The Effects of Cold, Electrical Stimulation, and Combination Cold and Electrical Stimulation on Sensory Perception

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Lindsey M. Philley
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This thesis titled

The Effects of Cold, Electrical Stimulation, and Combination Cold and Electrical Stimulation on Sensory Perception

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ABSTRACT

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The Effects of Cold, Electrical Stimulation, and Combination Cold and Electrical Stimulation on Sensory Perception

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Cryotherapy and sensory level interferential electrical stimulation (IFC) have been shown to be effective at producing analgesia. There is limited research on the anesthetic effectiveness of cryotherapy, IFC, and the combination of the two. This study compared the rates of onset of anesthesia and the duration of sensory effects between the three treatments. Semmes-Weinstein monofilaments were used to determine sensation every 2 min throughout a 20 min session for each treatment to determine the rate of onset of anesthesia. Sensation testing was conducted every 2 min following termination of the treatment to determine the duration of sensory effects. Results indicate a statistically significant difference in time to onset of anesthesia, as well as the time to return to baseline sensation level between the three treatment groups (p<.05). The combination treatment produced a more rapid onset of anesthesia and a longer duration of effects. Future research should explore onset and duration of analgesia.

Approved: ________________________________

Chad Starkey

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CHAPTER 1: INTRODUCTION

Musculoskeletal injuries affect one out of seven Americans. More than 215 billion dollars are spent annually on diagnosing and treating these injuries. The demands of physical activity can result in pain, the primary reason patients decide to seek medical attention. If excessive pain, it may prevent physical activity. A primary goal of athletic trainers (ATs) and health care professionals is to return the patient to the previous level of performance following injury. To accomplish this goal, pain must be alleviated.

Although pain has a protective quality that alerts the body of potential danger, it also negatively affects activity level. When analgesia is achieved the patient may progress through a rehabilitation protocol that otherwise may have been limited. Alleviating pain for an extended period of time may hasten return to competition.

Pain-relieving modalities are frequently used. While it has been shown that cryotherapy and sensory level interferential current electrical stimulation (IFC) produce analgesia, they also affect cutaneous sensory receptors. With these treatments sensation is altered, and ultimately lost, causing anesthesia.

Cryotherapy is typically administered using an ice bag applied directly to the skin. Cryotherapy decreases cell metabolism and reduces nerve conduction velocity, thereby decreasing the rate of sensory impulses delivered to the central nervous system. As the skin temperature decreases 5°C, alterations in neurologic sensation begin to occur. When skin temperature is lowered by 7.4°C, sensory nerve conduction velocity is reduced by 33%. Sensation typically returns to the skin after the tissue rewarms to approximately 15.6°C.
IFC also affects sensation. Sensory level nerves are stimulated before motor level or noxious level nerves because they are larger and more superficial. To activate sensory level nerves using electrical stimulation, the intensity is increased to the point at which a muscle twitch is felt, and then the output is decreased by approximately 10%. Through the process of accommodation, the constant barrage of stimuli from the electrical current causes the depolarization threshold of the subcutaneous sensory nerve fibers to increase. When the threshold is increased, more intense stimulus is needed in order for an action potential to be achieved. Sensory level IFC targets the sensory level receptors, including mechanoreceptors, responsible for the sensation of touch. By increasing the depolarization threshold of mechanoreceptors, sensation can be reduced. IFC also uses the Gate Control Theory to produce analgesia. By stimulating sensory nerves, the pain impulses sent from the nociceptive nerves are blocked from reaching the brain.

Multiple studies have examined the pain-reducing efficacy of cryotherapy; others have examined IFC. However, little research has been conducted on the anesthetic effects of using a combination treatment of cryotherapy and IFC. The cold application slows nerve conduction velocity and the repolarization of pain fibers. IFC reduces sensation by increasing the depolarization threshold of the sensory nerve fibers, especially the mechanoreceptors and A-β fibers carrying touch and pressure stimulus. The combination of both modalities may reduce the time to onset of anesthesia or result in a longer duration of anesthesia posttreatment. However, very little information on the combination of the two has been found in the literature.
Cryotherapy and IFC are used daily. A combination treatment of cryotherapy and IFC is also being used. Further research is needed to discover the technique that produces the quickest onset of anesthesia, as well as the longest duration of anesthesia post treatment.

Statement of the Problem

While there is a significant amount of literature proving the analgesic effectiveness of cryotherapy and IFC, there is limited research on the anesthetic effectiveness of the combination of the two. There is also a limited amount of literature focusing on the rate of onset of anesthesia and the duration of effects of cryotherapy and IFC alone. An understanding of the rates of each will provide better treatment options.

Purpose

The purpose of this thesis is to examine the anesthetic effect of cryotherapy, IFC, and the combination of concurrent cryotherapy and IFC. The primary aim of this thesis is to determine which of these three frequently used techniques induces anesthesia the quickest and produces the longest duration of effects after the termination of the treatment.

Significance of the Study

This thesis is an attempt to determine the anesthetic effectiveness of three commonly used treatment techniques. While numerous studies have shown that cryotherapy and IFC are both effective pain-relievers, this thesis will examine and compare the onset and duration of the anesthetic effects. This thesis will also examine the onset and duration of anesthesia during a combination cryotherapy and IFC treatment,
which, to my knowledge, has not yet been described in the literature. Determining which treatment induces anesthesia the fastest and which treatment causes the longest duration of anesthesia, will identify more efficient treatment options.

Research Questions

The research questions guiding this thesis are:

1. Is there a significant difference in the time to onset of anesthesia between an ice bag, sensory level IFC, and a combination treatment?

2. Is there a significant difference in the time to return to baseline sensation level post treatment between an ice bag, sensory level IFC, and a combination treatment?

Null Hypothesis

\( H_{01} \) There is no significant difference in the time to onset of anesthesia between an ice bag, IFC, and a combination treatment.

\( H_{02} \) There is no significant difference in the time to return to baseline sensation level post treatment between an ice bag, IFC, and a combination treatment.

Delimitations of the Study

Delimitations of this study include:

1. Participants in this study were college-aged (18-26).

2. All subjects were free of underlying pathology.

3. Each of the three treatments were applied for 20 min bouts.

4. The treatments were performed on the participants’ dominant leg.
Limitations of the Study

Limitations of this study include:

1. The baseline sensory level was unique to each participant.
2. The amount of testing time following the termination of the treatments varied for each participant.

Definition of Terms

*Analgesia.* Inability to feel pain.

*Anesthesia.* The participant cannot feel the 6.65 evaluator (300 g of pressure) touching the skin; loss of sensation.

*Athletic trainer (AT).* Health care professionals who collaborate with physicians to optimize activity and participation of patients and clients. ATs specialize in the prevention, assessment, treatment and rehabilitation of injuries and illnesses.

*Cryotherapy.* The therapeutic application of any substance to the body that removes heat from the body, resulting in decreased tissue temperature.¹

*Interferential current electrical stimulation (IFC).* Transectaneous application of alternating medium-frequency electrical current for therapeutic purpose.¹⁶

*Intensity.* Strength of the electrical stimulation current. Should be strong but comfortable.¹⁶
CHAPTER 2: REVIEW OF LITERATURE

The purpose of this literature review is to examine the current state of research as it pertains to the sensory effects of three common treatment techniques. Cryotherapy, IFC, and a combination of the two are used frequently to provide analgesia. The mechanisms by which analgesia, as well as anesthesia, are obtained have been researched. However, to my knowledge of the current state of research, it has not been determined which of these three techniques induces anesthesia at the quickest rate or for the longest duration after the treatment has ended. The purpose of the study behind this literature review is to examine the anesthetic efficacy of cryotherapy, IFC, and a combination treatment. In this literature review pain, cryotherapy, IFC, and the effects of each will be discussed.

Pain

Pain is the sum of several components. Perception of pain, the somatosensory information associated with pain, the mechanisms by which pain travels through the nervous system, its interpretation in the brain, and palliative treatments are all topics of research. Pain encompasses physiological and psychological factors. It is neither solely somatic, nor solely psychogenic, but involves both components.\textsuperscript{18}

\textit{Pain Perception}

Pain is very subjective and each person responds to painful stimuli differently.\textsuperscript{2} Under the same amount of pain-inducing stimulus some individuals may react with intense sensations of pain while others may hardly notice it. There are various reasons behind these altered responses. Pain threshold and pain tolerance are different for each
individual. Factors such as personality, gender, culture and race, fear and anxiety, and knowledge of the pain all determine how an individual responds to painful stimuli.2

**Pain Threshold**

Pain threshold has been defined as “the level of noxious stimulus required to alert the individual to possible tissue damage.”11\(^{p31}\) Pain threshold is subjective and unique to each individual. Threshold differences vary between men and women, with women typically having lower thresholds.19 Altering pain thresholds in each individual has been studied. In one study, after multiple exposures to the same painful stimulus, the threshold fell lower, thus inducing pain more quickly.20 However, in another study conducted by the same researchers, it was discovered that in a few of the subjects pain threshold rose after exposure to painful stimulus. In other subjects there was little to no effect on pain threshold.20 Here the data are inconclusive as to whether pain threshold can be increased or decreased after multiple exposures to noxious stimuli. This may be due to the population chosen for these studies. Each study used only seven participants, all males, with a wide age range (28-60 years).20 Using a larger population size with more defined inclusion and exclusion criteria might affect the outcome.

**Pain Tolerance**

Pain tolerance differs from pain threshold and is defined as “a measure of how much pain a person can or will withstand.”11\(^{p32}\) It is thought of as “the amount of pain or “quantity” of exposure (cold water, pressure, heat) that an individual can or will endure.”11\(^{p32}\) Pain tolerance can be compared to the amount of pain an individual can withstand before failure, such as passing out. Pain tolerance also varies from person to
person, but patterns have shown that females typically tend to have a lower pain tolerance level than males.\textsuperscript{19}

\textit{Personality}

It is generally accepted that individuals who have not been exposed to the hardships of the world would have a lower pain tolerance and thus experience higher pain levels. However, there is no clinical evidence to prove this.\textsuperscript{2} One study compared an individual’s level of self-efficacy to their pain tolerance levels. Self-efficacy can be thought of as an individual’s belief that one can successfully perform a task or accomplish an achievement that will produce a desired outcome.\textsuperscript{18} Bandura suggested the self-efficacy theory in which if an individual truly believed that a task could be accomplished and the individual had the required motivation, the goal would be easier to achieve.\textsuperscript{18} The self-efficacy theory can be applied to pain as well. It has been discovered that those individuals who believe they have a low self-efficacy have also shown lower pain tolerance levels, whereas efficacious individuals show higher pain tolerance levels.\textsuperscript{18}

\textit{Gender}

Studies have shown that females typically have lower pain thresholds and pain tolerance levels than males. Females also report more pain than males.\textsuperscript{2} There are numerous reasons to account for these differences. Because of the menstrual cycle and childbirth, females are more likely to experience recurrent pain.\textsuperscript{2} Another explanation for the decreased thresholds and tolerance levels for females is the difference in blood pressure. Women generally have lower blood pressures than men of the same age. Studies have revealed individuals with hypertension have a decreased pain sensitivity.\textsuperscript{19} It
has also been noted that a family history of hypertension or cardiovascular problems related to stress had an effect on pain perception. The same study also examined thermal stimuli, in which case the females claimed the stimuli to be more unpleasant than the males did.

*Culture and Race*

Research on pain perception compared to culture, ethnicity, and race has produced mixed results. One study determined that there were no ethnic differences in the amount of pain reported by individuals in the United States. However, another study claimed that ethnicity and culture has a large influence on pain perception, response to pain, and communication of pain. Social factors contribute a great amount to how the patient responds to a painful stimuli. Another study determined that Whites showed the highest pain tolerance, while African Americans showed the second highest, and Asian Americans showed the lowest.

*Fear and Anxiety*

How an individual interprets pain has an effect on the perception of that pain. If the individual is in constant fear of pain and is focusing solely on the negative aspects of pain, then the individual is more likely to experience pain for a longer duration. Also, if an individual is anxious and trying to avoid a painful stimulus, pain-related symptoms are more likely to be reported. Hypervigilance is the constant attention to threat of a painful stimulus and can lead to catastrophizing and worrying about experiencing pain, which can lower the pain threshold.
Knowledge of Pain

The amount of knowledge an individual has about their pain may affect pain perception. Some individuals may seek out all of the information they can about their pain, while others may want to avoid the pain and push it away. Both techniques can be helpful in diminishing pain. However, these approaches should be individually based for each person and what they prefer. For those that need all of the information, until they have all the facts, they will worry and fret, thus increasing their pain symptoms.²

While it is clear that psychological factors have a large impact on pain, it is also important to examine the somatic components of pain. Nerve conduction, thermoreceptors, mechanoreceptors, nociceptors, and the Gate Control Theory all have an effect on pain.

Nerve Conduction Velocity

Nerve conduction is the process of an electrical impulse traveling along the neuron to arrive at the brain where it can be interpreted.²¹ Nerve conduction velocity is the rate at which the impulses are sent. Nerve conduction velocity has a linear relationship to nerve fiber diameter.²¹ Therefore, the larger the diameter of the fiber, the faster the transmission is sent. For smaller nerves, a greater stimulus is needed to activate the receptor.²¹ Nerve conduction velocity is also related to the myelination of the nerve fiber. Myelin is the sheath that surrounds the nerve fiber. Nerves with large amounts of myelination will transmit the impulse faster than nonmyelinated fibers.²² The type of fiber that is being excited will also determine the rate of nerve conduction velocity. This review of literature will look mainly at the research done on cutaneous sensory nerves.
The sensory nerves can be divided into two main categories depending on axon size and myelination: A-fibers and C-fibers.

*A-fibers*

A-fibers are further categorized into A-β and A-δ fibers. A-β fibers have a large diameter and are myelinated. They have a very quick nerve conduction velocity, around 1.2-40 m/s. They detect non-noxious stimuli, such as mechanical sensations of touch and proprioception.\(^{23}\)

A-δ fibers have a smaller diameter than A-β fibers, as well as less myelination surrounding the nerve. A-δ fibers have a slower nerve conduction velocity than A-β fibers, at approximately 10-20 m/s.\(^ {24}\) A-δ fibers are classified as either low-threshold, D-hair mechanoreceptors, or A-δ mechanonociceptors. The A-δ mechanonociceptors detect high-intensity, noxious stimuli. Studies of these receptors showed that they only respond to damaging stimulation to the skin. A-δ mechanonociceptors have a much higher threshold than A-β fibers. A-δ mechanonociceptors are also considered to be thermosensitive. It has been shown that about 12% of these fibers are sensitive to heat, with a threshold of approximately 42°C. About 50% are cold sensitive with a threshold around 8°C.\(^ {23}\)

*C-fibers*

C-fibers have a small diameter and are unmyelinated. Because of this the nerve conduction velocity of C-fibers is much slower than A-β and A-δ fibers. C-fibers have a conduction velocity ranging from 0.3-1.2 m/s.\(^ {23}\) Even though the nerve conduction velocity is much slower, C-fibers are much more abundant than A-fibers. Generally C-
fibers respond only to noxious stimuli. However, research has shown that there are a number of C-fibers that respond to pleasant touch rather than pain. All of the remaining C-fibers are responsible for detecting all types of painful stimuli, including heat, mechanical pressure, and chemical stimuli.\textsuperscript{23}

First and second pain sensations have been examined to determine which of the fibers, A or C, is responsible for each type of pain sensation. First pain sensation is considered to be localized to one area, short-lasting, and pricking. Second pain is considered to be over a broader area, longer-lasting, and burning. Studies have shown that A-δ fibers are responsible for first pain, while C-fibers are responsible for second pain transmission.\textsuperscript{24}

\textit{Myelination}

Isochronicity is the ability of information to be sent from presynaptic neurons along different pathways, yet still arrive at the postsynaptic cells at the same time. This is achieved through changes in nerve conduction velocity due to axon diameter, length, and the amount of myelination present. There are numerous places within the body that an impulse must pass through before a sensation is noticed.\textsuperscript{24} It must travel from the receptor along the neuron pathway to the dorsal ganglion root to the brain, and then back down the pathway to trigger a response. It has been noted that once the impulse reaches the brain, the nerve conduction velocity drastically slows. Therefore, the total nerve conduction time is dependent upon how long the impulse stays in the brain before it is transmitted back to the neuron.\textsuperscript{24}
Myelination of the nerve fiber is a critical component in nerve conduction velocity. In an unmyelinated fiber the nerve conduction velocity is equivalent to the square root of the diameter of the nerve. In order to have a nerve conduction velocity that was ten times greater, the diameter would have to be 100 times greater, which is highly unlikely to happen. Therefore in order to achieve a faster nerve conduction velocity, the nerve fiber must be myelinated.²⁴

*Temperature Effects on Nerve Conduction Velocity*

Numerous studies have discovered that ambient temperatures have a direct effect on nerve conduction velocity. One such study examined the sciatic nerve of frogs. Rosenberg and Sugimoto took a baseline temperature of 78.8°F (26°C) and reduced it to 38.3°F (3.5°C). The researchers noted a marked decline in nerve conduction velocity, dropping from 33 m/s to 6 m/s. Until about 53.6°F the drop in conduction velocity was relatively slow. However, after this marker, conduction velocity dropped at a considerable pace.²⁵

Other studies have also shown similar results. Cooling of the phrenic nerve in a dog and the tibial nerve in rats and hamsters also slowed nerve conduction velocity.²⁵ These findings are helpful in understanding how cooling a nerve affects conduction velocity. However, each of these studies was performed on animal subjects instead of humans. It is still important to note that by decreasing the nerve conduction velocity, the transmission of an impulse will be slowed. This is partially the reason behind the idea of a cold application treatment to the skin. Cooling the cutaneous nerves will slow the conduction velocity and slow the rate of transmission of impulses, resulting in anesthesia.
**Somatosensory**

The body has many systems in place to ensure protection for itself. There are sensory fibers located throughout the body that detect potentially harmful stimuli. There are multiple somatosensory systems arranged in the body with specific receptors designed to detect specific stimuli. These receptors include thermoreceptors, mechanoreceptors, and nociceptors.

**Thermoreceptors**

Receptors that are designed to sense temperature changes alone and not mechanical stimuli are known as thermoreceptors. Thermoreceptors can further be subdivided into warm and cold receptors, each with its specific function. Warm and cold receptors serve functions that are oppositely correlated to each other. Warm receptors overshoot in frequency on sudden warming and show inhibition under sudden cooling. Cold receptors overshoot on sudden cooling and show inhibition under sudden warming.

At a constant body temperature both warm and cold thermoreceptors show a static frequency that stays constant. Warm receptors are monomodal, in that they only discharge in one temperature range. Maximal firing rates for warm receptors occur between 40 and 50°C. Cold receptors are bimodal, in that they fire in two different temperature ranges. Maximal discharge rates for cold receptors lie between 25 and 30°C and again at a temperature above 45°C. Warm thermoreceptors are innervated by C-fibers, while cold thermoreceptors are innervated by A-δ fibers.
**Mechanoreceptors**

Those receptors that are designed to detect mechanical stimulus, such as a touch and pressure, are known as mechanoreceptors. Mechanoreceptors can be classified by their nerve conduction velocities, determined by the nerve diameter and amount of myelination. Nerve fibers that have a large diameter and are myelinated are typically low-threshold mechanoreceptors, which activate A-β fibers. Low threshold mechanoreceptors can further be divided into rapidly and slowly adapting. Rapidly adapting mechanoreceptors respond to movement of the skin and not to a constant pressure on the skin. Slowly adapting mechanoreceptors respond to both movement and a constant indentation of the skin.

Certain classifications of A-δ fibers are classified as low threshold mechanoreceptors, including the D-hair fibers. D-hair fibers are the most sensitive mechanoreceptor located in the skin. These fibers have a very low threshold and large receptive fields. Other A-δ fibers are also considered to be mechanoreceptors that detect fast mechanical and heat pain. However, the molecular mechanisms behind the workings of mechanoreceptors are still unknown. Further research into the transduction process is needed to fully understand these mechanisms.

Mechanoreceptors convert the sensation of pressure into action potentials that send stimuli to the brain. Mechanoreceptors possess a neuronal membrane through which mechanically gated ion channels pass. When mechanoreceptors sense pressure, the channel opens, which allows sodium to pass into the receptor. As the sodium ions flow into the receptor, it becomes depolarized and produces an action potential that sends
the sensation of touch along its afferent fiber. When more pressure is applied to the skin, more action potentials are generated and the frequency of transmission is increased.\textsuperscript{11}

\textit{Nociceptors}

The third type of specialized sensory receptors are designed to respond to painful stimuli and are called nociceptors. Nociception is the process by which an individual is able to sense damaging stimuli.\textsuperscript{23} As defined by the International Association for the Study of Pain, a nociceptor is “a receptor preferentially sensitive to a noxious stimulus or to a stimulus which would become noxious if prolonged”\textsuperscript{23(p1090)}. It is important to note that there is a difference between pain and nociception. Pain almost always involves an emotional component, while nociception is strictly somatic.\textsuperscript{23}

There are multiple divisions of nociceptors, which have already been discussed. A-\(\delta\) and C-fibers are typically responsible for detecting pain. However, there are numerous subdivisions of C-fibers. A large portion of C-fibers are polymodal in that they respond to multiple types of noxious stimuli, such as thermal, mechanical, and chemical.\textsuperscript{23} There are also C-fibers which are not polymodal. One type is C-fibers that are sensitive to noxious cold. While it is accepted that these fibers exist, there is dispute among researchers as to their abundance.\textsuperscript{23}

A phenomenon of nociceptors that is designed to protect the body is called sensitization. Nociceptors have a property known as plasticity that allows them to adjust to the incoming stimuli. After a nociceptor has been continually exposed to the same threatening stimuli, it is able to adjust in a few ways. The nociceptor can either become nonresponsive, can respond at a reduced threshold, or can produce a response of a much
greater magnitude. Sensitization is seen most commonly during an inflammatory response where the sensitivity of the nociceptor is increased to protect the body from further injury.\textsuperscript{23}

\textit{Gate Control Theory}

Melzack and Wall developed their theory of the pain sensation control, dubbed the “Gate Control Theory” in 1965.\textsuperscript{29} The Gate Control Theory is based upon three spinal cord systems and input from sensory receptors. The three systems include the substantia gelatinosa, located in the dorsal horn, the dorsal column fibers that travel toward the brain, and the first central transmission cells in the dorsal horn, also known as T cells.\textsuperscript{30}

There are three main mechanisms behind how each of the three spinal cord systems works. The substantia gelatinosa was given the name of the “gate control” because it modulates which impulses are transmitted to the T cells. Within the dorsal column there are afferent fibers that control which stimuli activate specific brain processes that will alter the gate control response. The T Cells are responsible for response and perception of stimuli by activating neural mechanisms.\textsuperscript{30}

The main idea behind the Gate Control Theory is that excitations and inhibitions of nerve fiber types responsible for detecting pain can be controlled.\textsuperscript{29} Sensory receptors, thermoreceptors, mechanoreceptors, or nociceptors receive a stimulus and transmit this impulse along the afferent pathway to the dorsal horn. Here the substantia gelatinosa is responsible for “opening and closing” the “gate” to certain impulses before they reach the T cells.\textsuperscript{30} The fibers of the dorsal column will transmit certain impulses to the brain,
depending on which sensory receptors are activated, the brain will respond accordingly, and transmit the appropriate response back to the T cell to produce a sensation.\textsuperscript{30}

Typically the gate is held in a relatively open position because it is constantly bombarded by impulses without a specific stimulus. These impulses typically travel on small myelinated or unmyelinated nerves. However, if large diameter myelinated fibers can be triggered through touch sensation, then the large diameter fibers will travel faster than the small myelinated fibers and temporarily close the gate.\textsuperscript{30} Pain sensation travels along small diameter unmyelinated fibers, while mechanical sensation travels along large diameter myelinated fibers. Therefore, if mechanical sensation is produced, pain will be temporarily overridden.

Large diameter fibers adapt at a quicker rate than small diameter fibers. Therefore, if the stimulation of large diameter fibers is static, the fibers begin to lose their ability to close the gate, allowing it to reopen and the transmission of the small diameter fibers to continue. If the stimulation of the large diameter fibers can be continually changed through multiple stimuli, then the gate will remain closed and pain transmission will be reduced for a longer period of time.\textsuperscript{29,30}

The validity of the Gate Control Theory has been in question since its inception. There are researchers who believe it is not an accurate representation of pain control. A study conducted by Nathan and Rudge reviewed the principles behind the Gate Control Theory. The aims of their study were to examine the effectiveness of large diameter nerve fibers in stopping pain, as well as raising the pain threshold to noxious stimuli. They used seven male subjects with an age range of 28 to 60 years. Radiant heat was
applied to the distal phalanx of a finger as means of a noxious stimulus. A threshold level was taken before testing began and was measured as the length of time of heating. In most cases of this study blood flow to the limb was occluded by means of a sphygmomanometer. After multiple exposures to the thermal stimulus, the pain thresholds where compared. Results varied, with pain threshold levels decreasing in some cases and with no effect in others.20

In another attempt the researchers applied electrical stimulation to the upper arm. The current output was constant at 0-50 mA with a delivery of rectangular pulses. The duration was between 50 and 500 microseconds with a frequency between 15 and 180 pulses/second. The electrical stimulation was used in order to reduce C-fiber pain. However, results were also inconclusive. In two of the seven subjects the pain was abolished. In one of the subjects the pain was decreased, and in two of the subjects there was no effect.5,20 The researchers behind this study viewed the Gate Control Theory as ineffective despite the inconclusive results and small subject size.20

Cryotherapy

Cryotherapy is “the therapeutic application of any substance to the body that removes heat from the body, resulting in decreased tissue temperature.”1(p395) Cryotherapy is one of the most commonly used modalities for the treatment of athletic-related musculoskeletal injuries.3 One study has shown that in order to achieve analgesia with cryotherapy, the skin temperature should be cooled to at least 13.2°C.5 Cryotherapy has been shown to be effective in providing analgesia for acute pain.4
The application of cryotherapy produces many effects on the body. Blood flow, metabolism, oxygen utilization, and inflammation are all affected. Cryotherapy plays a role on the stimulation of nociceptors, thermoreceptors, and mechanoreceptors. It also produces changes in nerve conduction velocity, sensation, and depolarization threshold.

**Nociceptors, Thermoreceptors, Mechanoreceptors**

The theory behind cryotherapy is that cooling the tissue will slow the activity of nociceptors and delay transmission of painful stimuli to the brain. Following an initial injury, nociceptors are activated. The brain detects this stimulus, and signals the body to increase motor activity in the injured area, resulting in a muscle contraction. If these contractions are consistent, muscle spasms develop, which may lead to a decrease in blood flow to the area, resulting in hypoxia. The muscle spasms then lead to further pain, and ultimately a process known as the pain-spasm-pain cycle. With the application of cryotherapy early on, the action of the nociceptors can be slowed, resulting in slower transmissions of painful stimuli, thus reducing the chance of the pain-spasm-pain cycle occurring.

Thermoreceptors detect change in the skin’s temperature. When a cooling agent is applied to the skin, thermoreceptors are activated and send this stimulus to the brain. When thermoreceptors are activated, the transmission of noxious stimuli from the nociceptors is blocked. Therefore, when thermoreceptors detect a change from cryotherapy, the thermal stimulus blocks the painful stimulus from the nociceptors.

Mechanoreceptors are responsible for detecting changes in movement and pressure applied to the tissue. When cryotherapy is applied via an ice bag
mechanoreceptors sense the pressure on the skin from the bag of ice and transmit this signal to the brain. The resultant cooling of the mechanoreceptors because of the cold application slows the rate at which the mechanical stimuli is sent to the brain. When the conduction of the impulses is slowed, cutaneous sensation to touch or pressure is lessened, resulting in anesthesia.

**Effects of Cryotherapy**

The application of cryotherapy alters a few of the body’s functions. Numerous studies have shown that cryotherapy reduces tissue temperature, blood flow, metabolism, oxygen utilization, inflammation, and muscle spasm. Cryotherapy has been shown to cool tissue temperatures at a depth of 2 to 4 cm. Cryotherapy is believed to cause vasoconstriction of blood vessels, thus reducing blood flow. An ice wrap placed on a knee for 20 min reduced arterial blood flow by 38% and soft tissue blood flow by 26%.

After an initial injury has occurred, a major concern is secondary injury. Hypoxia, or the lack of blood flow to an area, is one of the main catalysts of secondary injury at an injured site. Hypoxia leads to ischemia, involving inadequate oxygen, fuel substrates, and waste removal.

By reducing the tissue temperature, metabolism, the rate of chemical reactions, is slowed. Because of this, there is a reduction in the need for adenosine triphosphate (ATP). The decreased need for ATP reduces the need for oxygen in the injured area as well. With the injured area demanding less oxygen, there is less of a chance that hypoxia, ischemia, and, ultimately, secondary injury will occur. In turn, the healing
process as a whole can be shortened because the demand of injured and dying tissue is diminished.³

After a musculoskeletal injury is sustained, immediate treatment and care is needed to prevent further secondary injury to the area to insure faster healing rates. Cryotherapy is one of the most common modalities applied immediately following an injury because of its ability to slow metabolism, reduce blood flow and the need for oxygen, as well as the need for ATP at the injured site.¹²

*Cryotherapy and Pain*

Numerous sources have deemed cryotherapy effective in decreasing pain.⁴,⁵,⁶-⁸ Along with its ability to slow the body’s metabolic actions in order to help prevent or slow secondary injury, cryotherapy is also commonly used to decrease pain and provide analgesia. Application modes and times can vary, but it is considered that cryotherapy is an inexpensive and effective intervention for pain.⁵

Denegar and Perrin conducted a study comparing the changes in perceived pain before and after a cryotherapy session applied over the elbow flexor muscles. Participants performed elbow flexor exercises before the cryotherapy was applied to induce delayed onset muscle soreness (DOMS). Perceived pain was then established by using the Graphic Pain Rating Scale and having the participant place a mark on a 12 cm line to describe the pain. Plastic bags filled with crushed ice applied for 20 min were the cryotherapy source. Following the cryotherapy session, participants were asked to place a mark on the pain scale again indicating their pain level after the treatment. The study revealed that cryotherapy had a significant reduction in perceived pain.⁸
Several other studies have reviewed the effectiveness of cryotherapy in reducing perceived pain. One conducted by Cleakley, McDonough, and MacAuley examined the effects of a continuous 20 min cryotherapy treatment versus an intermittent 10 min cryotherapy treatment on perceived pain in patients with ankle sprains. A 10 cm visual analogue scale was used to quantify pain. Results showed that pain improved for both groups after cryotherapy was applied. Pain on activity also decreased for both groups. However, the intermittent group experienced significantly lower levels of perceived pain than the continuous group. The intermittent group maintained tissue temperatures of 10-15°C for longer periods of time than the continuous treatment group did. Therefore, this study suggested that intermittent cooling provide more efficient short term analgesia, but that both cryotherapy applications showed decreases in perceived pain.\(^7\)

Studies reviewing the application of various modes of cryotherapy also showed the effectiveness of producing analgesia. Hubbard and Denegar agreed that cold application was more effective in reducing pain in the short term, but its long term effects needed more research.\(^6\) They also found that applying cryotherapy after minor knee surgery was more effective at reducing pain that applying no form of cryotherapy.\(^6\) Another study done by Green, de Rosayro, and Tait found that cryotherapy was successfully used to induce analgesia for acute thoracic pain.\(^4\)

Pain Tolerance and Pain Threshold

Algafly and George researched the effect of cryotherapy on pain tolerance and pain threshold. As previously stated in this review of literature, pain tolerance is defined as “a measure of how much pain a person can or will withstand,”\(^5(p31)\) while pain
threshold is defined as “the level of noxious stimulus required to alert the individual to possible tissue damage.” Algafly and George hypothesized that the application of cryotherapy would increase pain tolerance and pain threshold. Both categories were assessed by using a pressure algometer on the tibial nerve on both the treatment and control ankles. Algafly and George discovered that both pain tolerance and pain threshold were significantly changed by the application of cryotherapy. As the skin temperature decreased, there was a progressive increase in pain tolerance and pain threshold. There was a relative percentage change from the baseline to post treatment measures of pain tolerance and pain. The percentage change at 10°C for tolerance was 76% while the change for threshold was 89%. Therefore the study revealed that the application of cryotherapy can increase pain tolerance and pain threshold levels.

Sensation

Cryotherapy has also been shown to decrease cutaneous sensation. A study done by Rubley, Denegar, Buckley, and Newell examined the cutaneous sensation in the index finger and thumb after a cold immersion session. Semmes-Weinstein monofilaments were used to test sensitivity to pressure. Baseline testing using the monofilaments was administered before the 15 min cryotherapy session. Testing was also done once the treatment was completed. The participant was blinded while the monofilaments were pressed onto the palmar aspect of the distal phalanx of the thumb and forefinger. The monofilament was pressed onto the skin with enough force to make it bend where it was held in place for 2 seconds. The participant was instructed to respond with a “yes” if they
could feel the monofilament. The monofilaments were arranged by a numbered size that correlated with a gram value of pressure needed to bend the monofilament. The monofilament used increased in size until the participant answered “yes” consecutively.\textsuperscript{12}

The study concluded that after the application of cryotherapy the sensation of pressure was $0.108$ g higher than the baseline. Therefore, the sensation of pressure posttreatment was significantly higher, decreasing cutaneous sensation. It is thus believed that a decrease in cutaneous temperature may affect the sensory receptors. During the cryotherapy application the thermal receptors are intensely activated. Nociceptors are also activated due to the low temperatures. If a receptor is constantly activated, its threshold increases, which causes it to fire less frequently. The increased threshold may be the reason for the decreased sensation. Another common explanation for the decreased sensation relates to a decrease in nerve conduction velocity.\textsuperscript{12}

\textit{Depolarization Threshold}

The application of cold has an effect on all nerves. When cryotherapy is applied to the skin, the depolarization threshold of the sensory impulses is increased.\textsuperscript{11} An action potential is required for an impulse to be sent from the sensory receptor to the brain. During cryotherapy application action potential generation is delayed. One cause of the delay is related to the exchange of $\text{Ca}^{2+}$ and $\text{Na}^+$ that takes place at the gated ion channel on the receptor. The decreased tissue temperature resulting from the cold application causes increased friction between $\text{Ca}^{2+}$ and the gate. The increased friction reduces the number of $\text{Ca}^{2+}$ ion exchanges that lead to the production of action potentials. The
reduction in action potentials leads to the reduction in impulses being sent to the brain, resulting in altered sensation.\textsuperscript{5}

Continuous stimulation of a receptor can also lead to an increased depolarization threshold. A receptor adapts to constant stimulation by increasing the level at which an action potential is generated. The increased threshold results in the receptor firing less frequently. The increased threshold may also be responsible for the decrease in sensation of pressure following a cryotherapy application.\textsuperscript{12} Because mechanoreceptors and nociceptors are independent of each other, an increased threshold in mechanoreceptors may not be seen after cryotherapy. However, polymodal nociceptors that respond to thermal and mechanical noxious stimuli are activated concurrently. Polymodal nociceptors may permit the threshold to be increased for mechanoreceptors.\textsuperscript{12} Increasing the thresholds of the sensory nerves results in anesthesia.\textsuperscript{11}

\textit{Nerve Conduction Velocity}

The application of cryotherapy slows the body’s metabolism, reduces the need for oxygen, blood flow, and the activation of nociceptors to reduce pain. However, one of the most common reasons cryotherapy is applied is due to its ability to decrease nerve conduction velocity. Many studies have verified cryotherapy’s ability to slow the rate of nerve conduction velocity.\textsuperscript{1,3,5,7,12} It has been shown that nerve conduction velocity has a linear relationship to tissue temperature. As tissue temperature decreases, nerve conduction velocity in the efferent and afferent nerve fibers also decreases.\textsuperscript{12} The effects of cryotherapy on nerve conduction velocity are said to last up to 30 min after treatment.\textsuperscript{3}
Algafly and George also examined cryotherapy’s effect on nerve conduction velocity. In their study, the cutaneous temperature was lowered to 10°C, which took 26 min of cryotherapy to achieve, on average. Algafly and George compared the treatment ankle to the opposite control ankle and found that nerve conduction velocity for the treatment ankle was significantly reduced after the cryotherapy treatment when compared to the baseline measurement. Nerve conduction velocity was also significantly reduced in the treatment ankle compared to the control ankle. A 33% reduction in nerve conduction velocity was noted. Algafly and George also observed a 0.4m/s decreases in nerve conduction velocity for every 1°C decrease in cutaneous temperature.

Cryotherapy is able to reduce nerve conduction velocity by reducing the rate at which nerves transmit impulses to the brain. Reducing the rate at which synaptic transmission takes place decreases nerve conduction velocity. Increasing the time it takes for a nerve to depolarize and repolarize reduces the amount of times an action potential can be generated. Reducing the number of action potentials results in fewer transmissions being sent. The reduction in the frequency of transmission of sensory impulses results in a reduction in nerve conduction velocity. Decreasing the conduction velocity of a mechanoreceptor, reduces the amount of stimulus of touch or pressure being felt. This reduction in sensation, produced by cryotherapy, results in anesthesia.

Gate Control Theory

Cryotherapy may have an effect on the Gate Control Theory. A few others have found that cryotherapy may produce an antinociceptive effect on gate control. The pain impulses transmitted by A-δ and C fibers may be inhibited by other inputs, in this case,
cold sensation or the sensation of touch by the mechanoreceptors. Pain perception may then be blocked because the other inputs are closing the gate by reaching the brain at a faster rate.\textsuperscript{5} However, more research is needed on the basis of the Gate Control Theory.

\textit{Return to Participation}

A review of studies done by Hubbard, Aronson, and Denegar examined whether cryotherapy could hasten an athlete’s return to participation. The authors reviewed 4 articles using patients with ankle sprains and the use of cryotherapy. They discovered that 2 of the 4 articles they reviewed shown an earlier return to participation, while 1 of the articles supported the notion that cryotherapy contributed to an earlier return, but that the application of compression was the greater contributing factor. The last article reported no statistical difference in return to participation.\textsuperscript{3}

While the results of the four studies varied, it was shown that 42.1\% of the participants treated with cryotherapy returned to play by the second day, with 84.2\% returning by the seventh day. It also showed that participants with severe ankle sprains who used cryotherapy returned to participation on average after 7.3 days, while those who did not use cryotherapy returned on average after 10.2 days. Despite the small number of sources used for their research, Hubbard, Aronson, and Denegar concluded that the application of cryotherapy has a positive effect on returning an athlete to participation.\textsuperscript{3}

\textit{Interferential Current Electrical Stimulation}

Interferential current electrical stimulation (IFC) is the most common form of electrical stimulation used by clinicians in Europe and Australia, with growing popularity
throughout the world.\textsuperscript{9,10} IFC is noninvasive and produces an immediate effect.\textsuperscript{13,14} IFC has been used for reducing swelling, wound and fracture healing, and increasing muscle function.\textsuperscript{13} Multiple studies have revealed the analgesic effects of ICF.\textsuperscript{9-16} It has been shown to treat knee osteoarthritis pain, low back pain, fibromyalgia/myofascial pain, jaw pain, frozen shoulder pain, and bicipital tendinitis pain.\textsuperscript{10} Sensory level IFC targets large-diameter A-\(\beta\) fibers first. The sensory receptors are activated before motor or noxious receptors.\textsuperscript{11} By targeting A-\(\beta\) fibers and sensory receptors, IFC plays a role in producing anesthesia.

Despite the extensive use of IFC to relieve pain, information about the modality is limited.\textsuperscript{10} However, there are claimed advantages to IFC over other electrical stimulation currents. One advantage is IFC”s capacity to diminish skin impedance to its current.\textsuperscript{10,16} By reducing the resistance to the current, the discomfort delivered by the current is reduced and the treatment is more tolerable.\textsuperscript{16} Another reported advantage of IFC is its ability to generate an amplitude-modulated frequency (AMF) parameter. AMF is a low-frequency current generated deep within the treatment area.\textsuperscript{10,16} AMF is produced due to the interaction of two medium frequency currents mixing in the body.\textsuperscript{16}

IFC is a complex modality and an understanding of how it operates is needed, including the type of current and frequency typically used, as well as AMF settings and electrode alignment. Studies have revealed numerous types of pain treated as well as the physiologic and analgesic effects of IFC. Comparisons have also been made studying the effectiveness of IFC treatments versus other common treatments.
Concepts of IFC

Alternating Current, Kilohertz Frequency, and AMF

IFC is the “transcutaneous application of alternating medium-frequency electrical currents for therapeutic purpose.” It uses two alternating currents that have differing kilohertz frequencies to produce a resultant wave in the treatment area. A kilohertz frequency is delivered in order to overcome skin impedance and penetrate deeper tissues, while reducing the stimulation of unwanted cutaneous nerves. IFC produces interfering currents within the tissue. Using very high frequencies is not comfortable for the patient, therefore two currents that have different frequencies or are out of phase are used to reduce resistance.

The point at which the currents cross produces interference and a resultant AMF. Typically, one frequency is set at 4,000 Hz with the other frequency set between 4,050-4,250 Hz. The resultant AMF frequency is then 50-250 Hz, depending on the difference between the two original currents. It has been shown that AMF frequencies between 1-250 Hz produce an analgesic affect. For pain control, an AMF setting of 80-130 Hz is used to activate the pain gate mechanism described in the gate control theory. An AMF setting of 25 Hz or less stimulates the descending pain suppression mechanism.

Intensity

The current intensity will vary from patient to patient. However, for a sensory-level IFC treatment, it has been most commonly established to set the intensity at a strong but comfortable level. At this intensity patients should report a pins-and-needles-like
feeling, but no muscle contraction should be visible.\textsuperscript{16} To determine the strong but comfortable level, the intensity is turned up until a visible muscle contraction is noted. Then the intensity is turned back down until there is no further muscle contraction, but patients report a strong sensation that is comfortable to them.\textsuperscript{13} A strong but comfortable intensity has been shown to reduce pain better than a sham electrical stimulation treatment.\textsuperscript{13} One study suggests standardizing IFC intensities to a strong but comfortable level for all patients.\textsuperscript{13}

\textit{Electrode Placement}

IFC uses a quadpolar electrode arrangement where four electrodes are used. Carbon rubber electrodes or self-adhesive electrodes are typically used. The two electrodes from each channel are arranged so that they are diagonal to each other. The end formation is typically a square shape with the currents from each channel intersecting in the middle and causing interference.\textsuperscript{15} The middle of the treatment area is where the maximum frequency flows. There is a snowflake-shaped field that is produced between the electrodes where the current scans and flows laterally from its direct path to interact with the other current.\textsuperscript{15}

It is important to keep in mind nerve fiber orientation when placing the electrodes. Only those nerve fibers that are angled optimally between the electrodes will receive the fully modulated alternating current. The optimum alignment of the electrodes to the nerve fiber depends on the current intensities. If the intensities are equal, then the optimum angle alignment is $45^\circ$ to the electrode path. However, the intensities may never be truly equal due to skin impedance and the impedance of subcutaneous tissues
such as fat. Therefore, if the electrodes are arranged in a pattern that is not aligned with
the nerve fiber, the amount of actual stimulus affecting the nerve may be diminished or
vary from treatment to treatment.\textsuperscript{9}

\textit{Types of Pain}

Several studies have been done examining the effects of IFC on different types of
pain. They have shown that IFC treatments can be helpful in producing analgesia
unrelated to musculoskeletal pain. These studies have examined the analgesic effects of
IFC on inflammatory pain, mechanical hyperalgesia, ischemic pain, and cold-induced
pain.\textsuperscript{13,14}

\textit{Inflammatory Pain}

After an injury is sustained, pain due to inflammation in the area may result. The
pain may be ongoing or spontaneous. Spontaneous inflammatory pain is known as a
“continuous endogenous stimulation of nociceptors caused by the release of
inflammatory mediators that directly stimulate them.”\textsuperscript{14} This type of pain is typically
controlled through the use of nonsteroidal anti-inflammatory drugs (NSAIDs) to prevent
the sensitization of nociceptors.\textsuperscript{14}

A study done on rats examined the effects of IFC on inflammatory pain.
Inflammation was endogenously induced in rats” hind legs. An IFC treatment was
applied before the inflammation was induced, immediately after, and 2 hours after. The
study found that the IFC treatment applied during the first hour immediately after
inflammation significantly reduced the flinching behavior seen in rats when feeling pain.
The researchers determined that IFC is effective in reducing inflammatory pain in animal
models and that it should be considered for use in controlling acute inflammatory pain in humans.  

Mechanical Hyperalgesia

A study has also been done examining the effects of IFC on mechanical hyperalgesia pain. Hyperalgesia is the increase in neuronal membrane excitability. Mechanical hyperalgesia is a sensitization of nociceptors due to inflammatory mediators. Mechanical hyperalgesia was induced in the hind legs of rats using an injection of carrageenan. The study found that a 1-hour IFC treatment applied 2 hours after the injection significantly prevented a further increase in pain due to mechanical hyperalgesia.  

Ischemic Pain

Another study examined the effects of an IFC treatment on ischemic-induced pain. Ischemic pain was induced in participants by using the submaximal-effort tourniquet test, where a tourniquet was applied to the arm and the participants were asked to exercise the hand. This produced a deep aching pain in the arm. To objectify pain levels, the visual analog scale was used during the ischemic pain test while the McGill Pain Questionnaire was used to assess changes in pain following the treatment. Each participant received 22 min of IFC treatment. The results of the study showed that IFC reduced pain intensity when compared to the sham treatment. It was also reported that IFC has an elevating effect on pain threshold compared to the sham treatment as well.
Treatment Comparisons

IFC may be used alone or as a supplement to another treatment to provide analgesia. A systematic review was done comparing the analgesic effects of IFC alone versus a placebo, versus a comparison group, and IFC as a supplement to another treatment versus a placebo and versus a comparison group.\textsuperscript{10}

\textit{IFC Alone Versus Placebo Group}

Two studies were used to examine the effects of IFC alone compared to a placebo group. The two studies revealed opposite results. One study was conducted on knee osteoarthritis, while the other study was done on temporomandibular jaw pain. With very little sample size and differing results, it was indicated that IFC alone was not significantly better than a placebo.\textsuperscript{10}

\textit{IFC Alone Versus Comparison Group}

Two studies were also included in this treatment comparison. One study focused on acute low back pain while the other study focused on chronic low back pain. An IFC treatment was applied, while the comparison group consisted of manual therapy, traction, and massage. The results from these two studies indicated that IFC alone did not significantly lower pain more than the comparison group.\textsuperscript{10}

\textit{IFC as a Supplement to Another Treatment Versus Control Group}

Three studies were used for this comparison. The studies examined knee osteoarthritis, frozen shoulder, and acute low back pain. The visual analog scale was used to assess pain in these studies. When compared to the control group, the application
of IFC as a supplement to another treatment was 2 points better in reducing pain intensity.¹⁰

**IFC as a Supplement to Another Treatment Versus Placebo**

Five studies were included in this comparison. Osteoarthritis, chronic low back pain, and fibromyalgia were reviewed. Four of the five studies favored IFC as a supplement when compared to the placebo group. It was also found that IFC as a cointervention was significantly better at reducing pain intensity than the placebo.¹⁰

**IFC as a Supplement to Another Treatment Versus Comparison**

Five studies were also included in this comparison. Osteoarthritis pain, shoulder pain, and myofascial pain were reviewed. The comparison treatments, as well as the supplements to IFC, were hot packs, active range of motion, and myofascial release. The results from these studies indicated that IFC as a supplement to another treatment was no better than the comparison group at reducing pain intensity.¹⁰

**Physiologic and Analgesic Effects**

While the information about IFC is limited, there are a few theories pertaining to its mechanisms of action. Authors believe that IFC produces an effect on endorphin release, summation, neuron action potentials, pain suppression, and the gate control theory. Each has varied credibility and more research is needed on these topics.

**Endorphin Release**

One study has found that high and low frequency electrical stimulation may trigger the release of different opioids within the body. A team of researchers examined the amount of different opioid peptides in the cerebrospinal fluid of participants that had
undergone an electrical stimulation treatment. It was found that a 30 min treatment at 100 Hz produced a 49% increase in immunoreactive dynorphin A, which acts on the \( \kappa \)-opioid receptors. It was also discovered that low frequency stimulation of 2-4 Hz releases enkephalin, \( \beta \)-endorphins, and endomorphins. These act upon the \( \mu \)- and \( \delta \)-opioid receptors. Therefore, high and low frequency electrical stimulation, such as IFC trigger the release of opioid peptides, which may have an effect on producing analgesia.\(^{17}\)

**Summation**

It is believed that the kilohertz-frequency alternating current associated with IFC may have an effect on the threshold needed to excite sensory nerves. Gildemaster proposed that as the burst duration of the alternating current is increased, the threshold voltage needed in order to excite sensory nerves is decreased.\(^9\) In the alternating current wave-train, each consecutive pulse pushes the nerve fiber membrane closer to its threshold. Its threshold is reached when depolarization produces an action potential.\(^9\)

**Neural Block/Accommodation**

Constant stimulus from a kilohertz-frequency AC stimulator can result in direct conduction block of nerve fibers. Repetitive stimuli have an effect on the production of action potentials needed to elicit a response from the nerve fiber. As the intensity of the stimulus is increased, the responses of the large-diameter fibers are lost first, followed by the intermediate-diameter fiber responses, and lastly the small-diameter fiber responses are lost.\(^9\) Large-diameter fibers carry touch and pressure information from mechanoreceptors. It has been shown that at frequencies of 4 kHz or greater the firing frequency of nerve receptors decreased to zero in less than a second.\(^9\) Because the
responses of large-diameter fibers are lost first, anesthesia may be produced within a few min into an IFC application.

The stimulus from an IFC application is sufficient to produce a depolarization of a receptor’s membrane. The repetitive, constant stimulus increases the resting potential of the receptor to a higher than prestimulus level. The increased resting potential results in the decrease of discharge of action potentials. Accommodation develops when generation of action potentials decreases while the depolarization stimulus remains the same. A nerve experiencing accommodation requires a more intense level of stimulus to reach the depolarization threshold. Because the depolarization threshold is increased in A-β fibers, sensation may be altered, resulting in anesthesia.

After repetitive stimulation at a frequency up to its maximum, the action potentials in the axon will flow at the same rate as the stimulation. If the rate of stimulation rises above the axon’s maximum rate, then successive stimuli will fall within the absolute refractory period of the action potential before it. The stimuli within the absolute refractory period cannot produce another action potential until the previous stimulus has. In order to stimulate a refractory neuronal membrane to produce an action potential, a larger flow of current or larger stimulus is necessary. Because of this the nerve sensitivity decreases. If this larger current is consistently used, then the axon will eventually stop conducting its impulses, thus reducing the transmission of information. IFC sends a constant stimulus to the sensory nerve fibers, A-β fibers first. By decreasing the sensitivity of A-β nerve fibers, anesthesia can be achieved.
Descending Pain Suppression Mechanism

The descending pain suppression mechanism is mediated by the endogenous opiates. When nociceptive information is sent to the brain, it enters the spinal cord and eventually the thalamus. One of the other structures nociceptive information interacts with is the raphe nuclei. When the raphe nuclei send information back down the spinal cord, fibers descending from the raphe nuclei will release inhibitory neurotransmitters which are responsible for blocking further nociceptive information from being sent to the brain. IFC used with a frequency of 15 Hz will maximally affect the raphe nuclei fibers, thus decreasing pain.\textsuperscript{15}

Gate Control Theory

One of the most supported reasons for IFC producing analgesia is its effect on the gate control theory. Several authors have claimed IFC”s pain-relieving mechanism lies within the “pain gate theory.”\textsuperscript{10,14-16} The stimulus traveling along large-diameter myelinated afferent nerves, carrying sensory information from cutaneous receptors, takes precedence over the small-diameter unmyelinated sensory fibers, carrying pain information from nociceptors. Therefore, the sensory information closes the gate and prevents pain information from reaching the brain at a conscious level.\textsuperscript{15} Ultimately, IFC works via the gate control theory by stimulating large-diameter afferent fibers.\textsuperscript{16} The stimulation of A-\(\beta\) fibers inhibits the small-diameter fibers from firing. IFC applied at a high frequency (> 100 Hz) will stimulate larger A fibers, but will have little impact on smaller C fibers.\textsuperscript{14} Clinical experience has shown that at a frequency of 100 Hz or greater, IFC significantly reduces pain.\textsuperscript{15} While the stimulation of large-diameter fibers
via IFC has been shown to produce a rapid onset of analgesia, its duration of effects may be short-lived.\textsuperscript{10}

\textit{Placebo Effect}

It is important to keep in mind the potential for a placebo effect to occur during an IFC treatment. Once the electrodes are applied, there may be a psychological expectancy about receiving treatment. Pain thresholds may be increased simply due to psychological beliefs that pain will be treated, without the actual modality producing a therapeutic effect.\textsuperscript{16}

\textbf{Conclusion}

Pain affects individuals every day. It is the most common reason individuals enter the health care system.\textsuperscript{1} It is a complex, multi-faceted sensation that is triggered by somatic receptors and/or psychological factors. There are multiple nerve fibers within the body designed to detect specific sensations. These sensations are sent along different pathways to be interpreted by the brain. Pain sensations can be altered by decreasing rate at which the impulse travels along the nerve fiber (nerve conduction velocity), as well as through the Gate Control Theory.

Cryotherapy is one the most commonly used modalities to alleviate pain in individuals with musculoskeletal injuries. Cryotherapy works to decrease many of the body’s processes, including metabolism, blood flow, nociceptor activation, sensation, and nerve conduction velocity. The application of cryotherapy may also increase pain tolerance and pain threshold levels. Cryotherapy decreases sensation and produces anesthetic effects. It has also been found to be effective in hastening return to
participation. Cryotherapy is considered to be an inexpensive and effective intervention for pain.\textsuperscript{5}

IFC is commonly used throughout the world to treat multiple types of pain, including musculoskeletal pain, inflammatory pain, and ischemic-induced pain. IFC operates using an alternating current of differing kilohertz frequencies to produce AMF. IFC has been compared to different treatment options and has been used as a supplement to other modalities. IFC has been shown to be effective in producing analgesia and anesthesia through mechanisms such as endorphin release, neural block, and the gate control theory.

While the literature suggests that both cryotherapy and IFC are effective analgesics, very little research has been conducted on a combination of both treatments. The physiologic mechanisms of each modality have been shown to reduce pain; therefore, it is thought that using a combination of the two would also be effective in reducing pain. Literature has shown that IFC has a positive effect on analgesia when used in conjunction with other modalities, but cryotherapy was not listed.\textsuperscript{10} More research is needed on the combination treatment of cryotherapy and IFC. While both cryotherapy and IFC have been shown to be effective at producing analgesia, more research is needed on the anesthetic effects of each, as well as a combination of the two.
CHAPTER 3: METHODS

This thesis is focused on calculating the rate of onset of anesthesia and the duration of effects for an ice bag, IFC, and a combination treatment. These two research questions have guided this study:

1. Is there a significant difference in the time to onset of anesthesia between an ice bag, sensory level IFC, and a combination treatment?
2. Is there a significant difference in the time to return to baseline sensation level post treatment between an ice bag, sensory level IFC, and a combination treatment?

Research Design

A repeated measures ANOVA design was used in this study. The independent variables in this study were treatment type (ice bag, IFC treatment, combination treatment), and treatment time (20 min). The dependent variables were baseline sensation level, the amount of time to reach anesthesia, and the amount of time to return to baseline after termination of the treatment.

Identification of the Population

Fifteen healthy subjects (4 males, 11 females; age = 21.53 ± 2.1 years; dominant leg 2 left leg, 13 right leg) with no local infection of either lower extremity, unhealed muscle, tendon, or bone injury in the lower extremities, systemic infection, exposed metal implants in the lower extremity, cancerous lesions in the lower extremity, local cardiovascular and/or neurologic inhibition including peripheral vascular disease, venous insufficiency, or Raynaud’s disease, pregnancy, implanted cardiac pacemaker, or
epilepsy volunteered for this study. Participants underwent a standard orthopedic screen to assess neurologic status. All participants signed an approved consent form and were informed they could withdraw from the study at any time without penalty. The Ohio University Institutional Review Board approved this study.

Instrumentation

There are several instruments selected for this thesis. A medical history questionnaire (MHQ) identified the presence of any of the following conditions that would exclude them from participating in the study: local infection of either lower extremity, unhealed muscle, tendon, or bone injury in the lower extremities, systemic infection, exposed metal implants in the lower extremity, cancerous lesions in the lower extremity, pregnancy, implanted cardiac pacemaker, or epilepsy.

Touch Test™ Sensory Evaluators (Semmes-Weinstein Monofilaments) provide a non-invasive evaluation of cutaneous sensation levels throughout the body with results that are objective and repeatable. The evaluators range in thickness from 1.65 to 6.65. The number on the evaluator correlated with the amount of pressure in grams needed to bend the monofilament wire.

A Chattanooga Intelect® Legend XT 2 Channel System is an electrotherapy system used for the relaxation of muscle spasms, prevention or retardation of disuse atrophy, increase local blood circulation, maintaining or increasing range of motion, symptomatic relief and management of chronic, intractable pain, post-traumatic acute pain, and postsurgical acute pain. It is capable of producing monophasic, biphasic and interferential currents.
The ice bag used for the cryotherapy application was a modified gallon-sized Ziploc® bag with a 28.3 cm² hole cut out of the middle. This bag contained 1 kg of crushed ice. The plug ice bag was a smaller bag of ice that was applied over the hole of the larger ice bag. This bag contained 0.09 kg of crushed ice. Preliminary testing indicated that there was no significant difference in skin treatment temperature between our modified bag and a standard ice bag at any time point.

Data Collection Procedures

Fifteen healthy, college-age volunteers participated in this study. Testing during this study was performed by a licensed athletic trainer. Potential participants attended an orientation session before the study began to receive information about the study and ask any questions. Consent forms were distributed and signed by participants. The MHQ was used to identify the presence of any of the exclusionary criterion. After completion of the MHQ and approval for participation, dates and times were established for the participants to attend their study sessions.

Each participant underwent each of the three sessions: one ice bag, one sensory level IFC, and one combination treatment. A Latin squares table determined the treatment order for each participant. There was at least 1 day between each testing session.

Participants reported to room E207 in Grover Center for testing. A portion of the anterior thigh of the dominant leg, determined by asking the participant which leg they would kick a ball with, was shaved using a disposable razor and cleaned with an alcohol swab to remove dirt and oils on the skin.
Participants were placed supine on a treatment table. A curtain was drawn across the abdomen in order to block vision of the lower extremity. A baseline sensory level sensation test was done prior to the start of each session using Touch Test™ Sensory Evaluators. The evaluators range in thickness from 1.65 to 6.65. The number on the evaluator correlated with the amount of pressure in grams needed to bend the monofilament wire. Participants were asked to say “yes” when they felt an evaluator touch their skin. The 1.65 evaluator was applied to the participant’s skin first. If the participant did not report feeling the 1.65 evaluator, then the next size up was applied and so on until the participant reported feeling the monofilament. The first Touch Test™ Evaluator the participant reported feeling was their baseline evaluator.

After the baseline sensory status was determined, the participant underwent either an ice bag, IFC, or a combination treatment. An 8x8 cm target area was marked on the anterior thigh, centered between the ASIS of the hip and the superior pole of the patella, bisecting the leg. Each treatment lasted 20 min.

For the ice bag treatment, the prefabricated ice bag containing 1 kg of crushed ice was applied to the treatment area. The hole in the ice bag was centered over the target marked on the anterior thigh. The plug bag containing 0.09 kg of crushed ice was placed over the hole of the larger bag to ensure the entire testing area was being cooled.

For the IFC treatment a quadpolar electrode arrangement was placed around the target area, with the contiguous borders of each electrode placed 8 cm apart. The intensity was increased until the participant experienced a slight muscle contraction. The intensity was
turned down by 10% to where no contraction was seen or felt and a strong but comfortable sensation was felt.

For the combination treatment the ice bag treatment and IFC treatments were applied simultaneously over the same area using the protocols previously described.

Sensory testing was conducted every 2 min to test the onset of anesthesia. After the first 2 min of the treatment, the baseline monofilament was applied to the skin first. If the participant did not report feeling the baseline monofilament, then the next size was applied until the participant reported feeling a monofilament being applied to their skin. If the participant did not report feeling the 6.65 evaluator (300 g of pressure), the largest monofilament, then we determined the participant reached anesthesia.

After the 20 min treatment concluded, the Touch Test™ Evaluators were applied every 2 min, starting with the largest monofilament to be felt. The monofilaments were decreased in size until the participant reported feeling their baseline monofilament. Once the participant's sensory level returned to baseline, an additional testing using the baseline monofilament was conducted for a 2 min interval to confirm the participant had returned to their baseline sensation level. If the participant did not report feeling their baseline monofilament after the additional 2 min interval, then testing resumed until the participant reported feeling the baseline for two consecutive 2 min intervals. This determined the duration of anesthesia. Once the participant reported feeling the baseline evaluator for two consecutive 2 min intervals, the session was terminated.
Statistical Analysis Procedures

Statistical Package for the Social Sciences (SPSS) 18.0 was used in the analysis of these data. Power analysis was conducted, taking into consideration the repeated measures design of the data. The effect size was based on piloted data. The power analysis indicated that a total sample of 15 participants were needed based on an effect size of 0.4 and alpha level at 0.05 to achieve a power of 0.8. A repeated measures ANOVA test was used to determine the differences of means between the three groups. Pairwise comparisons were conducted to compare the data between groups.
CHAPTER 4: RESULTS

The purpose of this chapter is to analyze the data for the time to onset of anesthesia between an ice bag, IFC, and combination treatment. It will also present the differences between the time to return to baseline sensation post-treatment between the three treatment groups.

Time to Onset of Anesthesia

The results for research question “is there a significant difference in the time to onset of anesthesia between an ice bag, sensory level IFC, and a combination treatment” indicated a significant difference between the three groups ($F_{2,12} = 21.75; P < .05$). The mean time to anesthesia for an ice bag was $18.67 \pm 2.23$ min, IFC $16.80 \pm 5.99$ min, and combination treatment $8.80 \pm 4.59$ min. (see Figure 1). Pairwise comparisons demonstrated a statistically significant difference in the time to anesthesia between combination treatment and the ice bag ($MD = 9.867; P < .05$). There was also a statistically significant difference between combination treatment and IFC ($MD = -8.000; P < .05$) (see Table 1).
Figure 1. Mean time to anesthesia with error bars representing standard error of the mean. Combo = Combination treatment; IFC = Interferential current electrical stimulation; *Indicates significant difference at $P < .05$ between combination treatment and IFC; †Indicates significant difference at $P < .05$ between combination treatment and ice bag.

Table 1

Time to Anesthesia Pairwise Comparisons

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mean Difference</th>
<th>Std. Error</th>
<th>$P$</th>
<th>95% Confidence Interval for Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combo</td>
<td>-9.867</td>
<td>1.373</td>
<td>0.000*</td>
<td>-13.597 - 6.136</td>
</tr>
<tr>
<td>Ice</td>
<td>-1.867</td>
<td>1.518</td>
<td>.717</td>
<td>-2.258 - 5.991</td>
</tr>
<tr>
<td>IFC</td>
<td>-8.000</td>
<td>1.841</td>
<td>0.002*</td>
<td>-13.004 - 2.996</td>
</tr>
</tbody>
</table>

Combo = Combination treatment; IFC = Interferential current electrical stimulation; *Indicates significant difference at $P < .05$. 
Time to Return to Baseline Sensation

The results for research question “is there is a significant difference in the time to return to baseline sensation post treatment level between an ice bag, sensory level IFC, and a combination treatment” indentified a significant difference between the three groups ($F_{2,12} = 12.548; P < .05$). The mean time to return to baseline for an ice bag was 9.47 ± 5.73 min, IFC 4.27 ± 6.27 min, and combination treatment 13.73 ± 6.36 min (see Figure 2). Pairwise comparisons showed a statistically significant difference in the time to return to baseline sensation level post-treatment between combination treatment and IFC ($MD = 9.467; P < .05$). (See Table 2).

![Figure 2. Mean time to return to baseline post treatment with error bars indicating standard error of the mean. Combo = Combination treatment; IFC = Interferential current electrical stimulation; *Indicates significant difference at $P < .05$ between combination treatment and IFC.](image-url)
Table 2

Time to Return to Baseline Sensation Pairwise Comparisons

<table>
<thead>
<tr>
<th></th>
<th>Mean Difference</th>
<th>Std. Error</th>
<th>P</th>
<th>95% Confidence Interval for Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lower Bound</td>
</tr>
<tr>
<td>Combo</td>
<td>IFC</td>
<td>9.467</td>
<td>1.454</td>
<td>.000*</td>
</tr>
<tr>
<td>Ice</td>
<td></td>
<td>4.267</td>
<td>2.083</td>
<td>.179</td>
</tr>
<tr>
<td>Ice</td>
<td>IFC</td>
<td>5.200</td>
<td>2.073</td>
<td>.075</td>
</tr>
</tbody>
</table>

Combo = Combination treatment; IFC = Interferential current electrical stimulation; *Indicates significant at P < .05.

Conclusion

We found a significant difference in the time to onset of anesthesia between an ice bag, IFC, and combination treatment. The combination treatment had the most rapid onset of anesthesia. A significant difference in the time to return to baseline sensation level post treatment between an ice bag, IFC, and combination treatment was identified. We found that the combination treatment had the longest duration of sensory effects post treatment.
CHAPTER 5: DISCUSSION

A significant difference in the time to onset of anesthesia between an ice bag, IFC, and combination treatment was identified. A significant difference was also identified in the time to return to baseline sensation level post treatment between the ice bag, IFC, and combination treatment.

**Time to Onset of Anesthesia**

Our findings demonstrated a significant difference in the time to onset of anesthesia between combination treatment and the ice bag and IFC, with combination treatment reaching anesthesia faster. There was no significant difference between the ice bag and IFC. These findings suggest that the combination of ice and IFC results in a more rapid onset of anesthesia compared to an ice bag or IFC treatments alone.

**Ice Bag**

The mean time to onset of anesthesia for the ice bag was 18.67 ± 2.23 min. To date studies have not examined the time to onset of anesthesia for ice. Our study supports that ice produces anesthesia. There are a few possible mechanisms explaining the decreased sensation. Cryotherapy has an effect on the exchange of Ca\(^{2+}\) and Na\(^{+}\) at gated ion channels on mechanoreceptors.\(^5\) When mechanoreceptors sense pressure, Ca\(^{2+}\) signals the channel to open and allow Na\(^{+}\) to pass into the receptor, resulting in depolarization and an action potential leading to the sensation of touch or pressure.\(^11\) Cryotherapy causes increased friction between Ca\(^{2+}\) and the gate, resulting in a reduction in action potential formation, leading to fewer impulses being sent to the brain, causing anesthesia.\(^5\)
Cryotherapy also reduces sensation by decreasing nerve conduction velocity, resulting in fewer impulse transmissions to the brain.\textsuperscript{1,12} A prior study identified that cooling the tissue at a temperature above 12°C resulted in a relatively slow reduction in nerve conduction velocity. However, at 12°C nerve conduction velocity decreased at a considerable pace.\textsuperscript{25} Pilot data for our study identified mean cutaneous temperature as 16.5°C at 20 min of ice bag treatment. Tissue temperature in our study did not reach 12°C and the point where nerve conduction velocity dramatically decreases, according to previous literature.\textsuperscript{25} It is possible that during our ice bag treatment a slower rate of decreased nerve conduction velocity was experienced, which may have attributed to the longer onset rate of anesthesia. It is possible that cutaneous cooling may have been achieved more dramatically if compression had been added. If the tissues could have reached 12°C earlier in the treatment, it is possible that the onset of anesthesia could have been achieved faster.

\textit{Interferential Current Electrical Stimulation}

The mean time to onset of anesthesia for IFC was 16.80 ± 5.99 min. To date studies have not examined the time to onset of anesthesia for IFC. Our results could not be compared to prior studies. Our study supports the anesthetic effect of IFC. Accommodation is one possible mechanism for the decreased sensation.\textsuperscript{15} During an IFC treatment sensory nerve fibers are under constant stimulation from the electrical impulses. The maximum rate of action potential formation is achieved. The impulses begin to fall within the relative and/or absolute refractory period.\textsuperscript{15} The sensitivity of the
nerve decreases. For the sensory nerve to continue conducting the stimulus must be removed or a greater stimulus must be added.15

Another possible explanation for the decreased sensation is IFC”s effect at the spinal level. It is proposed that applying peripheral electrical stimulation could result in the release of endogenous opioids at the spinal and supraspinal levels.31 It is also proposed that peripheral electrical stimulation triggers the release of peptides and enkephalins.11,32

The placement of the electrodes could have been a factor in producing anesthesia. Studies have determined that applying the electrodes in a specific location according to nerve fiber orientation can affect the modulation of the current.9 In our study the electrodes were placed 8 cm apart for each participant. If the electrodes had been arranged in a unique manner to each participant”s nerve fiber orientation, it is possible that anesthesia may have been achieved faster.

**Combination Treatment**

The mean time to anesthesia for combination treatment was 8.80 ± 4.59 min. The significant differences in time to onset of anesthesia were between combination treatment and ice bag (MD = -9.867, \( P = .000 \)) and between combination treatment and IFC (MD = -8.000, \( P = .002 \)). Our results identified that combining ice and IFC resulted in achieving anesthesia in almost half the time than the ice bag and IFC treatments alone.

To date studies have not examined the anesthetic effects of combining ice and IFC, although prior studies have examined other effects of combination treatments. It was identified that a cold application, a transcutaneous electrical nerve stimulation
(TENS) application, and a combination of cold and TENS resulted in a significant analgesic effect for participants experiencing delayed onset muscle soreness (DOMS). It is unknown which of the three treatment groups had the greatest analgesic effect.

Previous literature has identified that using IFC in combination with other modalities was no better at reducing pain than other modalities such as TENS, ultrasound, or hot packs. One study compared the effects of cold water immersion, cathodal high voltage pulsed current (CHVPC), and a combination of the two on edema formation after injury. There was no significant difference between treatment groups.

Our results determined that neither ice alone nor IFC alone were able to produce anesthesia faster than the other. There was no benefit of using ice versus IFC in terms of time to onset. It is thought that if cryotherapy and electrical stimulation produce anesthesia by different mechanisms, then applying them in combination might result in a greater treatment effect. Combining the mechanisms by which ice and IFC produce anesthesia should reduce the time to onset. It is possible that the constant stimulus from IFC increased the resting potential of the mechanoreceptors to a higher than pre-stimulus level. The increased resting potential resulted in the decrease of action potential formation. Fewer action potentials were generated and less stimulation was transmitted to the brain. It is possible that the ice bag also reduced the number of action potential formations by increasing the friction between Ca²⁺ and the gated ion channels on the mechanoreceptors. Decreasing nerve conduction velocity also reduced the number of
impulses that are sent to the brain. As impulse transmissions were reduced the production of action potentials to produce new transmissions became delayed.

It is conceivable that IFC and the ice bag contributed to decreasing action potential formation that would lead to the sensation of touch from the monofilament. As each decreased the number of action potentials that were produced, the amount of sensation being sent to the brain was also decreased. It is possible that combining both mechanisms of the ice bag and IFC to reduce the number of sensory transmissions achieved a faster onset of anesthesia than either mechanism or treatment alone. Our results support the efficacy of using ice and IFC together to achieve a more rapid onset of anesthesia.

Time to Return to Baseline Sensation Level

Our findings demonstrated a significant difference in the time to return to baseline sensation level post treatment between an ice bag, IFC, and combination treatment. There was a significant difference between combination treatment and IFC. There was no significant difference between combination treatment and the ice bag. There was no significant difference between the ice bag and IFC. These findings suggest that the combination of ice and IFC results in a longer duration of sensory effects post treatment compared to an IFC treatment alone.

Ice Bag

The mean time to return to baseline sensation post treatment for the ice bag was 9.47 ± 5.73 min. Previous literature has identified that the effect of cold on nerve conduction velocity may last up to 30 min post treatment. There are a few possible
reasons for the discrepancy in the length of duration of effects. The previous study did not list the methods or parameters describing how nerve conduction velocity effects 30 min post treatment were achieved. The duration of effects may have been affected by the depth of the nerve or the length of cooling. It is also possible that the mechanism for producing anesthesia in our study was not decreased nerve conduction velocity. The reduced sensation could have been attributed to an increased friction between Ca\textsuperscript{2+} and the gated ion channel on mechanoreceptors or another mechanism.

In our study the duration of effects may have been affected by the treatment time. In one study, the ice was applied for 20-31 min in order to achieve sufficient cooling of the tissues. For our study, it is possible that the duration of effects post treatment could have been lengthened if the treatment time was extended beyond 20 min. The depth of cooling may also affect the duration of sensory effects. It is possible that cooling deeper tissues may take more time to rewarm and return to baseline sensation levels.

*Interferential Current Electrical Stimulation*

The mean time to return to baseline sensation post treatment for IFC was 4.27 ± 6.27 min. Previous literature has identified that the effects of IFC could last at least up to 30 min post treatment. If the theory of accommodation is applied, during the IFC treatment action potential formation was reduced due to the overload of stimuli. Once the stimuli were removed, the nerve could continue conducting, but an approximate 4 min latency period was seen before full sensation returned. Another possible option is the effect of IFC at the spinal level, including the release of enkephalins. Prior studies have identified enkephalin to have a half-life of 2-3.9 min. Our results are more
comparable to the half-life of enkephalin, but we did not examine the mechanisms and cannot be sure of the cause for the 4 min return to baseline sensation.

Combination Treatment

The mean time to return to baseline sensation post treatment for combination treatment was 13.73 ± 6.36 min. There was a significant difference between combination treatment and IFC ($MD = 9.467; P = .000$). Combination treatment resulted in a longer duration of sensory effects post treatment. A relatively fast baseline sensation return was identified for IFC. The duration length for the combination treatment could possibly be attributed to combining the effects of cryotherapy and IFC.

There was no statistical difference between combination treatment and ice bag ($MD = 4.267; P = .179$). However, combining ice and IFC compared to ice alone produced a longer duration of effects. Combining the mechanisms of ice with the mechanisms of IFC had a greater effect on time to return to baseline sensation than the mechanisms of ice alone.

There was no significant difference between ice and IFC ($MD = 5.200; P = .075$). In terms of duration of effects post treatment, there is no benefit in using ice compared to IFC. The mechanisms of ice alone had no greater effect on time to return to baseline sensation than the mechanisms of IFC alone.

Studies have not examined the duration of sensory effects for combining ice and IFC. It is suggested that combining the two would result in greater treatment effects.$^{33}$ Our results identified that when compared to IFC, combination treatment produces a longer duration of effects post treatment. When compared to ice, combination treatment
does not produce a significantly longer duration of effects. However, ice does not produce a significantly longer duration of effects compared to IFC. Combining the mechanisms of ice and IFC produces a longer duration of effects that the mechanisms of IFC alone.

Limitations

This study used Semmes-Weinstein monofilaments to test sensation. The monofilaments were designed to test cutaneous sensation levels of the hands and feet. In this study the monofilaments were used to test cutaneous sensation levels of the anterior thigh. Although not used for their intended purpose, the Semmes-Weinstein monofilaments provided a repeatable, objective measure of sensation.

A similar study was done using Semmes-Weinstein monofilaments to test sensation in the hand and fingers after an ice immersion. The monofilaments were used to measure sensitivity to pressure by pressing the monofilament against the skin until it bent. The monofilament was held in place for 2 seconds and was then removed. Monofilament size was increased until the participant reported feeling the monofilament. The results showed that sensation of pressure was statistically significantly higher after the ice immersion than at baseline ($F_{1,352} = 9.09, P \leq .003$). These procedures are similar to the procedures used in this study.

Clinical Significance

Our results demonstrated that using a combination of ice and IFC resulted in a more rapid onset of anesthesia compared to using the treatments individually. There is a significant benefit of using combination treatment compared to isolated ice or IFC.
treatments in terms of onset of anesthesia. If the treatment goal is to reduce the patient’s sensation in the least amount of time, combination treatment should be the option used. In a clinical setting, reducing sensation quickly could be used for the treatment of wounds, including cleaning.

Our results indicated that using a combination of ice and IFC resulted in a longer return to baseline sensation post treatment compared to IFC. There is a significant benefit in using combination treatment compared to IFC in terms of duration of sensory effects after treatment termination. Our results identified that there was no significant difference in duration of sensory effects between combination treatment and ice bag. There is no added benefit in using combination treatment compared to an isolated ice bag. There is also no significant difference in time to return to baseline sensation between IFC and ice bag. There is no added benefit in using an ice bag compared to IFC in terms of duration of sensory effects post treatment.

While there is no statistical benefit in combining ice and IFC compared to an isolated ice bag, combination treatment does provide a longer duration of sensory effects compared to an IFC treatment. There is no added benefit in using an ice bag compared to an isolated IFC treatment. If the treatment goal is to provide the patient with the longest duration of sensory effects once the treatment is terminated, combination treatment should be the option used. An ice bag is the next best treatment option, compared to IFC.

While the need for producing anesthesia in a clinical setting may not be relevant, the results of our study are quite significant in understanding the relationship between ice and IFC working together.
Future Research

Future research should examine the onset and duration of analgesia between a cold application, IFC application, and combination of the two. Cryotherapy and IFC have been shown to be effective at producing analgesia, but the rates of onset and duration have not been compared. Both modalities are frequently used as analgesics. A study comparing the time to onset and duration of analgesia would benefit the clinical setting in determining which treatment option would be most beneficial to the patient.


The following research study has been approved by the Institutional Review Board at Ohio University for the period listed below.

**Project:** The Effects of Cold, Electrical Stimulation, and Combination Cold and Electrical Stimulation on Sensory Perception

**Researcher(s):** Lindsey Philley
Andrew Krause

**Advisor:** Chad Starkey

**Department:** Recreation & Sport Sciences

Anne Loucks, Ph.D., Chair
Biomedical Institutional Review Board

**Approval Date:** 07/06/2010

**Expiration Date:** 06/30/2011

This approval is valid until expiration date listed above. If you wish to continue beyond expiration date, you must submit a periodic review application and obtain approval prior to continuation.

The approval remains in effect provided the study is conducted exactly as described in your application for review. Any additions or modifications to the project must be approved by the IRB (as an amendment) prior to implementation.

Adverse events must be reported to the IRB promptly, within 5 working days of the occurrence.
APPENDIX B: IRB AMENDMENT APPROVAL

The amendment, detailed below, and submitted for the following research study has been approved by the Institutional Review Board at Ohio University.

Project: The Effects of Cold, Electrical Stimulation, and Combination Cold and Electrical Stimulation on Sensory Perception

Amendment: Increase enrollment from 12 to 15. Change "analgesia" to "anesthesia" in protocol. Informed Consent Form revised.

Primary Investigator: Lindsey Philley
Co-Investigator(s): Andrew Krause

Advisor: Chad Starkey
Department: Recreation & Sport Sciences

Robin Stack, CIP, Human Subjects Research Coordinator
Office of Research Compliance

Date: 11/24/2010
Protocol Expiration Date: 6/30/2011
Title of Research: The effects of cold, electrical stimulation, and combination cold and electrical stimulation on sensory perception.

Researchers: Lindsey Philley, Dr. Chad Starkey, Dr. Andrew Krause

You are being asked to participate in research. For you to be able to decide whether you want to participate in this project, you should understand what the project is about, as well as the possible risks and benefits in order to make an informed decision. This process is known as informed consent. This form describes the purpose, procedures, possible benefits, and risks. It also explains how your personal information will be used and protected. Once you have read this form and your questions about the study are answered, you will be asked to sign it. This will allow your participation in this study. You should receive a copy of this document to take with you.

Explanation of Study
The purpose of this study is to examine the effect on sensation of cold application, sensory-level electrical stimulation, and both a cold application and electrical stimulation. You will participate in each of the three treatment groups. Testing during this study will be done by Lindsey Philley, who is a licensed athletic trainer. Sensory evaluators (wires much like fishing line) will be used to test skin sensation on the front of your thigh. Your dominant leg, the leg you use to kick a ball, will be tested. The cold application group will undergo an ice bag treatment, with skin sensation tested every 2 min. Once you can no longer feel the evaluators touching your skin, numbness will have been achieved and the time will be recorded. After the 20 min treatment, the ice bag will be removed and the evaluators will continue to be applied to your skin for a period of time. The same procedure will be used for the other two treatment groups. During the sensory electrical stimulation treatment, four electrodes will be placed on your skin and the intensity will be turned up until a slight muscle contraction is felt, then the intensity will be turned down to where it will feel “prickly”, but not painful. The combination treatment will be the same as the electrical stimulation group. However, an ice bag will be applied on top of your thigh between the electrodes. We will evaluate your level of sensation during the treatment (ice, electrical stimulation, or both) and following the end of the treatment. The post-treatment sensory testing will continue until you reach the pre-test level of sensation. Each testing session will last 1 hour. Subsequent testing will occur between 2 to 5 days from the last treatment session.
We request that you not engage in vigorous exercises three hours prior to your scheduled sessions.

**Exclusionary Criteria**

College students aged 18 to 26 will be recruited for this study. You will be given a Medical History Questionnaire to identify the presence of any of the following exclusionary conditions:

- Local infection of either lower extremity
- Unhealed muscle, tendon, or bone injury in the lower extremities
- Systemic infection
- Exposed metal implants in the lower extremity
- Cancerous lesions in the lower extremity
- Local cardiovascular and/or neurologic inhibition including peripheral vascular disease, venous insufficiency, or Raynaud’s disease.
- Pregnancy
- Implanted cardiac pacemaker
- Epilepsy

Participants will undergo a standard orthopedic screening to assess their neurologic status.

**Risks and Discomforts**

The risks for this project are minimal. You will experience a cold sensation during the ice bag application. The typical sensations associated with cold application are cold, burning, aching, and numbness. However, these discomforts will dissipate relatively quickly after the ice bag has been removed. You will experience a tingling sensation during the electrical stimulation treatment. This sensation may be comparable to the area feeling as if it has “fallen asleep.” The tingling sensation will subside shortly after the treatment has been stopped.

You may end the treatments at any time if discomfort levels become too great. You may remove yourself from the study at any time and for any reason without penalty.

**Benefits**

While there are no direct benefits to you as an individual the scientific community will benefit as follows: By determining the efficacy of a common clinical technique, this study will provide a better understanding of the rates of onset of anesthesia, as well as the duration of anesthesia while using three different modality options.
Confidentiality and Records
- Your information will remain confidential throughout the study and will not be shared with anyone else other than the investigators of the study.
- All files including informed consent, key codes linking you to the data and the data itself will be stored in a locked cabinet in Dr. Starkey’s office E170 Grover Center.
- You will have an assigned specific ID number for the study. The key codes to connect your ID number to the data files will be destroyed as soon as the connection has been made by using a micro-cut shredder. The signed informed consent and data records will be stored for three years after completion of the study.

Additionally, while every effort will be made to keep your study-related information confidential, there may be circumstances where this information must be shared with:
* Federal agencies, for example the Office of Human Research Protections, whose responsibility is to protect human subjects in research;
* Representatives of Ohio University (OU), including the Institutional Review Board, a committee that oversees the research at OU.

Compensation
There will be no compensation for participating in this study.

Contact Information
If you have any questions regarding this study, please contact: Lindsey Philley – (765) 461-8891, lp255409@ohio.edu, Dr. Andrew Krause - (740) 593-4648 (krausea@ohio.edu), or Dr. Chad Starkey – (740) 593-1217, starkeyc@ohio.edu
If you have any questions regarding your rights as a research participant, please contact Jo Ellen Sherow, Director of Research Compliance, Ohio University, (740)593-0664.

By signing below, you are agreeing that:
- you have read this consent form (or it has been read to you) and have been given the opportunity to ask questions
- known risks to you have been explained to your satisfaction.
- you understand Ohio University has no policy or plan to pay for any injuries you might receive as a result of participating in this research protocol
- you are 18 years of age or older
- your participation in this research is given voluntarily
- you may change your mind and stop participation at any time without penalty or loss of any benefits to which you may otherwise be entitled.

Signature ___________________________________________ Date ____________

Printed Name ___________________________________________ Version Date: [05.26.10]
## APPENDIX D: MEDICAL HISTORY QUESTIONNAIRE

### Medical History Questionnaire

**Subject Code Number:**

<table>
<thead>
<tr>
<th>Question</th>
<th>Y</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Do you have decreased sensation in your legs?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Have you sustained any leg injury in the last six months that required medical attention?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Do you have any exposed metal implants in your legs?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Are you currently taking antibiotics?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Have you ever been diagnosed with cancer?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Are you currently pregnant or is there a chance that you may be pregnant?</td>
<td></td>
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</tr>
<tr>
<td>7. Have you ever been diagnosed with epilepsy or have ever had a seizure(s)?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Have you ever been diagnosed with a heart condition?</td>
<td></td>
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<tr>
<td>9. Do you currently wear a cardiac pacemaker?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. Are you currently experiencing any numbness or tingling due to vascular or nerve related diseases including peripheral vascular disease, venous insufficiency, or Raynaud”s disease?</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

If you answered “Yes” to any of the questions above please use the space provided below to explain.
APPENDIX E: TOUCH-TEST™ SENSORY EVALUATOR INSTRUCTIONS

The Touch-Test™ Sensory Evaluator (Semmes-Weinstein Monofilaments) provide a non-invasive evaluation of cutaneous sensation levels throughout the body with rest are objective and repeatable. Using Touch-Test™ Sensory Evaluator is indicated in diagnoses including nerve compression syndromes, peripheral neuropathy, thermal injury postoperative nerve repair. Each Touch-Test™ Sensory Evaluator is individually calibrated to deliver its targeted force within a 5% standard deviation.

**Instructions:** These instructions are written for threshold testing with individual Touch-Test™ Sensory Evaluators, and for comparative testing and color mapping with the Touch-Test™ 5 Piece Hand Kit, the Touch-Test™ 6 Piece Foot Kit and the Touch-Test™ 20 Piece Full Kit. Color mapping enables progression or regression of sensory neuropathy to be documented. When worsened sensibility is detected proper intervention can be implemented. Conversely, improved sensibility would indicate effective treatment intervention.

1. Rest the patient's extremity on a stable, padded surface. Testing should be done in a quiet area to help the patient fully attend to the testing procedure. Obstruct the patient's vision by using a shield or by having the patient look away.
2. Explain the testing procedure to the patient and instruct the patient to respond when the stimulus is felt by saying “touch” or “yes”. Nonverbal patients may tap the table lightly when the stimulus is felt.
3. Note any areas of callus, abrasion, scarring or other blemishes by drawing on the recording form (Hand Screening Form NC12750-1 or Foot Screening Form NC12749). While testing, proceed from distal to proximal and from small to large monofilaments.
4. It is not necessary to test every area of the skin when performing an evaluation. Checks may be done over areas innervated by different nerves. For the hand, test the palmar surface of the index finger and thumb to evaluate median nerve function; test the little finger and hypothenar eminence to evaluate the ulnar nerve; and test the dorsum of the hand to evaluate the radial nerve (see Figure 1). For the foot, test the sites indicated in Figure 2.
5. Press the filament at a 90° angle against the skin until it bows. Hold in place for 1.5 seconds and then remove (see Figure 3). For monofilaments from 1.65 to 4.08 apply the stimulus in the same location up to three times to elicit a response. A single response indicates a positive response. For filaments 4.17 through 6.65, apply the stimulus one time only.
6. To test with the Touch-Test™ 5 Piece Hand Kit (NC12772), the Touch-Test™ Six Piece Foot Kit (NC12773) or the Touch-Test™ 20 Piece Full Kit (NC12775), begin with the 2.83 filament. If the patient responds to the stimulus in all sites, normal cutaneous sensation can be documented and the examination is complete. If the patient does not respond to the stimulus, choose the next largest monofilament and repeat the process.
7. When the patient indicates a response, record the result using the colored pencil that corresponds to the color on the handle of the Touch-Test™ Sensory Evaluator (Colored Pencils Set NC12756). When representing monofilaments of the same color, note which monofilament size was used (see Figure 4). Threshold levels indicated in Figure 5 can be used to interpret test results.

**Figure 1**

**Figure 2**

**Figure 3**

**Figure 4**

Sample of Documented Progress:

*If testing with the 5.07 only, follow instructions #1-#5. Then apply the 5.07 to the test sites shown in Figure 2. Record results using X to indicate each site with sensation and # for lack of sensation.

Note: Touch-Test™ Sensory Evaluators are precision instruments. Care should be taken at all times to protect the integrity of the nylon filament. The filament may be cleaned with a mild instrument disinfectant. Substantially bent or kinked monofilaments must not be used for testing and should be discarded.
### Figure 5—Touch-Test™ Sensory Evaluator Chart

<table>
<thead>
<tr>
<th>Product Number</th>
<th>Evaluator Size</th>
<th>Target Force*</th>
<th>Representation</th>
<th>Hand &amp; Dorsal Foot Thresholds</th>
<th>Plantar Thresholds</th>
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</thead>
<tbody>
<tr>
<td>NC12775-01</td>
<td>1.65</td>
<td>0.008</td>
<td>Green</td>
<td>Normal</td>
<td>Normal</td>
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<tr>
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<td>0.04</td>
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<td>0.07</td>
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<tr>
<td>NC12775-05</td>
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<td>0.16</td>
<td>Blue</td>
<td>Diminished Light Touch</td>
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</tr>
<tr>
<td>NC12775-06</td>
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<td>0.4</td>
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<td>NC12775-07</td>
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<tr>
<td>NC12775-08</td>
<td>4.08</td>
<td>1</td>
<td>Purple</td>
<td>Diminished Protective Sensation</td>
<td>Diminished Light Touch</td>
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<tr>
<td>NC12775-09</td>
<td>4.17</td>
<td>1.4</td>
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<tr>
<td>NC12775-10</td>
<td>4.31</td>
<td>2</td>
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</tr>
<tr>
<td>NC12775-11</td>
<td>4.56</td>
<td>4</td>
<td>Red</td>
<td>Loss of Protective Sensation</td>
<td>Loss of Protective Sensation</td>
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<tr>
<td>NC12775-12</td>
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<td>6</td>
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<tr>
<td>NC12775-13</td>
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<td>8</td>
<td></td>
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<tr>
<td>NC12775-14</td>
<td>5.07</td>
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<td>NC12775-15</td>
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<tr>
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<td>300</td>
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<td>Deep Pressure Sensation Only</td>
<td>Deep Pressure Sensation Only</td>
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* Individually calibrated within a 5% standard deviation.

### Touch-Test™ Sensory Evaluators and Accessories:

<table>
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<tr>
<th>Product Number</th>
<th>Description</th>
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<tbody>
<tr>
<td>NC12775</td>
<td>Touch-Test™ 20 Piece Full Kit</td>
</tr>
<tr>
<td>NC12774</td>
<td>Touch-Test™ Complete Foot Kit (6 Piece Kit, Screening Forms, Colored Pencils)</td>
</tr>
<tr>
<td>NC12773</td>
<td>Touch-Test™ 6 Piece Foot Kit (2.83, 3.61, 4.31, 4.56, 5.07, 6.65)</td>
</tr>
<tr>
<td>NC12771</td>
<td>Touch-Test™ Complete Hand Kit (5 Piece Kit, Screening Forms, Colored Pencils)</td>
</tr>
<tr>
<td>NC12772</td>
<td>Touch-Test™ 5 Piece Hand Kit (2.83, 3.61, 4.31, 4.56, 6.65)</td>
</tr>
<tr>
<td>NC12775-14</td>
<td>Touch-Test™ Sensory Evaluator 5.07 (10 grams of force)</td>
</tr>
</tbody>
</table>

▲ See NC12775-01 thru NC12775-20 for Individual Replacement Touch-Test™ Sensory Evaluators ▲

<table>
<thead>
<tr>
<th>Product Number</th>
<th>Description</th>
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</thead>
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<tr>
<td>NC12749</td>
<td>Foot Screening Forms (pad of 100)</td>
</tr>
<tr>
<td>NC12750-1</td>
<td>Hand Screening Forms (pad of 100)</td>
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<tr>
<td>NC12756</td>
<td>Colored Pencils Set</td>
</tr>
<tr>
<td>NC12780</td>
<td>Touch-Test™ Training Video-FREE</td>
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The following reference can be used for more detailed instructions:

APPENDIX F: DATA

**Descriptive Statistics**

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<tr>
<th></th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>N</th>
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<td>2.225</td>
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<td>min to anesthesia IFC</td>
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**Source**

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<th>F</th>
<th>Sig.</th>
<th>Observed Power a</th>
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</thead>
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</table>

a. Computed using alpha = .05

**Pairwise Comparisons**

<table>
<thead>
<tr>
<th>(I) factor1</th>
<th>(J) factor1</th>
<th>Mean Difference (I-J)</th>
<th>Std. Error</th>
<th>Sig. a</th>
<th>95% Confidence Interval for Difference a</th>
</tr>
</thead>
<tbody>
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<td>IFC</td>
<td>1.867</td>
<td>1.518</td>
<td>.717</td>
<td>-2.258 – 5.991</td>
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<td>.002</td>
<td>-13.004 – -2.996</td>
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</table>

Based on estimated marginal means
a. Adjustment for multiple comparisons: Bonferroni.
* The mean difference is significant at the .05 level.
### Descriptive Statistics

<table>
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<tr>
<th></th>
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### Source

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<th>Observed Power</th>
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### Pairwise Comparisons

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<th>(J) factor1</th>
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<th>Std. Error</th>
<th>Sig. a</th>
<th>95% Confidence Interval for Difference a</th>
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Based on estimated marginal means
a. Adjustment for multiple comparisons: Bonferroni.