Evidence of altered kinesthesia about the knee following increased skin temperature

by

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ABSTRACT

EVIDENCE OF ALTERED KINESTHESIA ABOUT THE KNE FOLLOWING INCREASED SKIN TEMPERATURE

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Introduction: Skin information does contribute to knee joint position sense (Collins et al., 2005; Edin, 2001). It remains unclear if increased skin temperature can affect dynamic joint position sense (DJPS) about the knee. Purpose: To determine how increased skin temperature can affect knee DJPS. Method: Participants (n=11; F= 6) were seated in a HUMAC NORM dynamometer (CSMi Medical Solutions, Stoughton, MA). Participants pressed a trigger when they perceived their left knee reached a 90^{o} angle. Five extension and five flexion trials were performed at baseline ($28.74 \pm 2.43\,^{o}C$). Skin temperature was increased ($38.05 \pm 0.16\,^{o}C$) and the protocol was repeated. Directional error (DE), absolute error (AE) and precision absolute error (PAE) were calculated. Results: Increasing knee-skin temperature improved extension AE ($p= 0.032$). Discussion: Information from muscle spindles may be preferentially weighted over information from cutaneous afferents during knee extension. Conclusion: Increased knee-skin temperature improves DJPS during knee extension.

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1. JPS: Joint position sense
2. IP Joint: Interphalangeal Joint
3. CNS: Central nervous system
4. PIP Joint: Proximal Interphalangeal Joint
5. MCP Joint: Metacarpophalangeal Joint
6. FA: Fast adapting
7. SA: Slow adapting
8. TRP: Transient Receptors Protein
9. DJPS: Dynamic joint position sense
10. DE: Directional error
11. AE: Absolute error
12. PAE: Precision absolute error
13. Avg: Average

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1. INTRODUCTION & LITERATURE REVIEW

1.1 Proprioception, kinesthesia and why is it important research?

Proprioception has long been defined as the awareness of limb position in space (Sherrington, 1907; Proske & Gandevia, 2009). The awareness of limb position was originally believed to utilize information provided to the central nervous system (CNS) by specific receptors regarding conscious movement or activity (Proske & Gandevia, 2012). When defined separately from proprioception, kinesthesia is believed to require multiple sensory systems, integrating four components of sensory awareness; (a) passive motion sense, (b) active motion sense, (c) joint position sense (JPS), and (d) the sense of heaviness (Elangovan et al., 2014). A widely accepted definition of proprioception states that proprioception includes the senses of limb position and movement, the sense of tension or force, effort, and balance (Proske & Gandevia, 2012), while the sub-component known as kinesthesia, specifically refers to the sense of limb position and movement. More recently, proprioception has been used to reference static tasks, while the term kinesthesia has been used to characterize the awareness of limb positioning during dynamic tasks (Aman et al., 2015).

This research will use the most recent definition of proprioception, where kinesthesia remains a component of proprioception, while referring to the awareness of limb position during dynamic tasks. Muscle spindles (Mccloskey et al., 1983), joint receptors (Clark et al.,1985; Macefield et al., 2016) and skin (Collins et al., 2005; Meyer et al., 2004), all contribute sensory information for proprioception and kinesthesia. Sensory feedback is required for the generation of smooth and coordinated actions (Ribeiro & Oliveira, 2007) and for effective planning of future movements. Accurate dynamic joint position sense (DJPS), referring to awareness of joint position through

movement (Verschueren et al., 2002), is critical for carrying out discrete multi-segmental movements (Cordo et al., 1994) of daily life.

1.2 Overview of muscle spindles

Muscle spindles, consisting of many intrafusal muscle fibres, are stretch sensitive receptors located deep within the belly of skeletal muscle. These receptors generate monosynaptic reflexes, and contribute to the coordination of locomotion, and awareness of limb position (Akay et al.,2014; Goodwin, et al., 1972; Poppele & Terzuolo, 1968). Each muscle spindle has three distinct components; 1) non-contractile intrafusal muscle fibres with contractile components on either end, 2) a large-diameter myelinated afferent axon that relays sensory information to the central nervous system (CNS) and 3) a small-diameter efferent axon that relays motor commands to the periphery (Boyd, 1962). These fusiform-shaped receptors are found parallel and in tandem with one another, and are parallel to the surrounding extrafusal muscle fibres (Cooper & Daniel, 1963). Elastic tissue and reticulin, surround the intrafusal and extrafusal fibres, with a greater concentration around intrafusal fibres (Cooper & Gladden, 1974). Located between the fibres endings and the elastic tissue are the afferent endings. Changes in muscle length increases the tension on the elastic tissue, causing deformation of the afferent ending.

The population of muscle spindles within each muscle is unique. In humans, 28 muscle spindles were recorded within the fourth lumbrical of the hand (Banks, 2015). Conversely, the gluteus maximus, with its much larger size and mass, displayed a spindle population of 629. (Banks, 2015). Furthermore, muscle spindle size can also vary across different muscle groups. The lumbricals of the hand are almost 600 times smaller at 1.3 g, than the average 748 g gluteus maximus muscle (Banks, 2015). However, as seen in muscles of the calf region, the relationship between muscle

spindle density and spindle location is non-linear (Banks, 2015). Despite being located in the same physical region and of similar size, the soleus muscle has a greater population of muscle spindles (408 spindles; 0.94 muscle spindles/g) than the gastrocnemius muscle (156 spindles; 0.4 muscle spindles/g) (Banks, 2015). It is postulated that spindle density within each muscle is dependent on the functional role of the muscle, rather than muscle location within the body.

1.3 Muscle Spindle Morphology

Located along the equatorial region of the non-contractile unit of the muscle spindle, two distinct receptor endings are found; nuclear bag fibres and nuclear chain fibres. Named for their contiguous single strand formation, ~10-20/strand (Cooper & Daniel, 1963), nuclear chain fibres are sensitive only to static length (Boyd et al., 1977). Nuclear bag fibres are ~1.5x smaller than nuclear chain fibres (Cooper & Daniel, 1963). Within the nuclear bag fibres are bag-like nuclei. Each nuclear bag fibre can contain up to 100 nuclei, with 2-5 nuclei across the widest section of the fibre (Cooper & Daniel, 1963). The nuclear bag fibres are classified into one of two groups, based on their unique sensory contributions (Boyd, 1962). Dynamic bag fibres (Bag I) have a high sensitivity to contractile velocity of muscle fibres, while static bag fibres (Bag II) have a high sensitivity to changes in length and position of muscle fibres. In feline models, the ratio of the nuclear bag fibres to nuclear chain fibres is unequal within the spindle, with an average ratio of 4-5 nuclear chain fibres to 2-3 nuclear bag fibres (Boyd, 1962). However, sensory ending proportions within muscle spindle is not uniform across mammals. Human muscle spindle biopsies have shown greater morphological complexity than rat and feline muscle spindles (Soukup & Thornell, 1999). The muscle spindles located in the neck and lumbrical muscles of the hand contain an increased number of muscle spindles, with the population of fibres per spindle ranging from 8-11 (Cooper & Daniel,

1963). This increased spindle population in humans is likely due to the increased number of chain fibres (Cooper & Daniel, 1963).

1.3.1 Muscle Spindles and sensory afferent innervation

The afferents associated with non-contractile components of muscle relay sensory information regarding stretch to the CNS. These afferents are classified by their diameter, and are not uniformly distributed along the intrafusal fibre capsules. Primary (type Ia) afferents are largest in diameter at 12-20μm, and form annulospinal connections with the associated intrafusal fibres (Hunt, 1954). The Ia afferents innervate nuclear chain, nuclear bag1 and nuclear bag2 fibres. However, type II afferents are smaller, with an average diameter between 4-12μm (Hunt, 1954). Type II afferents display a flowerspray ending, which innervates nuclear chain and nuclear bag2 fibres (Hunt, 1954). The type II afferent termination associated with nuclear bag2 fibres is what functionally delineates the bag2 fibres from nuclear bag1 fibres. Nuclear bag fibres are further classified as dynamic bag fibres (type I; high sensitivity to velocity) and static bag fibres (type II; high sensitivity to length and position).

1.3.2 Muscle Spindles and coding movement

As described above, muscle spindles provide information regarding movement velocity (Grill & Hallett, 1995) and muscle length (Cordo et al., 2002). Furthermore, it appears that these receptors are directionally dependent, increasing their responses during directional ramp and hold stretches, with peak firing during the greatest muscle length (Roll, Bergenheim, & Ribot-Ciscar, 2000). However, these receptors appear to provide information most relevant to JPS throughout the mid-ranges of motion (Cordo et al., 2002). Macefield and colleagues (2005) determined that stimulation of single sensory afferents did not always correspond to an individual's perception of movement. This finding would suggest that the activation of multiple sensory units within a muscle are

responsible for proprioception within a muscle (Cordo et al., 2002; Ribot-Ciscar & Roll, 1998; Roll et al., 2000). The response of a larger spindle population from multiple muscles acting about a joint are required for the coding of relative joint and limb positions (Ribot-Ciscar & Roll, 1998; Vallbo & al-Falahe, 1990). The concept of multiple muscle spindle populations contributing to proprioception has been explored during passive movement, and vibration induced illusions. Gilhodes et al (1986) applied vibration to biceps and triceps brachii, two ago-antagonist muscles about the elbow joint. When the vibration frequencies were the same across both muscles, participants did not perceive illusionary movement about the elbow. However, when the two muscles were vibrated at different frequencies, movement was experienced such that the muscle with the greater frequency was being stretched. Furthermore, the relationship between ago-antagonist muscles has shown importance for coding movement velocity (Ribot-Ciscar & Roll, 1998). Microneurographic data obtained from the peroneal nerve in humans (Ribot-Ciscar & Roll, 1998) suggests that the direction of slow movements may be determined on the basis of the spindle discharge rate. Spindle discharges are greater in the stretched muscle than in the shortened muscle, and therefore movement velocity might be correlated with the difference between the ago-antagonist spindle activity (Ribot-Ciscar & Roll, 1998).

1.3.3 The fusimotor system

Skeletal muscles are innervated by three functionally distinct efferent neurons: alpha (α), beta (β) and gamma (γ) motor neurons. Extrafusal muscle fibres, responsible for generating contractile force, are innervated by α-motor axons. Changes in extrafusal fibres length, as well as velocity, can alter the firing rate of intrafusal fibres (muscle spindles). During alpha motor neuron excitation and contraction of extrafusal fibres, the length of the intrafusal muscle fibres decrease. This change in length is what creates slack along the spindles, decreasing their

sensitivity (Cooper & Gladden, 1974). In these instances, the fusimotor system shortens the contractile ends of the muscle spindles (Boyd, 1976; Hulliger, 1984), thereby increasing the sensitivity of these fibres. Shortening of the contractile ends of spindles pulls on the central non-contractile region, keeping the spindle taught. Increasing intrafusal muscle fibre tension readies the sensory region of the spindles, thereby optimizing the intensity of the sensory feedback relayed to the CNS (Proske & Gandevia, 2009). The fusimotor system is a system through which the CNS controls muscle spindle sensitivity (Proske & Gandevia, 2009). Together, muscle spindles and their associated fusimotor neurons modulate the tensile force of extrafusal muscle fibres. The α-motor axons are not a component of the fusimotor system.

Gamma motor neurons are specific to mammalian species. In lower vertebrates, such as reptiles and amphibians, β-motor neurons innervating intrafusal fibres appear to branch from the larger α-motor neurons innervating contractile extrafusal fibres (Smith et al., 1973). Due to this connection to the α-motor neurons, β-motor neurons are also referred to as 'skeletofusimotor' axons (Scott, Kummel, & Illert, 1995). Although unclear for many years regarding the presence of β-motor neurons in mammalian species, several electrochemical and neuroanatomical studies have concluded the presence of dual-innervation by β-motor neurons (Adal & Barker, 1965; Bessou, Emonet-Dénand, & Laporte, 1963; Bessou & Laporte, 1962). Beta motor neurons innervate both static and dynamic fibres in approximately 70% of muscle spindles in both cats and humans (Manuel Hulliger, 1984; Scott et al., 1995). The function of β-motor neurons is not fully understood in humans, and will not be discussed further.

The γ-motor neurons innervate the contractile ends of the intrafusal muscle fibres, and do not contribute to contractile force (Leksell, 1964). The fusimotor system functions through the γ-motor neuron pool. De-efferented spindles in feline models have shown that removal of gamma motor neuron output removes all fusimotor activation (Matthews, 1963), as the fusimotor system is the only known system to alter the contractility of muscle spindle contractile units. However, not all γ-motor neurons are of the same classification. Fusimotor axons reflect the functional properties of their respective motor endings, and are thereby classified as static or dynamic (Bessou & Laporte, 1962; Bessou et al., 1966; Brown et al., 1965). Selective activation of the dynamic γ-motor axons increases the dynamic firing rate of dynamic nuclear chain and dynamic nuclear bag1 endings. Conversely, activation of static axons of γ-motor neuron increases firing rates of static nuclear bag fibres, with no change to dynamic firing rates (Bessou & Laporte, 1962). Dynamic γ-motor neurons innervate dynamic nuclear bag fibres, while static γ-motor neurons innervate static nuclear bag fibres and all nuclear chain fibres (Boyd et al., 1977)

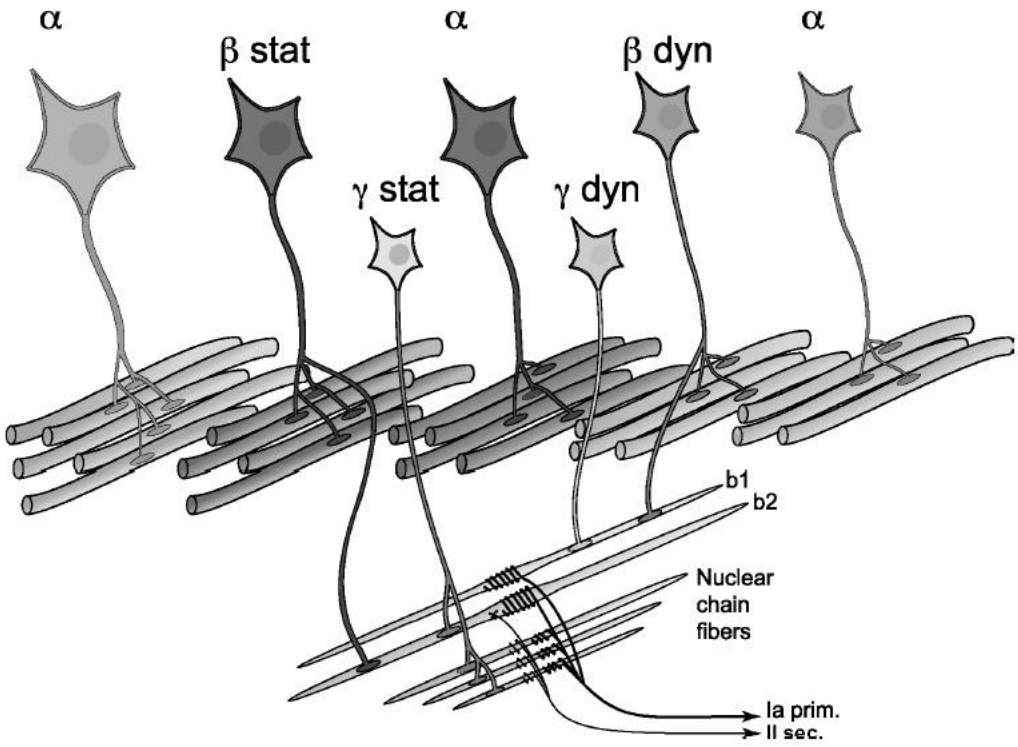

Figure 1: Illustration of the interaction between alpha motor neurons: extrafusal muscle fibres. Static beta-motor neurons (β stat) are shown to innervate both extrafusal fibres, as well as nuclear bag2 fibres. Dynamic beta motor neurons (β dyn) are shown to innervate both extrafusal muscle fibres and nuclear bag1 fibres. Similarly, dynamic gamma motor neurons (γ dyn) innervate nuclear bag 1 fibres only, while static gamma motor neurons (γ stat) innervate both nuclear chain fibres and nuclear bag2 fibres. Ia primary afferents relay information to the CNS from all intrafusal fibres, while secondary (II) afferents only relay information from nuclear chain fibres and nuclear bag2 fibres. (Manuel & Zytnicki, 2011)

1.3.4 Contributions to proprioception

McCloskey et al. (1983) examined proprioceptive involvement of muscle spindles in the halluces longus by pulling the exposed tendon to induce muscle lengthening. The participant reported the experience of joint rotation about the first digit of the foot providing solid evidence of spindle involvement in proprioception. The contractile ends of the intrafusal muscle fibres receive motor innervation from the CNS, and have been shown to contribute to changes in velocity and changes in muscle length (Goodwin et al., 1972; Houk et al., 2013). Efferent motor output (γ-motor neurons) to the contractile region of the muscle spindle causes the central region of the muscle

spindle to be stretched. Increases in muscle spindle stretch results in activation of the afferent γ-neurons, which will be described in greater detail later in this review. Interestingly, following changes in muscle length, static discharges from muscle spindle populations have shown a linear relationship to the specific joint angle throughout the intermediate ranges of motion (Cordo et al., 2011). However, the relationships between spindle sensitivity to muscle length and spindle sensitivity to movement velocity are distinct from one another. Research regarding muscle length and velocity at both the ankle and proximal interphalangeal (PIP) joints found that when muscle length changed at extremely low velocities (<1°/minute), no appreciable difference in the participant JPS acuity was shown to occur, compared to movements at greater velocities (Clark et al., 1985). Furthermore, muscle spindle sensitivity is not consistent across all joints. Clark & Burgess (1986) compared the dynamic and static awareness of the PIP hinge-joint with the metacarpophalangeal (MCP) condyloid-joint in the index finger of the hand and found that although both joints function to carry out coordinated flexion-extension movement, static sensitivity was not found to be uniform between the two joints. With increased velocity of rotation (0.01-2.13°/second) no decrements were found in JPS about the MCP joint whereas, JPS about the PIP joint showed that movements into both flexion and extension <1.67°/second were detected with extremely low acuity. This research collectively shows that muscle spindles are sensitive to both changes in length and velocity. However, changes in muscle length and movement velocity are two distinct variables, which are detected individually detected by muscle spindles.

Muscle spindle information has also been shown to be functionally relevant during locomotion. In mouse models, removal of type Ia and type II afferent information resulted in locomotor deficits

(Akay et al., 2014). Genetic mutation of the early growth response 3 gene (Egr3) selectively impairs type Ia and type II muscle spindles (Akay et al., 2014). During a treadmill walking task at 0.2m/s, the mutated-Egr3 mice showed a significant change in muscle activation patterns, with a delay in activation of the Iliopsoas (hip flexor), and earlier activation of the tibilias anterior (ankle flexor) and semitendonosus (knee flexor) (Akay et al., 2014). During a horizontal ladder walking task, the Egr3 mice exhibited a 30% foot-drop error rate, compared to only a 2% foot-drop error rate in wildtype mice (Akay et al., 2014). This data reveals that efficient locomotor patterns and coordinated stepping movements in the mammals requires intact ongoing proprioceptive feedback. In humans, individuals with a history of lower leg injuries have reported less accurate JPS about their injured joint than individuals without a history of lower leg injuries (Bali et al., 2011). Proprioception of the knee and ankle joints has also been shown to deteriorate with age, which may contribute to decreased performance of sensorimotor tasks and increased postural sway (Goble et al., 2009; Madhavan & Shields, 2005; Verschueren et al., 2002).

1.3.5 Augmenting proprioception

Deficits to proprioception and postural control are shown to occur in older adults (Goble et al., 2009; Madhavan & Shields, 2005) and is prevalent for individuals with a history of joint injury (Macefield et al., 2016; Macefield et al., 2013; Relph & Herrington, 2016). It has been proposed that augmenting sensory information could be used to offset proprioceptive deficits. During the swing phase of gait, the distance from the hip joint to the center of the toe (leg length), must be less than the distance of the hip to the floor (Moosabhoy & Gard, 2006). This difference between leg length and hip-floor distance is important to avoid tripping and subsequent injuries related to falling. Decreased length during the swing phase of gait is achieved by altering the height of toe clearance, and changes to knee joint angles of 1.5-2^{o} have shown to significantly alter gait

(Moosabhoy & Gard, 2006; Winter, 1992). Muscle spindles are sensitive to augmentation, with many researchers having looked at the effects of vibratory stimuli on spindle firing frequency and the functional implications of these changes (Brumagne et al., 1999; Gilhodes et al., 1986; Goodwin et al., 1972; Roll & Vedel, 1982). Vibration of the soleus muscle in felines has been shown to selectively activate the Ia primary endings. These authors suggests that this provides evidence that only primary muscle spindle afferents are sensitive to vibration (Brown et al., 1967). In humans, vibratory stimuli has been shown to enhance the perception of muscle lengthening in the agonist muscle (Roll & Vedel, 1982; Albert et al. 2006; Gilhodes et al., 1986; Schofield et al., 2015). Vibratory stimulation between 60-80 Hz over the tendon of the biceps brachii created the illusion of elbow flexion, while the same frequency of stimulation placed of the Triceps tendon resulted in the perception of elbow extension (Roll & Vedel, 1982). Vibration intensity targeting muscle spindles has also been correlated to joint movement velocity. Vibration frequencies between 10-120 Hz were used over the biceps and triceps brachii (Roll & Vedel, 1982). As frequency increased from 10-60 Hz, perceived elbow velocity also increased. Peak firing frequency of the spindle afferents was found to occur when frequency of vibration was between 60-70Hz (Roll & Vedel, 1982). Goodwin et al. (1972) also applied 100 Hz vibration to the biceps brachii and triceps brachii muscles. During this study, participants reported greater judgment error regarding joint angle, with the increased error caused by the perception of increased muscle length. However, the firing frequencies were only altered when a vibratory stimulus was placed directly over the muscle. No changes in spindle firing frequency was elicited when vibration targeted the elbow joint directly, or the skin overlying bone (Goodwin et al., 1972). Collectively, this research suggests that muscle spindles are sensitive to vibration, inducing the perceptual illusion of muscle lengthening. This research suggests that muscle spindles are used for proprioception and

kinesthesia. Furthermore, the ability to use information from muscle spindles regarding joint position can be altered by mechanical applications.

1.4 Overview of skin and cutaneous receptors

Human skin is a multi-layered organ, responsible for regulation of core body temperature (Schepers & Ringkamp, 2010), protecting soft tissues from harmful damage or pathogens and detection of tactile sensations (Vallbo & Johansson, 1984). Humans have two different skin types; glabrous skin and hairy (non-glabrous) skin. Hairy skin covers areas of the body such as the forearm, torso, back, and face, while glabrous skin covers areas such as the palms of the hand and soles of the feet. Glabrous skin contains similar receptors as those found in hairy skin, with recordings from four tactile receptors (SAI, SAII, FAI, FAII) in both hairy (Aimonetti et al., 2007; Edin & Abbs, 1991; Edin, 2001) and glabrous skin (Vallbo & Johansson, 1984; Vallbo et al., 1995). In addition to the SAI, SAII and FAI receptors, hairy skin also contains field units and hair follicle units (Edin, 2001), which will be described later. This review will place a greater focus on the mechanosensitive properties of hairy skin receptors.

1.4.1 Cutaneous receptors and afferent innervation

Mechanosensitive receptors (mechanoreceptors) found in hairy skin are responsive to mechanical force applied to skin or hair follicles (Olson et al., 2016). Low threshold mechanoreceptors are more sensitive to innocuous stimuli, while high threshold mechanoreceptors respond to noxious stimuli (Olson et al., 2016). Each mechanoreceptor is innervated by an associated afferent nerve. Aß afferent nerves have rapid conduction velocities (average of 40-60 m/s), due to the thick myelination and large diameter (Olson et al., 2016). The A∂ fibres have moderately sized axons, however these afferents have a lower conduction velocity (average~20 m/s) due the thin layer of myelin covering the axons (Olson et al., 2016). C-fibres are known to have the slowest conduction

velocity of the three fibres types (<2.5 m/s), due to their small diameter and unmyelinated axons. A∂ and C-fibres do not innervate cutaneous receptors, and are associated with thermal detection and pain-perception of free nerve endings. These sensory endings will be described later in this review.

Cutaneous mechanoreceptors, specifically, are associated with Aß afferents (Olson et al., 2016). Together the mechanoreceptor and associated afferent nerve form a sensory unit. These units are distinguishable by the size of their receptive field and their unique firing characteristics in response to specific mechanical stimuli. Cutaneous mechanoreceptor nomenclature and classification varies across the literature, as these receptors can be named by their receptor ending or the unique response of their associated afferent. However, a consistent defining characteristic for all classifications of cutaneous mechanoreceptors is the ability for these receptors to adapt to stimuli and the size of their receptive fields. Fast adapting mechanoreceptors [FA type I (FAI) and FA type II (FAII)] respond to the onset and offset of a stimulus, with receptor type referencing the size of the receptive field. Type I receptors have small and well-defined receptive fields. In contrast, Type II mechanoreceptors display quite broad, undefined, receptive borders. Slowly adapting mechanoreceptors [SA type I (SAI) and SA type II (SAII)] also respond to the onset of new stimuli. However, unlike the on-off response of FA receptors, the SA receptors elicit a sustained response until the stimulus is removed completely. The following sections will detail the anatomy and function of these units.

1.4.2 Type I receptors & sensory contributions

The Merkel Disc receptor is part of the SAI sensory unit, located superficially within the epidermis. The Merkel Disc has the most basic structure of all the cutaneous mechanoreceptors, with only a

single layer of cells encapsulating the SAI afferent. The SAI receptor is most sensitive to indentation, specifically edges and curvature of objects (Johnson, 2013), where the depth of indentation is found to be linearly related the magnitude of the receptor response. Meisner's Corpuscles are part of the FAI sensory unit, and are also found to reside superficially within the papillary folds of the epidermal layer of the skin. These receptors are most sensitive to punctate stimuli (Järvilehto et al., 1981). Microneurography recordings have shown that FAI receptors located near MCP and PIP joints of the hand responded to articular movements, indicating that they may be involved in proprioception about joints not pertaining to skin stretch (Edin & Abbs, 1991). However, FAI receptors located in the skin over the MCP and PIP joints, anterior thigh lower leg have still been shown to elicit high frequency responses to bi-directional skin stretch, with preferential response to joint flexion (Aimonetti et al., 2007; Edin & Abbs, 1991; Edin, 2001).

In the glabrous skin of the hand the FAI and SAI receptors have been reported to have receptive field sizes of 12.6 mm^2 and 11 mm^2 respectively (Vallbo & Johansson, 1984). In the foot, Type I receptors located in both the hairy and glabrous skin have been recorded with receptive field sizes between 25-100 mm^2 (Lowrey et al., 2013; Strzalkowski et al., 2017; Trulsson, 2001). Stimuli below the threshold of the targeted mechanosensory unit, regardless of the receptive field size, will not be detected. Within these receptive fields are areas of increased sensitivity, known as "hot spots". Type I receptors have been shown to have several hot spots within their receptive fields, while Type II receptors only display a single area of increased sensitivity.

1.4.3 Type II receptors & sensory contributions

In humans, type II receptors reside in the dermal layer of hairy skin. Both type II mechanoreceptors are quite large, and are found within deep layers of the skin (Iggo & Muir, 1969; Iggo & Ogawa,

1977). In the dorsum of the human hand, the average receptive field size of SAII receptors are 28 mm^2, while the receptive field of the FAII unit encompassed an entire digit (Edin & Abbs, 1991). The Pacinian Corpuscle, which is believed to be the mechanoreceptor associated with the FAII sensory unit, is onion-like in its structure with multiple cell layers protecting a single afferent terminal. The afferent terminal is extremely sensitive to mechanical deformation. The Pacinian Corpuscles are most sensitive to high frequency input, as the multiple layers about the receptor act to filter low frequency deformations by dampening the frequencies (Johnson, 2013). The Ruffini Ending is the cutaneous receptor most sensitive to skin strain. This SAII receptor is similar in its structure to a muscle spindle. The Ruffini Endings are parallel to the skin, with the polar ends of this receptor attaching to the surrounding dermal collagen fibres (Chambers et al., 1972). Research examining skin strain over the anterior thigh and lower leg has determined that SAII receptors are most sensitive to unidirectional skin stretch caused by ankle and knee flexion (Aimonetti et al., 2007; Edin, 2001). Sensory information from cutaneous mechanoreceptors sensitive to stretch, have also been shown to contribute to proprioception around the ankle, knee, elbow and the interphalangeal (IP) joint of the hand (Collins, 2005; Edin, 2001; Mildren, 2017, Lowrey 2010). Collins et al. (2005) stretched the skin about the IP joint of the hand, where participants reported sensations of IP joint movement. The researchers concluded this was a result of information received through Ruffini Endings within the skin.

1.4.4 Mechanoreceptors specific to hairy skin

FAII receptors have yet to be located within the skin of the anterior thigh (Edin, 2001). Edin (2001) recorded from the femoral nerve innervating the thigh. Interestingly, only Edin (2001) has reported a third type of receptor in this region of the body; the SA III unit. The SAIII unit is responsive to multi-directional skin stretch and have appear to have a greater representation in skin over the

anterior thigh (SAIII: 10) than the SAII receptors (SAII: 2) (Edin, 2001). This unit displays a similar receptive field size to SA I receptors. However, unlike SAI units, the SAIII unit displays only a single spot of high sensitivity (Edin 2001). As shown in Table 1, the SAIII receptors, which dominate the anterior thigh, are sensitive to skin stretch in multiple directions. The receptor terminal of these afferents remain uncharacterized. However, it is proposed that this receptor resides in a similar superficial location as Merkel disc receptors, between the dermal and epidermal layers of skin (Edin, 2001).

Table 1: Slowly adapting afferents in hairy skin (Edin, 2001).

	SAI	SAII	SAIII
Multiple hot spots	●	○	○
Small, demarcated receptive field	●	○	●
Omnidirectional strain sensitivity	●	○	●
High skin strain sensitivity	○	●	●
Regular interspike intervals	○	●	●

** Open circle = Absent. Closed circle = Present.*

In hairy skin, fast adapting sensory units associated with hair follicles have been recorded. The hair follicle unit, also referred to as the hair follicle afferent (Templeton, 2012), has a large, irregular-shaped receptive field. In work conducted in the hairy skin of the forearm, hair follicle units have a recorded median receptive field area of 113 mm^2, which contain many clusters of sensitive spots (Vallbo et al., 1995). The hair follicle afferent can innervate up to 20 individuals hair shafts, and is sensitive to manipulation of these hair shafts (Vallbo et al., 1995). In research conducted in skin over the human thigh the hair follicle unit displays the largest sensory unit population, with 40% of all recorded sensory units being characterized as hair follicle units (Edin, 2001). However, despite high sensitivity to deformation of hair follicles, hair follicle units were

not sensitive to skin deformation when the knee joint was passively flexed (Edin, 2001). While these hair units are extremely sensitive to small deformations of the hair shaft perhaps gross joint movements did not deform the nearby hair shaft, which could explain the lack of activation to skin deformation (Edin, 2001).

Field units have been recorded in hind leg of felines (Burgess et al., 1968) as well as the skin of the forearm in humans (Vallbo et al., 1995) and in the human thigh (Edin, 2001). First recorded in the hairy skin of cats, these units display oval-shaped receptive fields with distinct boundaries (Burgess et al., 1968). These units are variable in their adaptation to stimuli, with some units displaying fast adaptation, while other units display adaption similar in rate to SA cutaneous receptors (Burgess et al., 1968). Relative to the hair follicle unit, field units display large receptive fields. However, they do not respond to movement of the hair shaft alone, with the greatest response being elicited with hair shaft and skin deformation (Burgess et al., 1968; Edin, 2001), the field units do not respond to manipulation of the hair shaft.

1.4.5 Augmenting proprioception

Increased thresholds of cutaneous receptors have been reported in older adults and individuals with diabetic neuropathy (Priplata et al., 2006; Priplata et al., 2003). Sub-threshold vibration applied to the foot sole, targeting cutaneous receptors, has been shown to improve time-to-task-completion and reduce postural sway during standing balance tasks (Miranda et al., 2016; Priplata et al., 2002; Priplata et al., 2006; Priplata et al., 2003) as well as altering perceptual thresholds (Hur et al., 2014; Liu et al., 2002; Ross et al., 2007). Sub-threshold vibration is believed to improve postural stability by increasing the strain on receptor membranes and subsequently altering ion permeability (Priplata et al., 2006). It is the subsequent change in ion permeability which brings the cutaneous

receptors closer to threshold (Priplata et al., 2006). At the knee, increasing cutaneous feedback using physiotherapy tape has been shown to improve the threshold to detect passive movement in healthy young adults (Torres & Trindade, 2016). Similar to physiotherapy tape, elastic bandages are used to treat musculoskeletal disorders. Perlau & Frank (1995) tested the baseline proprioception of 54 young healthy adults. The elastic bandages were found to significantly improved knee proprioception during the entire protocol. Furthermore, it was concluded that the beneficial effects of the elastic bandages were inversely related to participants' inherent proprioceptive ability (Perlau & Frank, 1995). The mechanism behind improving proprioception with elastic bandages and physiotherapy tape is believed to rely on increasing the strain of the skin in select areas around the joint. Enhanced skin strain subsequently provides greater feedback, which ultimately results in improved muscular control (Edin, 2001). Textured materials have also been found to alter proprioception. Textured insoles have been shown to improve performance during upright balance tasks (Orth et al., 2013), while textured panels over the knee can alter joint position sense about the knee (Lamers & Reeves, et al., 2018). The proposed mechanism behind texture altering proprioception involves increasing the discharge rate of cutaneous receptors in contact with the textured material, altering cutaneous receptor feedback.

1.5 Overview of thermal detection

Thermal detection is a unique sensory modality of the skin, with sensations of noxious cold, cold, warm, and noxious warm (hot). No single nerve ending has been found to be responsible for detection of thermal stimuli. However, thermal sensation does involve two primary afferent nerves; the Aδ fibres and C-fibres (Schepers & Ringkamp, 2010), which relay information regarding thermal stimuli from across a large temperature range. The Aδ and C-fibres have been studied in both hairy and glabrous skin of primates (Konietzny and Hensel, 1983), felines

(Konietzny and Hensel, 1983) and humans (Davis, 1998; Yarnitsky & Ochoa, 1991). However, the primate and feline thermal detection mechanisms may be different from those of humans. Most notably in primates, the SAI receptor has distinct steady state firing rate, which can change in response to temperature fluctuations (Konietzny and Hensel, 1983). However, this finding has not been found in humans.

Human thermal detection can occur over regions of hairy skin, and glabrous skin. Within humans these skin regions are distinctly different, both in anatomy and function. Sensory neurons of the dorsal root ganglia in the spinal cord are thought to mediate thermosensation. These sensory neurons innervate free nerve endings, which terminate in the dermal and epidermal layers of the skin (Hensel & Schafer, 1984). Although there is no specific cutaneous receptor responsible for thermal detection alone, the free nerve ending is able to detect mechanical, chemical and thermal noxious stimuli (Schepers & Ringkamp, 2010), and has been recorded as detecting innocuous thermal stimuli (Schepers & Ringkamp, 2010).

1.5.1 TRPV ion channels

Along free nerve endings, researchers have determined six channels from the Transient Receptor Proteins (TRP) family to respond to distinct temperature changes (Patapoutian et al., 2003). TRP ion channels are known as transient receptor proteins (TRP) channels, which release specific ions in response to distinct changes in temperature. At the time of this review, six TRP channels have been identified in the human body (*Table 2*). The TRP channels involved in cold sensation result in afferent baseline firing between 17ºC - 27ºC. As temperature decreases below 17ºC, the firing rate of the cold-specific afferents decrease until they are eventually silenced. Free nerve endings associated with warmth-activated TRP channels, respond to temperatures above 33ºC. However,

a unique warm-sensitive ion channel (TRPV4) has been shown to respond to temperatures greater than 24ºC (Watanabe et al., 2002). TRPV1 and TRPV2 respond to noxious warm stimuli ≥42ºC. However, TRPV1 has also been shown to respond to chemical changes, such as low pH and capsaicin (Patapoutian et al., 2003). The TRPV3 and TRPV4 ion channels are regarded as responsive to innocuous thermal stimuli within the 34ºC-42ºC temperature range. These thermo-TRP ion channels have been found to exist at the terminal end of dorsal root ganglia neurons. The nervous system can distinguish between noxious and innocuous thermal stimuli through the activation of these various ion channels, which are located at the terminal end of an associated free nerve ending afferents (Park & Kim, 2013; Rutkove et al., 1997).

*Table 2: Transient Receptor Protein ion channels involved in thermosensation (Park & Kim, 2013). PNS= peripheral nervous system. *(Rigon, 2014)*

Name	Alternate Name(s)	Temperature Sensitivity (ºC)	Location/Distribution
TRPV1	Vr1	≥42	PNS, brain, spinal cord, skin, tongue, bladder.
TRPV2	Vr1	≥52	PNS, brain, spinal cord.
TRPV3	Vr3	≥33	Skin, PNS (human), widely expressed
TRPV4	OTRPC4,VR-OAC, Trp12,Vrl2	27≥42	Kidney, PNS, skin, inner ear, brain, liver, trachea, heart, hypothalamus, fatty tissue, endothelium.
Trpm8	CMR1	≤25	PNS, prostate (human).
TRPA1	Closely related to ANKTN1*	≤42	PNS.

1.5.2 Innocuous heat

As stated earlier, warm temperatures within the moderate range of 33-42^{o}C is shown to result from activation of the TRPV3 and TRPV4 ion channels along cutaneous free nerve endings. Afferent impulses in response to increasing warm temperatures have been recorded in nerve fibres innervating tongue, nose and skin tissue in primates (Hensel & Iggo, 1971; Hensel & Kenshalo, 1969; Iggo, 1969). The mechanosensitive mechanisms were minimized by altering temperature surrounding the tissue, allow thermal changes to occur by convection. The distinct firing rate of the recordings from the thermaosensitive fibres indicated that the fibres were not myelinated. Unlike many mechanosensitive endings, thermosensitive afferents have a background firing rate when skin temperature is 34^{o}C. Further research into warm cutaneous afferents in primates determined that afferents could be divided into two groups (Hensel & Iggo, 1971), which were later determined to be 1) innocuous and 2) noxious. Although both thermosensitive afferents increased their firing rate linearly with increased skin temperature, maximal firing rates did not occur at a consistent temperature. One group displayed a maximal firing rate at 41^{o}C, while the other group continued to increase firing frequency into a noxious thermal range. Through sequence homology, these differences in maximal firing frequency have been shown to correspond to the specific ion channels; TRPV3 and TRPV4. TRPV3 in heterogenous systems has shown activation between 34-38^{o}C, and continue to increase activation well-into noxious ranges. This ion channel shares 40% homology with TRPV1 (Peier et al., 2002; Smith et al., 2002; Xu et al., 2002). The TRPV4 channel is exclusively activated by innocuous warm-stimuli, and does not increase afferent activity beyond 38^{o}C, despite sharing 50% homology to the TRPV1 ion channel.

1.5.3 Noxious Heat

As previously described in section 1.4.2, Aδ fibres and C-fibres are involved in noxious and

thermal detection (Patapoutian et al., 2003). Free nerve endings with connections to the Aδ afferents are classified into two groups [Aδ Type 1; found in both glabrous and hairy skin, and Aδ Type II; found only in hairy skin] (Treede et al., 1995). The Type I Aδ afferents have a high heat threshold, with a median threshold >53^{o}C). In the primate model, Type I Aδ afferents displayed a delayed activation by ~5 seconds and a delayed peak discharge, from the onset of a 53^{o}C stimulus held for 30 seconds. However, they display an increase in the strength of their response over short duration stimuli (Treede et al., 1995). Recordings from Type II Aδ afferents show lower heat-pain threshold (median ~47^{o}C), however they are highly responsive to stimuli with onset latency of <1 second following a thermal stimulus at 53^{o}C held for 30 seconds. In addition to the Type I and Type II Aδ nociceptive afferents, C-fibre afferents are also capable of detecting noxious heat stimuli. C-fibre afferents recorded in radial nerve of humans have demonstrated a heat detection threshold of 40^{o}C (Van Hees & Gybels, 1981). In the distal extremities, dual-pain sensations can be experienced. The first sensation, often perceived as a sharp or pricking pain, occurs ~0.4 seconds following the onset of heat-pain. The second sensation is experienced ~1-2 seconds from the onset of the stimuli. Individuals describe this pain as a dull, burning sensation (Campbell & LaMotte, 1983). Despite a faster response to noxious thermal stimuli, C-fibre afferents have a slower conduction velocity due to their small axon diameter (Treede et al., 1995) and lack of myelination. The latency of the second sensation of pain correlates with the difference Aδ fibre conduction velocity and C-fibre afferent conduction velocity. The onset of dull and burning sensations is believed to be the delayed noxious stimuli perception from C-fibre afferents (Davis, 1998). Therefore, although receptor detection of noxious stimuli shows distinctly

1.5.4 Muscle spindles and temperature

Increased thermal stimuli in the innocuous temperature range induces the sensation of warmth. However these receptors quickly adapt to this sensation (Schepers & Ringkamp, 2010), and the perception of warmth dissipates. This same adaptation occurs when cool stimuli within the innocuous thermal range is applied to the skin. Thermal stimuli not only affect the conscious sensation of temperature, but can also influence the function of alternate sensory and motor systems through the fusimotor system (Wolf & Knutsson, 1975). In the feline model, increased muscle temperature has been shown to alter the nervous outflow of the myelinated primary (Ia) and secondary (II) afferents, with the greatest functional changes occurring with increased temperature. When the gastrocnemius muscle fibres are heated from 36^{o}C to 43^{o}C, type Ia afferent firing frequency increased by >100%. However, type II afferents do not respond uniformly to increases in temperature. Mense et al. (1978) recorded from six type II spindle afferents, and found a 50% increase in firing rate, while the remaining afferents either did not change or even decreased their rate of firing. When the tenissimus and gastrocnemius muscles in felines were cooled below 30^{o}C, type Ia afferent firing rate increased (Fischer & Schafer, 1999; Mense, 1978). The work of Sato et al. (1983) provided superficial heat over the tibialis anterior in feline models. This research showed that superficial heat only affected 43% of all muscle spindle afferent fibres. However, no other research has reported this lack of temperature effect on muscle spindle firing.

The research described only shows that the changes to spindle firing rate elicited with thermal fluctuation occurs during the static phase of muscle stretch. However, the change to spindle firing with temperature is also functionally relevant. It has been shown that decreased skin temperature decreases tonic reflexes of underlying muscles. Cooling the skin overlaying the popliteal fossa in feline models resulted in depressed stretch reflexes of the triceps surae (Wolf & Knutsson, 1975).

Collectively, this research shows that increases in the temperature of mammalian muscle spindles can increase the firing rate of the muscle spindle, and decreases in temperature can decrease the firing rate of muscle spindles. Functionally, temperature induced changes in spindle firing is relevant, as this can affect the efficacy of tonic reflexes.

1.5.5 Cutaneous receptors and temperature

In human subjects, recordings from cutaneous afferents have shown that cooling the glabrous skin over the foot sole acutely reduced the firing frequency of the cutaneous receptors (Lowrey, 2012). Functionally, cooling of the glabrous skin of the foot sole has been shown to reduce both postural stability (Billot et al., 2013; Mäkinen et al., 2005) and distribution of foot pressure during locomotive tasks (Nurse & Nigg, 2001). Furthermore, cooling the surface temperature of the skin using ice and cryotherapy has been shown to decrease JPS at the ankle and shoulder (Wolf & Knutsson, 1975). While cooling of the skin has been extensively researched in human models to examine function, little is known about the functional effects of heating skin. Burton et al. (1972) measured the effect of cooling on skin afferents (41^{o}C-25^{o}C) in anesthetized felines. In response to incremental decreases in temperature, SAII afferents displayed an increase in firing frequency. In human subjects, heating the glabrous skin over the soles of the feet reduced vibration thresholds of cutaneous receptors (Schlee et al., 2009; Schmidt et al., 2016). When presented with a constant thermal stimulus over a three minute window, SAII receptors in felines have shown progressive decreases in firing rates as temperature increases (17^{o}C-41^{o}C), with almost no activity at 41^{o}C (Burton et al., 1972). However, the functional implications of these incremental and constant changes in skin temperature of the hairy skin over the knee are not well studied.

1.6 Purpose

The purpose of this research is to determine the functional implications of increasing skin temperature on DJPS about the knee joint.

1.6.1 Specific Aims

This research aims to determine:

1) the effect of increased skin temperature on dynamic JPS (DJPS)

2) if cutaneous afferents play a significant role in DJPS of the knee

3) if DJPS of the knee is directionally dependent.

1.6.2 Hypotheses

Based on the animal literature and limited human literature (Burton et al., 1972; Ghaffarinejad et al., 2014; Mense, 1978; Sato, 1983), it is hypothesized that:

1) increased skin temperature to 38^{o}C will decrease DJPS about the knee,

2) skin does contribute to DJPS about the knee, and when skin information is decreased using topical anesthesia, DJPS will decrease about the knee and

3) DJPS about the knee will be directionally dependent; with greater accuracy during movements into knee flexion over movements into knee extension.

2. METHOD

2.1 General overview

Fourteen healthy young adults (F=8; 23 ± 3 yrs) were recruited. Subjects received verbal and written descriptions of all procedures. All participants provided written informed consent before participating in the experimental procedures. DJPS testing was conducted over two sessions, with the skin temperature and direction of joint movement protocols remaining constant between the first and second test days. Skin input was altered during one of the test days using topical anaesthetic (EMLA®, Astra Zeneca; 2.5% lidocaine, 2.5% prilocaine). The sequence of EMLA and NoEMLA DJPS testing was randomized across test days (Table 3). Permission to conduct this research was provided by the Research Ethics Board at the University of Guelph and complied with the declaration of Helsinki for human experimentation.

Table 3: Dynamic joint position sense (DJPS) protocol. Five trials were conducted for each movement direction (10 total trials for each condition). Participants alternated between a movement through knee extension and knee flexion. Participants always began with knee-extension followed by flexion.

Test session (Randomized)	EMLA		No EMLA	
Condition	1. No Heat	2. Heat	1. No Heat	2. Heat
Trials	i. Extension ii. Flexion	i. Extension ii. Flexion	i. Extension ii. Flexion	i. Extension ii. Flexion

2.2 Experimental setup

To minimize information provided by hair follicles, each participant had their left anterior thigh shaved prior to both NoEMLA and EMLA DJPS tests. Metallic Sharpie® was used to demarcate a rectangular box where EMLA cream would be applied and where the skin would be heated. This box was drawn over the distal third of the thigh (Figure 2). Participants were standing during all

skin demarcation protocols. Using this area, a circle was drawn, such that the middle of the circle was the same as the midline of the box. This was the area of skin which was to be measured for changes in temperature by the thermal camera. Participants were instructed not to remove the markings until the second session has been completed. This ensured that test sites remained consistent between test sessions.

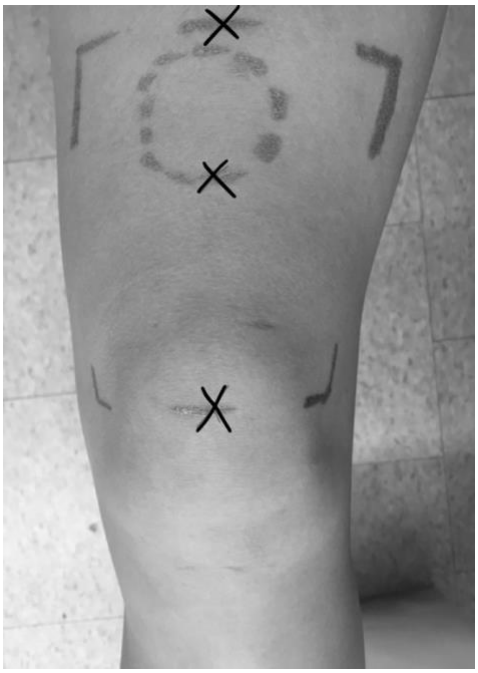

Figure 2: An anterior view of the knee with the black box indicating the location of greatest skin stretch. The base of the circle is the location from which thermal measurements were taken. Monofilament testing occurred at three sites along the midline of the demarcated box, with each site represented by a black X.

To determine which leg participants perceived as their dominant leg, participants were asked which leg they would use to kick a ball. Electromyography (EMG) was used to ensure the muscles of the lower left leg were inactive prior to motion and remained passive during joint position sense testing. It was important to minimize and monitor muscle activity in the synergistic, agonist, and antagonist muscles in order to focus on proprioceptive contributions from cutaneous receptors during knee movement. The skin was shaved and swabbed with alcohol prior to electrode

application. Two silver silver/chloride (Ag Ag/Cl) surface recording electrodes were placed on the skin over the quadriceps, hamstrings, and the gastrocnemius muscles of the left leg. These muscle groups cross the knee joint, contributing to knee flexion and knee extension. The electrodes were placed over the muscles group compartments, rather than targeting the specific muscles. This electrode placement was chosen because the purpose of the EMG for this research was to monitor and limit muscle activity about the knee joint throughout the protocol. Targeting each muscle would increase the number of electrodes on the skin, which could alter DJPS by affecting skin stretch. The recording electrodes were placed in a bipolar configuration. Electrode wires were secured with Transpore® tape ~2 cm in length on the lateral thigh. The ground electrode secured to the lateral malleolus of the right ankle with Transpore® tape.

Participants were seated in a HUMAC NORM dynamometer (CSMi Medical Solutions, Stoughton, MA), adjusted to suit each participant's comfort and leg length (*Figure 3*). Hip angle was recorded, and thigh length relative to the axis of rotation was measured to ensure participants could comfortably sit with their torso pressed firmly against the back of the dynamometer for the entire DJPS testing. Hip angle was maintained within a participant across testing sessions and was consistently 105 ± 4^{o} across participants. Participants were provided with a cushioned back support if they could not comfortably sit with their back pressed firmly against the back of the chair. All participants completed the DJPS protocol using their left (non-dominant) leg. The left ankle was anteriorly secured to the dynamometer arm using Velcro straps. Participant set up occurred over 20 minutes, which allowed the individual's skin temperature to acclimate to the ambient air temperature ($20.37 \pm 0.72^{o}C$) of the room (Gatt et al., 2015) (Figure 2).

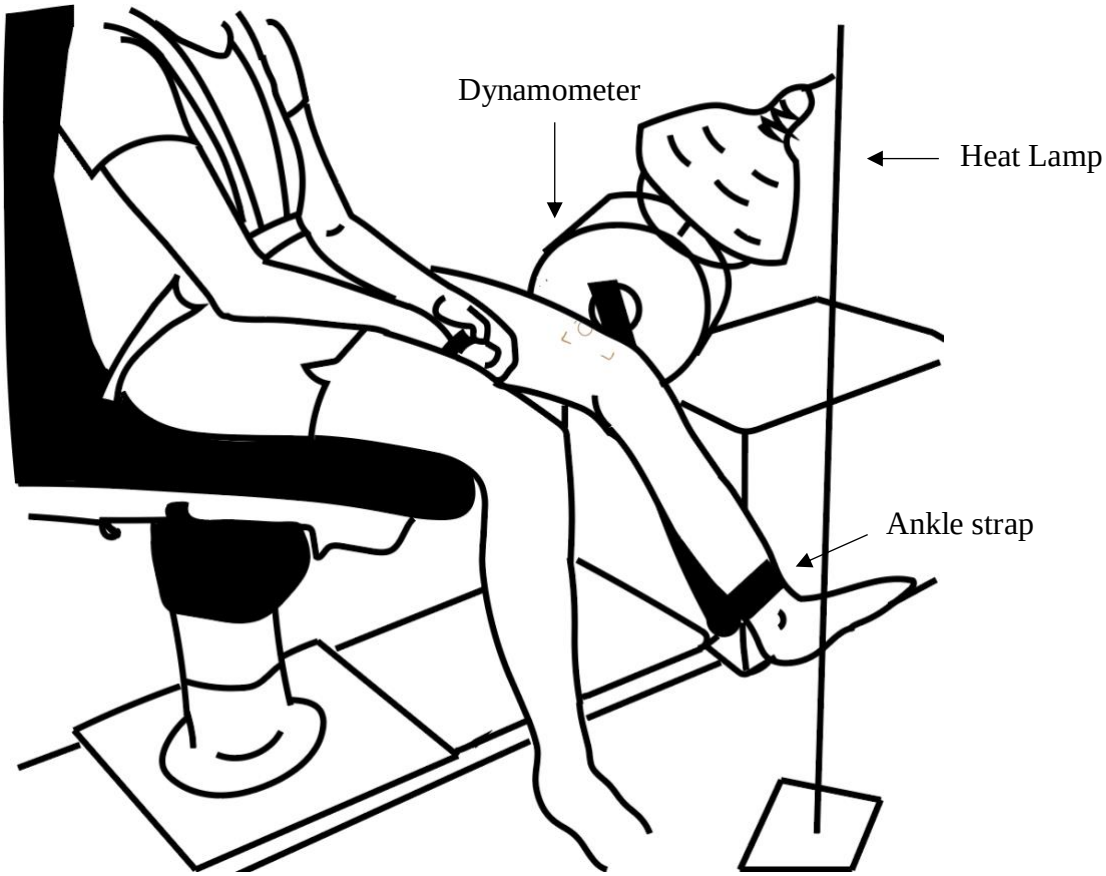

Figure 3: DJPS experimental set up. Electrode placement is not displayed. Ankle strap is covering the ankle, securing the leg to the dynamometer lever. Subject is secured to the seat with a harness. Heat lamp is anterior to the leg.

2.3 Increasing skin temperature

A 250W heating lamp (Zoo Med Laboratories Inc.; Sacramento, USA) was used to slowly increase the temperature of the skin over the knee from un-heated (baseline) skin temperature to 38 ± 0.5℃. Heat was always applied following baseline DJPS testing, to ensure that any changes to proprioception induced by heating would not affect baseline measurements. The temperature of 38ºC was chosen, as it was a warm temperature below nociceptive threshold. Sato et al. (1983) reported that the relationship between skin temperature and muscle spindles is parabolic, with spindle firing being the lowest at 35.1 ± 1.7 ºC, when skin temperature was heated and

cooled within a 20-40ºC range. Participants were told that the heated skin was to feel very warm but not painful, as 38ºC is below nociceptor threshold of 43ºC (Campbell & LaMotte, 1983; Tillman et al., 1995). The heating lamp was always >30 cm anterior to the leg. Prior to and following increasing skin temperature, individuals scored their perception of pain using a 10 cm visual analog scale (0=No pain, 10= intense pain) as shown in *Figure 4*. Once the skin over the knee was recorded to be at a temperature of 38 $\pm$ 0.5℃, the DJPS testing would begin.

Figure 4: The 10cm visual analog scale (VAS). The above VAS is not to scale.

A thermal camera (T10SC30, T430sc; FLIR® Systems Inc.) was placed ~1.5 m away from the participant and recorded changes in skin temperature. The thermal camera was focused on the skin within the circle drawn on the skin over the knee (*Figure 2*). This was to ensure that the desired temperature over the knee was measured by calculating the instantaneous temperature of the skin over the knee throughout each DJPS trial. Furthermore, photographs of the knee were taken at three time points within each DJPS trial; during the onset of extension trial #1, #3, and #5. These photographs were used as a record of skin temperature over the knee during DJPS testing.

2.4 DJPS protocol

Seated in the dynamometer, participants were instructed to remain relaxed with their eyes closed. Participants were instructed to allow their knee joint to be passively rotated by the dynamometer motor. Passive movement was monitored using EMG. Two sets of ten DJPS trials were conducted;

1) baseline knee-skin temperature and 2) heated knee-skin temperature of 38 $\pm$0.5℃. Knee angle orientation was as follows: 0^{o} = full knee extension, 180^{o} = large knee flexion such that the midline of the calf would be returned to the horizontal (*Figure 5*). The left knee began at an angle of 110^{o}. The knee was then extended at a velocity of 1^{o}/second, pausing at 70^{o} for two seconds and then returning to the initial knee angle of 110^{o} where the knee was held for another two seconds. Participants were instructed to indicate with the press of a trigger button, when they perceived their left knee to be passing through the angle of 90^{o}. A 90^{o} angle was chosen, as this angle is a common knee angle during activities of daily living and athletic performance, such as sit-to-stand tasks, weightlifting squats, and cycling. Previous research has also found individuals display greater proprioception about 90^{o} of knee flexion, than during more extreme angles, such as 115^{o} of knee flexion or 40^{o} of knee flexion (Lamers & Reeves et al., 2018). The passive sequence (extension-two second pause-flexion-two second pause) was repeated five times, therefore passing through an angle of 90^{o} ten times during each DJPS test which were: 1) baseline knee-skin temperature and 2) 38^{o}C knee-skin temperature. Participants were given the opportunity to rest between skin temperatures (after 10 trials).

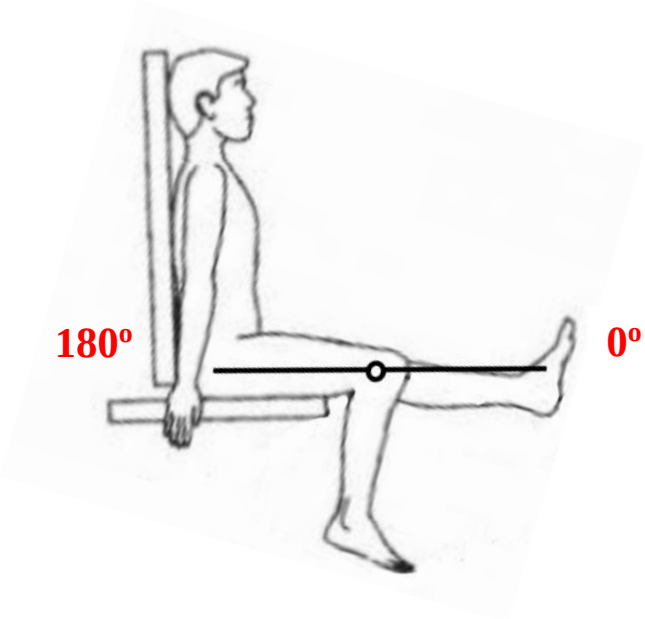

Figure 5: Knee angle orientation during DJPS trials. Extreme full extension = 0º, extreme flexion= 180º.

While the skin was at a baseline temperature, prior to data collection, 12 practice trials (six extension and six flexion) were conducted without providing a 90-degree reference angle. Cordo et al. (1994) conducted an accuracy-and-learning experiment using a similar DJPS protocol about the elbow. This research found that learning only reduced error variability for movements at the fastest velocity (min=17º/second, max=76º/second). It was concluded that proprioceptive triggering is not reliant on highly practiced sequences, but rather this information can be used for coordination during novel movement sequences as well. Twelve practice trials were chosen, to allow for participants to become accustomed to the DJPS protocol. The main DJPS protocol was 10 trials, which lasted ~7 minutes. Pilot testing showed that the first response was never representative of participant DJPS. Therefore, an additional passive sequence was added for practice trials. No feedback regarding DJPS performance was given during any of the trials, as participants were only practicing the timing of clicking the trigger when they perceived their non-dominant leg to reach 90º. Following the practice trials, the researchers manually moved the

left knee to a 90º reference angle. This reference angle was determined using a 12" 360° manual goniometer. Following a short rest, participants then began the main DJPS trials.

The main DJPS trials were defined as: DJPS trials where the participant had previously experienced the passive reference angle of 90º about their left knee, with the goal of clicking the trigger when they believed their left leg was at this reference angle. Again, no feedback regarding DJPS performance was given during any of the trials. The DJPS test procedures began after participants were shown where 90 º was. They consisted of ten trials (five extension + five flexion) while the skin temperature remained at baseline. After another short period of rest, the left leg was heated and DJPS protocol was repeated.

2.5 Modification of cutaneous afferent information

Mechanical changes are detected by the CNS through action potentials, which are recorded as the firing of a receptor. The action potentials are initiated and conducted due to the exchange of ions across receptor membranes. EMLA is a eutectic mixture, which affects sensitivity of cutaneous nerve endings by inhibiting the flux of ions through their respective sodium ion channels (Goede & Betcher, 1994). It is this reduction which blocks cutaneous sensation. Research has shown that there are certain individuals who are immune to the effects of EMLA, however this is often a symptom of a more prominent genetic disorder (Hakim et al., 2005). Reduction of skin sensation was completed by applying EMLA to the skin over the left knee demarcated with metallic Sharpie®. Heat and directional testing occurred on both test days, and the reduction of skin input was randomized between sessions. EMLA was applied in a thick layer to the skin and covered with a plastic occlusion dressing. The maximum dose (1 g/10 cm^2) of EMLA was applied to the skin two hours prior to DJPS testing. To determine the effect of the

EMLA cream, a tactile (touch) sensitivity test using Semmes Weinstein monofilaments was conducted prior to and two hours after application. Participants were seated with their eyes closed for all monofilament tests. One interval forced choice was conducted with a modified yes-no (Diamond et al., 1989) Semmes-Weinstein Monofilament test method over three locations around the knee; along the midline of the knee, denoted as the line between the lateral and medial condyles (*Figure 2*). These locations have been determined to elicit the greatest degree of stretch at 90^{o} of knee flexion (Macdonald et al. 2018). Detection threshold was determined to be the lowest monofilament which could be correctly determined by the participant 75% of the time.

2.6 Data analysis

EMG was monitored in real time with auditory biofeedback to the participant. The goal was to keep muscles relaxed and passive. Recordings which provided visual or auditory evidence of muscle activity resulted in the trial being discarded and repeated. Temperature from the first, third and fifth trials were recorded. Angular displacements about the reference 90^{o} were recorded using Windows LabChart 8. Outliers were removed by calculating three standard deviations away from the mean of each five-trial DJPS data (for each subject). A total of 35 of the 440 main DJPS trials were removed.

2.6.1 Dependent variables

For each participant, median directional error was calculated based on their triggered response (perceived 90^{o}) relative to the reference 90^{o} *(DE= perceived 90^{o} - reference 90^{o}).* An overshoot was defined as positive DE, whereby the participant pressed the trigger after their left leg passed through the reference 90^{o} angle. An undershoot was defined by the researchers as a negative DE, such that the participant pressed the trigger prior to their left leg reaching the reference angle. A

DE of zero indicated that the participant's left knee was at the 90º reference angle when the trigger was pressed. Absolute error (AE) was calculated as the absolute value of DE, thereby describing the magnitude of error, irrespective of the direction of lower limb movement.

Previous literature has shown that participants can be grouped based on JPS accuracy and JPS variability. Callaghan et al. (2002) reported individuals who had poor DJPS about their knee during passive angle reproduction tasks also showed large variability in their JPS responses (error >4º ± 8.9) compared to participants with good JPS (error <4º ± 2). The present research team calculated participant precision (PAE) to determine if participants were actually poor at determining DJPS about a reference target for this specific task, or whether the participants had poor DJPS in general. PAE was calculated as the difference between the maximum and minimum AE values for each condition. This calculated range was then expressed as a percent of the baseline range.

*PAE = (((Max Heat AE)- (Min Heat AE))/ ((Max Baseline AE)- (Min Baseline AE)))*100.*

2.6.2 Participant separation

Recently, the application of EMLA to the forearm has been shown to enhance manual dexterity of the hand and increased short-interval intracortical inhibition (Petoe et al., 2013). This research monitored the effect of the topical anesthesia using Semmes-Weinstein monofilament scores before and after EMLA application. This research found that increasing skin sensitivity thresholds to 4 g from baseline (2.74 g) over the forearm with EMLA induced a change in perception, and subsequently manual dexterity at the hand (Petoe et al., 2013). This research is evidence that increasing skin sensitivity thresholds to ~4 g is effective in altering proprioception. In the current

work, participants with Post-EMLA monofilament thresholds above 4 g were categorized as Responders. Participants with post-EMLA skin sensitivity scores less than 4 g were categorized as Non-Responders.

2.7 Statistical analysis

All statistical analyses were conducted using the program SAS (Version 9.3; SAS Institute Inc., Cary, NC).

2.7.1 Separating data by direction

In order to compare between flexion and extension a three way repeated measures ANOVA was conducted (all participants; n=11) to determine the main effects of EMLA, temperature, and direction on DE (Brown Forsythe $p= 0.09$; Shapiro Wilks $p< 0.01$). The distribution of DE data was determined to be normal. To determine the main effects of EMLA, temperature, and direction on absolute error (AE), a three way repeated measures ANOVA was conducted (Brown Forsythe $p= 0.36$; Shapiro Wilks $p< 0.01$). The distribution of AE data was determined to be normal.

2.7.2 Effect of temperature and EMLA and error

Values for DE are both positive and negative, which indicate an overshoot or undershoot about the target angle respectively. Following the determination that DJPS during knee flexion is significantly different from DJPS during knee extension, AE becomes the only relevant variable, as we are concerned with data to support whether temperature increases or decreases total error about the target error (AE). Flexion and extension are two distinct movements and were analyzed separately. A two-way repeated measures ANOVA (EMLA (2) x temperature (2)) was used to analyze extension AE data (Brown Forsythe $p= 0.16$; Shapiro Wilks $p< 0.01$). Flexion data was not found to be homogeneous in variance (Brown Forsythe $p= 0.02$) or normally distributed

(Shapiro Wilks p= 0.04), and the data was assessed using the Friedman's Two-way Analysis by Ranks (EMLA (2) x temperature (2)). The Friedman's Two-way Analysis by Ranks (EMLA (2) x direction (2)) was used to analyze PAE data (Brown Forsythe p= 0.22; Shapiro Wilks p< 0.01).

2.7.3 Skin sensitivity

Participants were divided into two groups (Responders and Non-Responders), characterized by the change in Semmes-Weinstein monofilament scores across three different sites over the knee before and two hours following EMLA. The data was neither homogenous in variance (Brown Forsythe p= 0.04), or normally distributed (Shapiro Wilks p< 0.05). The Friedman's Analysis by Ranks (Response (2) x Condition (2) x Site (2)) was used to assess the data.

2.7.4 Participants separated using post-EMLA sensitivity thresholds

To determine how EMLA affected participant AE, the two groups were compared into flexion and extension separately. A three-way repeated measures ANOVA (Response (2) x EMLA (2) x temperature (2)) was used to analyze extension AE data (Brown Forsythe p= 0.41; Shapiro Wilks p< 0.01). Flexion data was also assessed using a three-way repeated measures ANOVA (Response (2) x EMLA (2) x temperature (2)) (Brown Forsythe p= 0.75; Shapiro Wilks p= 0.04).

3. RESULTS

3.1 Subject characteristics and exclusions

Fourteen young adults were recruited to participate in this study. Three were excluded due to a conservative timeline of 5 years since knee injury based on previous work (Baker et al 2002) (F=6; 23 $\pm$ 3 yrs). Individuals were 168.16 $\pm$7.82 cm in height, with an average weight of 66.35 $\pm$ 9.82 kg. All participants reported average hours of weekly activity (mean= 7.4 $\pm$ 2.7 hrs) and

average BMI was calculated as 23.19 ± 2.98 kg/m^2. During testing average air temperature was 20.37 ± 0.72 ºC.

3.2 Main Effects: Direction

Participants (n= 11) displayed a directional dependency with DJPS (F value = 344.56; p< 0.001), where participants would undershoot during knee extension (average DE about 90º = -3.631 ± 0.17 º) and overshoot the target angle during knee flexion (average DE = 3.198 ± 1.61º) (*Figure 6*). Across all participants, AE was statistically different between movements of flexion and extension (F value = 24.06; p= 0.006). Participant AE was 1.07º less during movements of flexion (*Figure 7*).

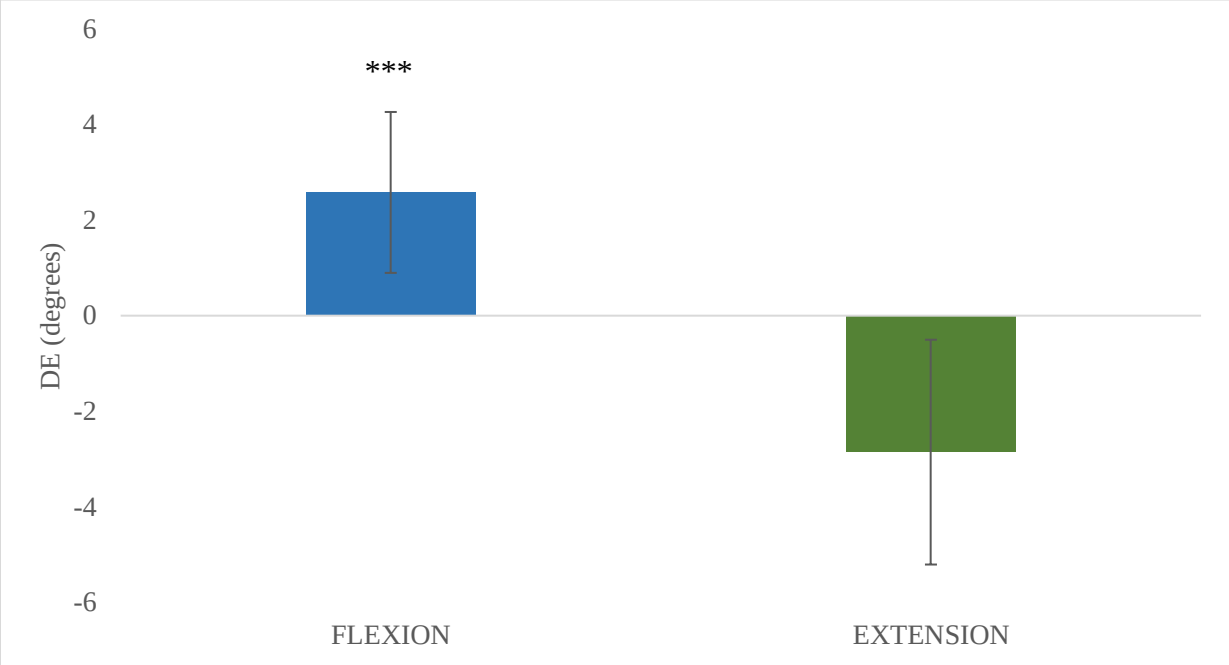

*Figure 6: DE across all participants and temperature conditions during movements of flexion and extension. Positive values indicate an overshoot (knee angle surpassed 90º when the trigger was pressed). Negative values indicate an undershoot (knee angle did not reach 90º when the trigger was pressed). Directional error (DE) was significantly different between the two passive knee movements (***p< 0.001). Participants would overshoot during passive knee flexion DE=2.58º; blue bar), and undershoot during knee extension (DE=-2.85º; green bar).*

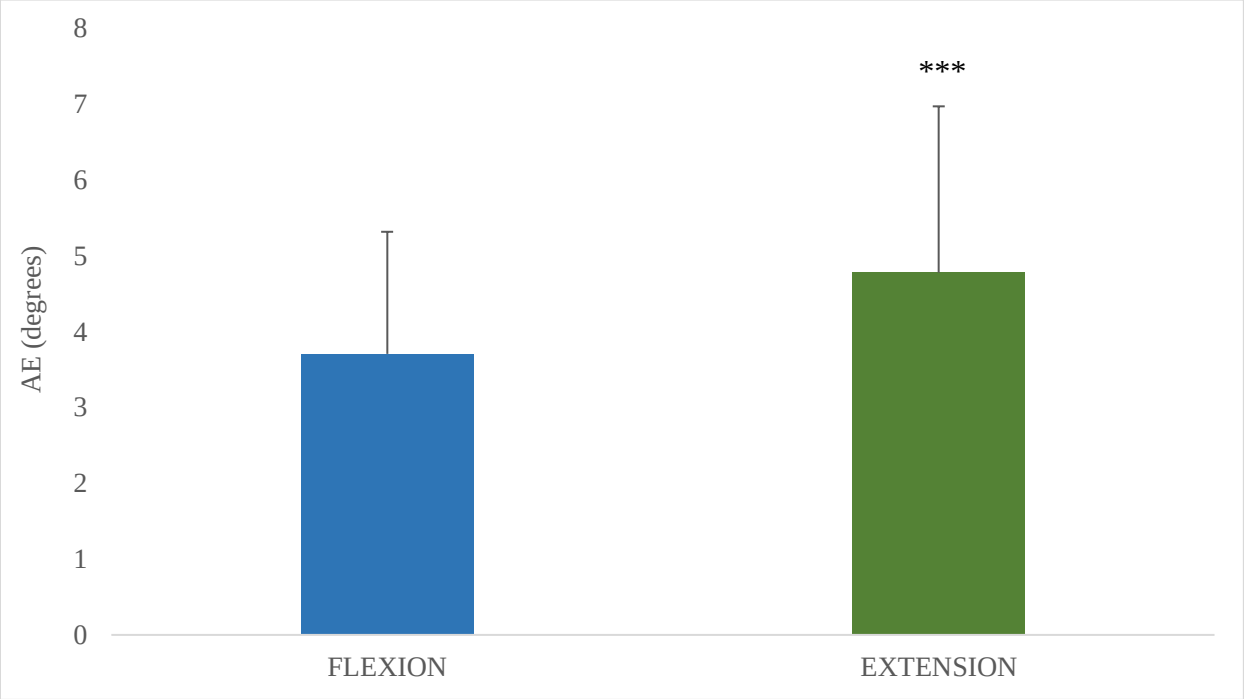

*Figure 7: The absolute value of each trial DJPS value was used to calculate the average AE error during movements of extension and flexion. The above depicts the effect of direction on AE averaged across all participants. Participants displayed a greater absolute error (AE) during movements passive knee extension (AE=4.78º; green bar) than during passive knee flexion (AE= 3.1º; blue bar)***p< 0.001.*

DJPS precision was calculated for each participant during each movement (*Table 4*). Although participants were more accurate (AE) at determining the angle of their knee during movements of knee flexion, participants were 5.17% more precise during passive knee extension.

Table 4: Average precision absolute error (PAE) across all participants during knee extension and knee flexion. PAE was calculated for each heated condition and expressed as a percent of baseline AE. Baseline AE = 100%. PAE< 100% represents an improvement in DJPS precision, PAE> 100% represents less DJPS precision.

Direction	Heat: NoEMLA (%)	Heat: EMLA (%)
Extension	153.57	84.93
Flexion	158.74	99.92

3.3 Main Effects: Temperature

Participants (n=11) began at an average baseline skin temperature of $28.74 \pm 2.43\,^{o}C$. Temperature of the skin over the knee was increased to $38.05 \pm 0.16\,^{o}C$ and remained within this temperature range for the duration of the heated DJPS protocol (*Table 5*). There was a main effect of temperature (F-value= 6.29; p= 0.031), where heat decreased DE. However, there was no main effect of heat and AE (F value= 3.29; p= 0.099). No interaction between temperature and direction was found to exist for values of AE (F-value= 3.83; p= 0.079). However, once AE was assessed in each direction separately, increased temperature was found to significantly reduce AE (F-value= 6.13: p= 0.032) during movements of passive knee extension.

Table 5: Skin temperature about the knee during passive knee extension during trial 1, trial 3, and trial 5.

		NoEMLA		EMLA	
Participant	**Trial**	**Baseline**	**Heat**	**Baseline**	**Heat**
1	1	29.4	37.5	25.4	37.9
	3	28.7	38.4	25.4	38.3
	5	28.7	38.0	25.4	38.5
2	1	26.5	37.5	26.1	37.8
	3	25.9	38.4	27.4	37.5
	5	25.7	38.2	27.6	37.8
3	1	28.8	37.0	29.5	37.8
	3	28.7	38.5	29.1	38.2
	5	28.9	38.1	29.2	38.0
4	1	27.2	38.4	28.7	37.8
	3	28.0	37.9	27.5	38.2
	5	26.1	37.9	27.5	38.3
5	1	26.9	37.9	27.2	37.6
	3	27.5	38.1	27.2	37.7
	5	28.3	38.3	26.4	38.2
6	1	28.2	38.1	25.6	38.3
	3	27.7	38.3	25.5	38.4
	5	27.1	38.3	25.5	38.1
7	1	24.7	37.7	28.2	37.9
	3	25.4	38.1	28.5	38.1
	5	25.5	37.7	27.5	38.3
8	1	29.3	38.0	27.9	37.9
	3	29.0	38.5	27.3	38.8
	5	28.1	38.3	27.8	37.8
9	1	29.4	38.3	29.9	38.3
	3	28.6	37.6	26.4	37.7
	5	29.8	38.0	26.4	37.7
10	1	28.2	37.6	26.4	37.7
	3	27.2	38.3	21.0	37.8
	5	27.7	38.2	27.4	37.9
11	1	26.9	37.6	25.0	38.0
	3	27.5	38.4	26.2	38.2
	5	27.7	38.3	28.2	38.2

AE during flexion movements were not affected by temperature (F value= 0.54; p= 0.465) (*Figure 8*). Baseline AE was 3.45 $\pm$ 1.86 ^{o}, which increased with temperature to 3.97 $\pm$ 1.86 ^{o}. However, during the heated knee extension trials, AE error was significantly closer to the 90^{o} reference angle (F value= 6.13; p=0.032) compared to baseline extension trials; AE baseline = 5.46 $\pm$ 2.39 ^{o} to AE heated=4.10 $\pm$ 1.97 ^{o}.

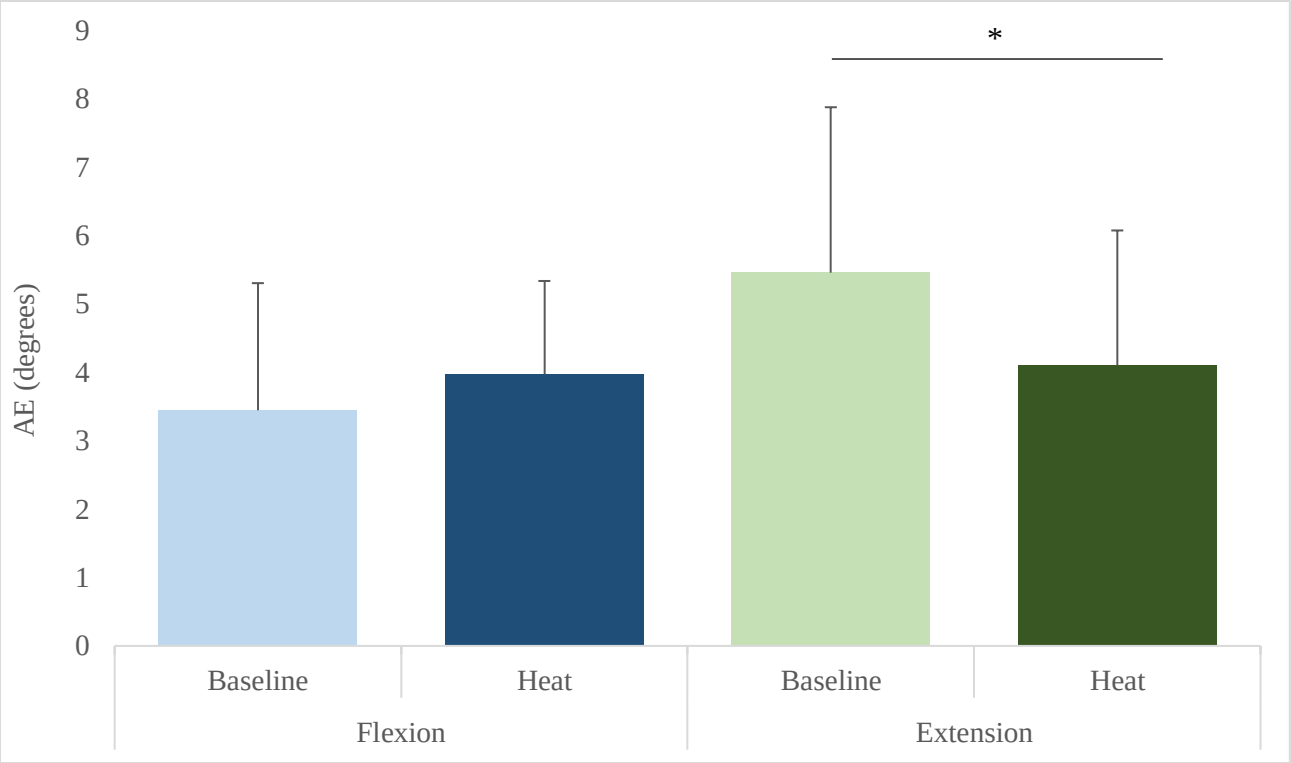

*Figure 8: AE during movements of passive knee flexion (blue) and passive knee extension (green). AE when the skin was at baseline temperatures are represented by light colours (flexion= light blue ;extension= light green). AE when the skin was at baseline temperatures are represented by light colours (flexion= light blue ;extension= light green). AE when the skin was heated to are represented by dark colours (flexion= dark blue ;extension= dark green). DJPS across all subjects, significantly improved with heat (*p=0.032) during movements of extension. No significant change in AE was found with increased skin temperature during passive knee flexion.*

3.4 EMLA and skin sensitivity

Skin sensitivity thresholds of each participant group categorized by site and condition are displayed in *Table 6.* Average participant monofilament scores across the three sites and prior to EMLA cream application was 0.355 ± 0.27 g.

Table 6: Skin sensitivity scores of the three tested sites on the skin above the knee. 1) Proximal site, 2) Middle site, and 3) Distal site. SWM= Semmes-Weinstein monofilament weight (g), Avg= average SWM threshold across sites 1-3. Standard deviations are within the brackets.

Condition	Site	Non-Responder		Responder (g)	
		SWM (g)	Avg (g)	SWM (g)	Avg (g)
PreEMLA	1	0.52 (0.387)	0.506 (0.34)	0.393 (0.378)	0.374 (0.262)
	2	0.365 (0.34)		0.344 (0.187)	
	3	0.633 (0.294)		0.384 (0.22)	
Post-EMLA	1	0.593 (0.427)	1.073 (1.079)	1.52 (1.527)	9.965 (1.937)
	2	1.66 (2.173)		26.48 (30.685)	
	3	0.967 (0.638)		1.894 (2.347)	
Post-Heat	1	0.352 (0.107)	0.541 (0.302)	0.432 (0.182)	0.581 (0.310)
	2	0.592 (0.385)		0.472 (0.313)	
	3	0.68 (0.415)		0.84 (0.434)	

There was a main effect of testing site on skin sensitivity (F-value=10.46; $p < 0.001$). However, skin sensitivity was not significantly different Pre-EMLA between the Responders (n= 5) and Non-Responders (n= 6) at the proximal (p= 1.0), middle (p= 0.916) or distal (p= 1.0) sites. Post-EMLA, the skin sensitivity was also not significantly different between the Responders and Non-Responders at either the distal (p= 1.0) or proximal (p= 0.99) sites. Skin sensitivity over the middle test site was increased in Responders Post-EMLA, with an average sensitivity of 26.48 ± 30.69 g. Over the middle test site post-EMLA, the two groups showed distinctly different skin sensitivity

thresholds, however this was not statistically significant (p= 0.39). The Non-Responders did not show a change in skin sensitivity Post-EMLA, average=1.662 $\pm$ 0.173 g. Post-heat, skin sensitivities of the Responders and Non-Responders were 0.54 $\pm$ 0.3 g and 0.58 $\pm$ 0.31 g, respectively.

3.5 Main Effects: EMLA all participants

EMLA did not significantly affect DE (F-value= 3.1, p= 0.109) or AE (F value= 1.39; p= 0.265). When AE was assessed within each direction separately, EMLA did not affect AE during passive knee flexion (F-value= 2.3; p= 0.633) or passive knee extension (F-value= 1.2; p= 0.733). EMLA was found to improve PAE scores for both passive knee movements (*Table 4)*. PAE during passive knee extension improved by 68.64% and passive knee flexion PAE improved by 58.82%. However, no effect of direction (F-value=0.64; p= 0.428) or EMLA (F-value=2.56; p= 0.117) was found for PAE.

3.5.1 EMLA and precision absolute error: Responders and Non-Responders

DJPS precision was determined for each group. During the NoEMLA DJPS testing, Responders improved their precision with heat by 16.29% compared to baseline temperature conditions (*Table 7*). Conversely, Non-Responders became less precise with heat, with PAE 221.71% of their baseline PAE. During EMLA DJPS testing, Responders displayed greater improvements in precision during the heated conditions compared to the Non-Responders for all conditions except EMLA during knee flexion where PAE increased relative to baseline.

Table 7: Heated PAE for Responders and Non-Responders. PAE was calculated for each heated condition and expressed as a percent of baseline AE. Baseline AE = 100%. PAE< 100% represents an improvement in DJPS precision, PAE> 100% represents less DJPS precision.

Group	Heat: Flexion (%)		Heat: Extension (%)	
	NoEMLA	EMLA	NoEMLA	EMLA
Responders	83.71	105.04	91.62	56.86
Non-Responders	221.27	95.66	205.19	108.33

3.5.2 EMLA and absolute error: Responders and Non-Responders

During movements of knee flexion, the Responder group displayed less AE at baseline (AE= 2.97 $\pm$ 1.8^o) compared to the Non-Responder group (AE= 4.24 $\pm$ 2.0^o) (*Figure 9*). The difference between the two groups' AE scores was reduced with heat, with Responder AE= 3.69 $\pm$ 1.58^o and Non-Responder AE= 3.69 $\pm$ 1.34^o.

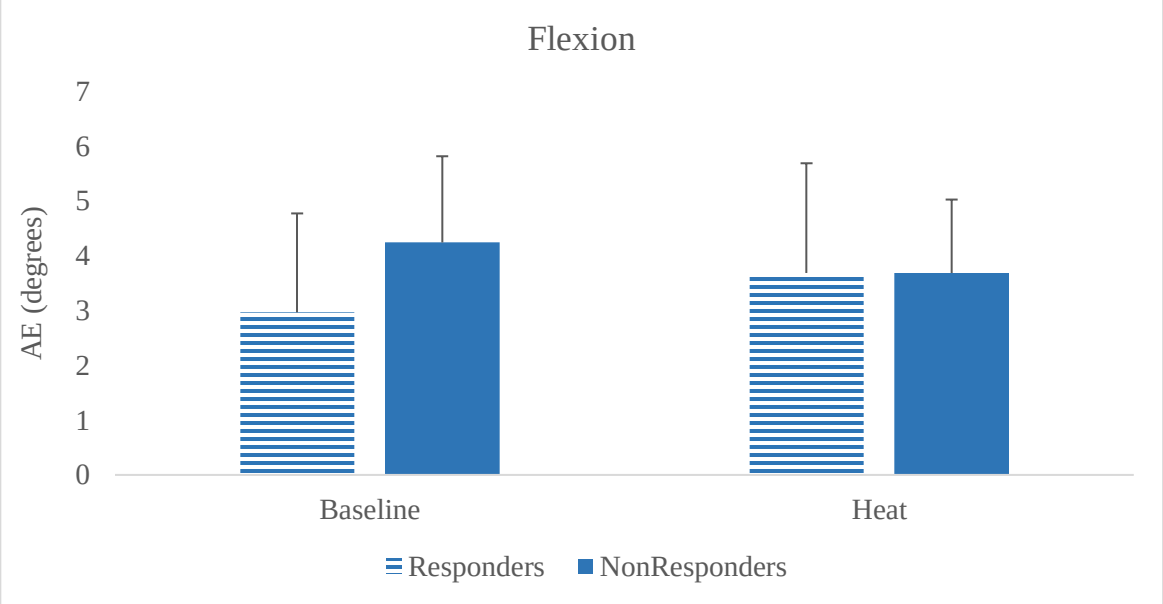

Figure 9: AE during movements of flexion. Data is presented for the Non-Responders (n=6) (striped), and Responders (n=5) (solid). AE= 0^o would indicate perfect DJPS about the knee.

During movements of knee extension, Non-Responders displayed less AE at baseline (AE= 4.53 $\pm$ 2.39^{o}) compared to Responders (AE= 4.97 $\pm$ 2.61^{o}) (*Figure 10*). When the skin over the knee was heated, the difference in AE between response groups was no longer present. Responder AE decreased by 1.76^{o} (AE=3.206 $\pm$ 2.53^{o}), while the Non-Responders improved their AE by only 0.32^{o} (AE= 4.21 $\pm$ 1.54^{o}). There was no significant effect of EMLA on AE between Responders and Non-Responders during movements of extension or movements of flexion and no significant effect of EMLA during either temperature condition.

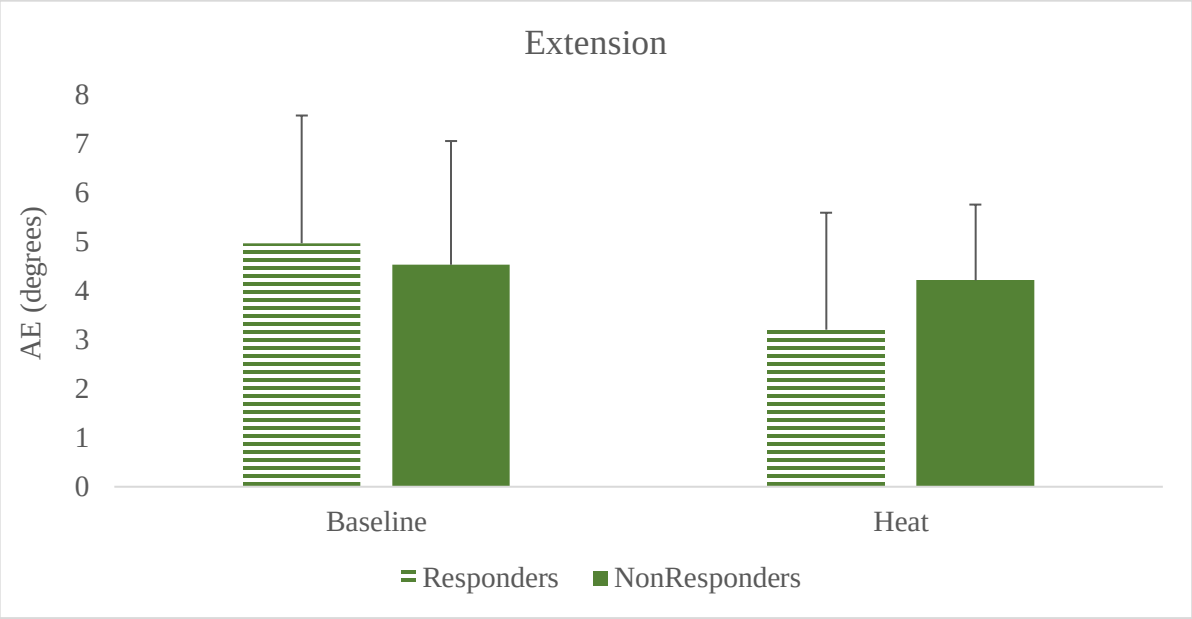

Figure 10: AE during movements of extension. Data is presented for the Non-Responders (n=6) (striped), and Responders (n=5) (solid). AE= 0^{o} would indicate perfect DJPS about the knee.

4. DISCUSSION

The objective of this thesis was to determine the functional implications of increasing skin temperature on DJPS about the knee joint. Based on the animal literature and limited human literature (Burton et al., 1972; Ghaffarinejad et al., 2014; Mense, 1978; Sato, 1983) we hypothesized that 1) increased skin temperature to 38^{o}C would decrease DJPS about the knee, 2) skin does contribute to DJPS about the knee, and when skin information is decreased using topical anesthesia, DJPS will decrease about the knee and 3) DJPS about the knee will be directionally dependent; with greater accuracy during movements into knee flexion over movements into knee extension. Our data support our hypotheses in that individuals were more accurate about a target knee angle through passive knee flexion than knee extension. When the skin temperature was increased, there was no change in DJPS during flexion. However, increased skin temperature did improve DJPS during passive knee extension, refuting our first hypothesis. Finally, EMLA, the topical anesthetic, was successful at reducing skin sensitivity in a sub-group of participants. However, we were not able to support our last hypothesis in that EMLA did not result in any changes to DJPS during flexion or extension at either skin temperature in any participant group.

4.1 Direction and absolute error

The cutaneous receptors sensitive to skin strain have been reported to be most sensitive to increased skin stretch in a single direction, specifically the direction which induces the greatest skin stretch (Edin & Abbs, 1991; Edin, 2001). For example, about the knee joint, cutaneous receptors located on the anterior thigh are most sensitive to knee-flexion (Edin, 2001). Knee flexion about 90^{o} has been shown to induce a large amount of longitudinal skin stretch about the knee (Macdonald et al., 2018), and may be optimal for many stretch-sensitive cutaneous

receptors. During movements of extension, the skin over the knee is not increasing tensile force through stretch, but rather knee extension decreases the amount of strain on the skin over the knee and anterior thigh, and thus retracts the skin. Aimonetti et al. (2007) found that cutaneous afferents located in the skin over the belly of the tibialis anterior were recorded to fire in response to both plantar flexion and dorsiflexion, with the greatest firing rate recorded during plantar flexion. This literature suggests that although cutaneous receptors along the anterior leg may respond to skin strain during movements of knee flexion and extension, these receptors are most sensitive to skin stretch during knee extension. The present research did not record afferent firing with microneurography. However, based on these previous findings it is proposed that the cutaneous receptors over the anterior thigh are most responsive to knee flexion over movements of knee extension.

Muscle spindles are also stretch-sensitive receptors, located between the extrafusal muscle fibres. These receptors are most sensitive to increases in muscle length and velocity of muscle length changes (Matthews, 1963; Roll et al., 2000). During movements of knee flexion, the muscles along the anterior leg, which are responsible for knee extension, are being stretched. The muscle stretch is detected by the knee-extensor muscle spindles as an increase in spindle discharge. Concurrently. the posterior muscles responsible for knee flexion are shortening. During movements of knee extension, the length of the anterior muscles decreases (signaled by a decreasing muscle spindle discharge) while the posterior muscle lengths increase, signalled by an increase in spindle discharge. The present research observed lower AE for movements into flexion. The concurrent increase in firing rate of both muscle spindle and stretch-sensitive SAII receptors are believed to explain lower AE scores during passive knee flexion than during

passive knee extension. Research evaluating JPS about the elbow in both healthy controls and individuals who had undergone total elbow arthroplasty for elbow articular lesions, found that JPS during passive movements into flexion (110^{o}) was more accurate than during extension (70^{o} and 50^{o}) (Lubiatowski et al., 2014). Improved kinesthetic performance about the knee during passive DJPS may be due to contributions of the muscle spindles and cutaneous receptors of the anterior thigh to kinesthesia about the knee. This conclusion is also supported by previous research, which found individuals to have improved JPS during movements of flexion over movements of extension at both the knee and elbow joints (Goble et al., 2009; Lubiatowski et al., 2014).

4.2 Temperature and absolute error

Participants displayed more accurate DJPS during passive knee flexion as compared to movements into knee extension. Interestingly, DJPS was not altered with temperature during knee flexion. When skin temperature over the knee was increased from baseline to 38^{o}C it was shown that absolute error was reduced during movements of extension only, with no significant change to absolute error during movements of knee flexion. This is thought to be due to how muscle spindles in the leg and cutaneous receptors of the anterior thigh contribute to kinesthesia during flexion and extension, and how temperature differentially affects these biomechanisms. These contributing mechanisms will be discussed in detail below.

4.2.1 Primary mechanism for DJPS; cutaneous receptors

The cutaneous receptor which has shown the greatest sensitivity to skin stretch is the SAII receptor. The relationship between the firing rates of SAII receptors and increased temperature of hairy skin has been shown to be non-linear (Burton et al., 1972). Specifically, the stretch-sensitive SAII receptors located in the hind limb hairy skin of cats show a parabolic response in

receptor discharges with increased temperature (Burton et al., 1972). Burton and colleagues (1972) demonstrated that peak firing of SAII receptors occurs between 27-29ºC, with firing reduced above and below these optimal temperatures in feline hairy skin. Chambers et al. (1972) also recorded from SAII units in the skin over the right hind limb in cats. They found the same parabolic increase in SAII discharge with increased temperature from 17-27ºC, with peak firing occurring at 27ºC, and decreasing from 28-40ºC.

In human research, cooling the glabrous skin over the foot sole below 27-29ºC acutely reduced receptor firing rate of all four types of cutaneous receptors (Lowrey, 2012). Following a 20 minute cooling protocol using ice packs (mean baseline temperature= 26.6 $\pm$ 3.7°C; mean cooled temperature=12.9 $\pm$ 4.4°C), SAI receptors were found to maintain their dynamic sensitivity, while static sensitivity was reduced or in some cases abolished. Functionally, with cooling, the SAI receptors behaved as FA receptors by responding to on/off stimuli, with minimal or no response to sustained pressure. This finding was not found to occur in SAII receptors, as both dynamic and static responses to sustained indentation were abolished with cooling. Lowrey (2012) did not report an optimal temperature range for any cutaneous receptors.

Collectively, this research shows that cutaneous receptors in humans are sensitive to temperature changes, subsequently altering their function. More specifically, the recordings from feline cutaneous afferents shows there to be an optimal temperature (27-29ºC), which falls within the same range as participant baseline skin temperature recorded in this research (28.7 $\pm$ 2.4°C). We suggest that based on feline literature, if information from cutaneous receptors were the primary

mechanism responsible for DJPS about the knee, increasing skin temperature about this region would likely reduce cutaneous firing, thereby negatively affecting DJPS.

4.2.2 Primary mechanism for DJPS; muscle spindles

Increasing the discharge rates of muscle spindles through mechanical vibration of the biceps brachii tendon and triceps tendon have been shown to alter proprioception (Goodwin et al., 1972; Roll & Vedel, 1982). As the frequency of vibration increased, firing frequency of the spindles increased, and the participants' perception of the illusionary joint movement velocity also increased. This research illustrates that altering the sensitivity of muscle spindles can in-turn affect proprioception.

Muscle spindles have also been shown to be sensitive to increases in temperature (Mense, 1978; Sato, 1983). Previous literature in the hind limbs of cats has suggested there may be a critical temperature, at which point the directional relationship between temperature and muscle spindle is completely altered (Sato, 1983). Cooling the muscle below $35.1 \pm 1.7^{o}C$ increases spindle firing, and warming past this temperature causes an increase in spindle discharge (Sato, 1983). Although at the time of this report, no other research has since explored this 'critical temperature'. Ghaffarinejad et al. (2014) compared the effects of deep heat using short wave diathermy using the contraplanar methods over the medial and lateral sides of the ankle compared to superficial heating through immersion of the lower leg in a water bath. Although both interventions increased skin temperature to $42^{o}C$ in young healthy males, only the deep heat was effective in penetrating the deeper tissues of the ankle. The increase in temperature about the ankle with short wave diathermy resulted in larger absolute angular error during active dorsiflexion, and decreased absolute angular error of passive plantar flexion. However,

superficial heat had neither positive or negative effects on the ankle JPS. It is proposed that the superficial heat did not sufficiently increase the temperature of the muscle. This would suggest that with increased temperature, muscle spindles are a primary source of proprioceptive information for JPS. Unfortunately, the researchers did not disclose whether their protocol was measuring DJPS or JPS, limiting the application of this work.

The present research did not directly record from muscle spindle or cutaneous afferents. However, previous literature would suggest that during movements of knee flexion, the CNS receives increased afferent signals from both muscle spindles and stretch-sensitive cutaneous receptors. When skin temperature is increased to 38^{o}C, the heat affects spindles and cutaneous input proprioceptive mechanisms differently, such that muscle spindle firing increases while cutaneous receptor firing decreases. When these two proprioceptive inputs are equally weighted within the CNS, the expected outcome of increasing temperature of both muscle spindle and skin would be no change in measures of proprioception. During passive knee flexion, heat did not affect AE about 90^{o}, suggesting that information from cutaneous afferents and muscle spindles are similarly weighted in the CNS during passive knee flexion. However, during passive knee extension, AE was altered with increased temperature.

The sensory weighting hypothesis states that information from each proprioceptive mechanism is weighted and then summated within the CNS (Horak, 2006; Nashner et al., 1982). This weighted summation of afferent signals are responsible for task-specific responses to environmental demands (Haran & Keshner, 2008; Horak, 2006; Nashner et al., 1982). The present research indicates that when the skin over the anterior thigh was heated, DJPS about the knee during

passive knee extension improved. It is proposed that with heat, proprioceptive information from muscle spindles in the anterior thigh may be preferentially weighted in the CNS over information from cutaneous afferents. However, the spindle information from shortening muscles do not singularly contribute to DJPS about the knee.

4.2.3 Antagonist muscles and contributions to proprioception

The perception of joint movement requires central awareness of movement from both shortening and lengthening muscle groups. In active muscles, the imbalance of proprioceptive feedback between the agonist and antagonist muscle groups is what generates the perception of movement direction (Gilhodes et al., 1986). During volitional movements about the elbow, Roll & Vedel (1982) concluded that this imbalance in ago-antagonist feedback favours information from the lengthening muscle. In active joint movement, reciprocal inhibition describes the synchronous process by which antagonist muscles relax to allow for agonist muscles to contract and enable smooth and coordinated actions (Feldman & Orlovsky, 1975; Latash, 2012; Sherrington, 1909). Inhibitory interneurons are under powerful control from the CNS, with a large number of inputs from both spinal and supraspinal inputs (Feldman & Orlovsky, 1975). In the present study all movements were passive, and during knee extension the lengthening muscles were located in the posterior compartment of the leg. In the context of DJPS, spindle sensitivity within the knee flexors increase during passive knee extension. It is possible that this increase in afferent feedback contributed to sensory reweighting.

4.3 Temperature and precision absolute error

Previous research in our lab has reported that vibration applied to the metatarsal of the foot sole did not increase AE during a 7° plantarflexion angle matching task (Mildren, 2015). However, variability about 7º of plantar flexion did significantly increase. The present research calculated

PAE as a measure of DJPS variability, with the purpose of discriminating between individuals who were accurate at determining the 90^{o} reference but with high variability about this angle from participants who were poor at determining the 90^{o} reference but with low variability about some incorrect angle. In our current research, the NoEMLA PAE measures indicate that with heat, the Responders improved DJPS variability while Non-Responders increased DJPS variability. No statistical differences in AE between the two groups with heat were found for either knee flexion or knee extension. However, during passive knee extension with heat, the PAE trends align with the changes in AE; Responders improved while Non-Responders became worse. Although there are no specialized temperature receptors within the skin, there are ion channels which become active at specific temperatures. The TRPV3 and TRV4 ion channels are responsive to innocuous thermal stimuli (34^{o}C-42^{o}C). These temperature sensitive channels have been found at the terminal end of free nerve endings and in the epithelial tissue of blood vessels (Johnson et al., 2014). At the time of this report, no research had been conducted regarding the density of these channels in the skin overlaying joints, or differences in ion channel density across individuals. The researchers postulate that across individuals and regions of the body, the density of free nerve endings and the density of the TRPV3 and TRPV4 channels are not uniform. Variable density in TRPV3 and TRPV4 ion channels over the knee may explain these differences in precision with heat. However, it remains unclear how activation of TRPV3 and TRPV4 ion channels affect DJPS about a local joint.

When assessing the effects of EMLA on PAE, knee extension precision improved for both groups, however this finding was not statistically significant (p=0.338). Power analysis revealed that the power for direction (β=0.053) and EMLA (β= 0.166) were low. Although not

statistically significant, this finding does suggest that during movements of knee extension information from cutaneous afferents from the anterior leg may not be a primary source of proprioceptive information. Reducing information from these afferents may be beneficial for individuals who require a high level of accuracy or precision during knee extension tasks. Previous work looking at movement adaptation to visual feedback during an aiming task recorded a decrease in muscle spindle activity with visuomotor learning (Jones et al., 2001). The researchers propose that in order to resolve conflicting information from vision and muscle spindles, the CNS reduces sensory signals from muscle spindles (Jones et al., 2001).

During passive knee flexion, EMLA did not uniformly alter PAE between Responders and Non-Responders; improving DJPS precision of Non-Responders, while Responders became less precise. EMLA is a eutectic mixture, which not only acts as an anesthetic but also can lubricate and add moisturize to the skin. A dehydrated epidermal layer has been characterized in the literature by a higher Young's modulus, meaning that the skin is stiffer (Choi et al., 2013). During shortening, dehydrated skin displays a higher number of skin folds, and larger amplitudes for each skin fold (Choi et al., 2013). This difference in skin deformation is likely to alter the deformation of the cutaneous receptors within the skin. Although skin moisture was not monitored during this research, moisturizing effect of EMLA could have been different between participants, based on each participants' baseline skin moisture level.

Although skin moisture could have been a contributing factor to changes in precision with EMLA and the different PAE scores between groups, the researchers propose that the dominant cause for the variable responses to EMLA may be explained by the relative weighting

hypothesis. Responders, who did show a high skin sensitivity to EMLA, may simply rely more heavily on cutaneous afferent information for DJPS about knee-joint during tasks which require high accuracy and precision.

4.4 Skin sensitivity and EMLA

4.4.1 Group responses to EMLA

Responder skin sensitivity thresholds Post-EMLA were 20.5x higher than Pre-EMLA skin sensitivity thresholds, indicating that these individuals responded to the lidocaine and that skin input was successfully blunted. However, EMLA was not an effective anesthetic for Non-Responders (n=6), whose skin sensitivity thresholds marginally increased by 0.04 g Post-EMLA.

4.4.2 Penetration depth of EMLA

When applied for 120 minutes, EMLA has been reported to affect sensation at depths of 3-5mm (Bjerring & Arendt-Nielsen, 1990; Goede & Betcher, 1994; Houk et al., 2013). The Semmes-Weinstein Monofilament sensory test targets FAI receptors (Johansson & Vallbo, 1979; Strazlkowski, 2015). In five participants, this depth was able to affect cutaneous receptors. The forced choice method was chosen to eliminate the subjectivity of participant responses. Several arguments could explain Non-Responders lack of response to the anesthetic effects of EMLA: 1) these individuals did not have receptors targeted by the Semmes-Weinstein Monofilament test in the area of skin 2) these receptors were located at a depth >5 mm 3) anatomical differences regarding nerve afferent location and sodium ion channel density or 4) varied concentration of the MCR1 gene within the skin.

To address the first possible source of EMLA resistance, microneurography conducted by Edin (2001) investigated the population of cutaneous receptors about the anterior thigh, lateral thigh, and knee (3 FAI, 2SAI, 2SAII, 10SAIII; 17 Hair follicle afferents). The three FAI receptors were all located within 10mm from the patella. At the time of this report, few studies have investigated cutaneous receptor density about the knee joint. However, the research that has been done indicates that although FAI receptors can exist over the skin of the thigh, these receptors display a low population in skin about the knee joint. However, baseline skin sensitivity scores were not significantly different across the two groups at any site pre-EMLA. Therefore, it is unlikely that the distribution of FAI receptors were unequal between Responders and Non-Responders. Furthermore, it is unlikely that the population of FAI receptors in the skin over the knee are >5 mm deep, as the combined thickness of the epidermal and dermal layers of the skin have been reported between 3-5 mm respectively (Lee & Hwang, 2002). Topical anesthetics reduce sensation by affecting the flux of sodium ions along the targeted nerve. The more superficial the nerve afferent is to the surface of the skin, the greater probability of penetration and the greater the anesthetic effect. The density of the sodium ion channel isoforms also varies between the CNS and the peripheral nervous system (PNS), and more specifically within the PNS (Wang et al., 2017). The depth of the associated afferents in the skin, as well as the distribution and density of the sodium ion channels along the sensory afferents could explain Non-Responder immunity to the anesthetic effects of the EMLA cream. Interestingly, research looking at the increased anesthetic requirements for individuals with red hair discovered a potential link between the MCR1 gene and inhalational anesthetic requirement (Liem et al., 2011). The MCR1 gene is expressed on the surface of melanocytes and functions to regulate intracellular signaling to the melanin biosynthetic pathway, which is responsible for pigment formation (Liem et al., 2011).

The red hair phenotype results from a mutation in the MC1R gene, which results in excess pheomelanin production which produces a yellow-red colour in melanocytes (Liem et al., 2011). Normal MC1R expression results in the predominant dark-brown melanocyte pigment (Liem et al., 2011). Liem et al. (2011) found that individuals with the red hair phenotype, a mutation of the MCR1 gene, had a 19% increased inhalational anesthetic requirement than black-brown hair controls. A potential fourth rationale for the different anesthetic effect of EMLA could be due to variations in MCR1 expression within the skin of participants.

4.4.3 Duration of anesthetic effect

Post-Heat EMLA sensitivity thresholds returned to baseline for the Responders, and remained at baseline for the Non-Responders. The anesthetic effect of EMLA is reported to persist for 60-120minutes after removal (Goede & Betcher, 1994). At the time of this report, no research has been conducted to determine whether heat can prolong or reduce the anesthetic period of EMLA. Both DJPS protocols (baseline and heat) were assessed well-within the effective time-window for EMLA. One research study did assess the effectiveness of EMLA cream in reducing painful sensations experienced with intravenous catheterization over the wrist (Liu et al., 2003). It was determined that heat can reduce the time-to-effect of the topical anesthetic. However, this research did not record changes in time-of-effectiveness. Although heat may affect how EMLA interacts with cutaneous afferents, the specific effects of heat on EMLA® remain undetermined.

4.5 Main effects: EMLA and absolute error

The EMLA cream did not have any significant effect on DJPS in either the Responder or Non-Responder groups. As outlined above, the depth of EMLA penetration has been recorded between 3-5 mm when applied to the skin for 120 minutes (Bjerring & Arendt-Nielsen, 1990;

Goede & Betcher, 1994; Houk et al., 2013). The receptor most sensitive to skin stretch is the SAII receptor, which is located deep within the dermis of the skin (Chambers et al., 1972). Research conducted on male and female cadavers recorded skin thickness over the anterior thigh in 17 adults (F=7) (Lee & Hwang, 2002). The average epidermal layer was found to be 1.4mm and 0.89 mm for males and females respectively (Lee & Hwang, 2002). The dermal thickness was recorded to be 1.01 mm and 0.99 mm for males and females respectively (Lee & Hwang, 2002). No significant differences in skin thicknesses were found to exist between males and females. This data suggests that based on depth of penetration, EMLA could have altered cutaneous mechanoreceptors and therefore DJPS, however no effect occurred. Cutaneous receptors sensitive to skin stretch induced by passive knee flexion and extension have been found across the anterior and lateral thigh (Edin, 2001). However, the present research only attempted to affect the region of skin which elicited the greatest stretch with knee flexion. Cutaneous receptors outside of this region, although not in skin shown to stretch the most, are still sensitive to skin stretch about the knee. These receptors were not targeted with EMLA, and were likely able to respond to changes in cutaneous stretch. Therefore, although EMLA was not effective for determining if cutaneous receptors play a primary role in DJPS about the knee, these receptors peripheral to the location of application likely contribute to DJPS about the knee and may be the explanation for our lack of differences between the EMLA and NoEMLA trials.

4.6 Limitations

4.6.1 Temperature measures

The purpose of this research was to determine the functional implications of increasing skin temperature on DJPS about the knee joint. This was achieved by heating the skin over the anterior thigh to 38^{o}C, targeting the area of greatest skin stretch. A limitation to this study was

that muscle temperatures were not directly measured. However, the method of measuring surface temperature to approximate muscle temperature has been shown to work relatively well. Previous work has shown that increasing skin temperature to 37-38ºC, corresponded to muscle temperatures of 36-37ºC, with an average discrepancy of 1.7ºC (Rutkove, 2001). It was also concluded that the improved accuracy achieved by measuring temperature from the structures beneath the skin would not be beneficial. In-dwelling thermodes make direct contact with the muscle structures and could potentially alter proprioception about the knee. Furthermore, thermodes placed over the skin would require taping placed over the skin of the thigh. As described in section 1.4.5, physiotherapy tape can alter proprioception about the knee and therefore any additional taping might alter proprioceptive feedback. The FLIR® 430sc and FLIR® 1030sc thermals cameras are reported to have measurement error of 2% for temperatures beyond 25ºC (FLIR, 2015b, 2015a). Therefore, the FLIR® thermal cameras were considered the best option to record temperature throughout the DJPS protocol.

4.6.2 Proprioceptive feedback from the posterior aspect of the leg

Participants were seated in a HUMAC NORM dynamometer (CSMi Medical Solutions, Stoughton, MA), with the popliteal fossa and proximal aspect of the gastrocnemius gently touching the chair when placed at a 90º angle. However, there were unavoidable limitations associated with participant set up. The pressure of the posterior aspect of the knee and lower leg was altered throughout the movement. As the leg moved through flexion and extension, the pressure of the leg on the dynamometer was altered. Participants could use these changes in proprioceptive feedback to improve their DJPS. During pilot work, foam was placed behind the knee to minimize pressure on the posterior leg. Unfortunately, the foam proved more of a burden on the protocol than an improvement, as the foam required constant readjustment and

participants still were able to feel the pressure of the chair. It was concluded that although participants could use the pressure on their posterior leg as proprioceptive feedback regarding joint angle, this pressure was consistent across all trials. Therefore, any changes to proprioception induced by posterior pressure on the leg would be consistent throughout all of the conditions. Furthermore, no feedback regarding performance was given to participants regarding their DJPS performance. Although participants may have used this information, there was no way for participants to conclude whether this feedback was helping for hindering their DJPS performance.

4.6.3 Localized increased temperature to the anterior compartment

The posterior aspect of the non-dominant leg was also not monitored for changes in temperature, as this study was only concerned with altering proprioceptive feedback from the anterior leg. During activities of daily living and athletic performance, temperature of the leg would increase for all compartments of the both legs. This research served to prove the concept that increasing temperature does affect DJPS, however, it remains unclear how increasing the temperature of both aspects of leg would affect DJPS about the knee.

4.7 Functional significance

The purpose of the present research was to determine the effect of increasing skin temperature on DJPS. During exercise, core temperature increases and it is critical that the skin be used to dissipate this heat. However, the external climate can drastically alter the degree to which heat dissipation occurs. Technical apparel companies have developed intelligent fabrics to enhance performance, regardless of the external environment. SUGOI® developed IceFil fabrics, strategically placed to reduce core temperature, and improve performance. Mizuno® Corporations developed their Breath Thermo technology, which captures the vapour molecules

dissipated from the skin, and utilizes this energy to generate heat. However, these fabrics are strategically placed for core temperature regulation. The present research is concerned with using temperature to optimize proprioceptive performance. When skin temperature over the knee was increased to 38°C, DJPS about the knee was altered, most notably during movements of knee extension. Furthermore, topical anesthetic placed only on the skin shown to elicit the greatest stretch did not affect absolute error. This research suggests that perhaps heat may not only be utilized to regulate core temperature, but may be a method to improve kinesthesia. Heat as a mechanism for improving proprioception may be of great value to individuals who require accurate DJPS about the knee during knee extension. The human body is not simply an input-output system, but rather a complex system which integrates incoming inputs and propagates outgoing motor commands. Improving DJPS through movements of knee extension may also be effective for indirectly enhancing reciprocal activation during knee flexion. Improvement of DJPS would benefit both sports enthusiasts and individuals undergoing knee-injury rehabilitation Furthermore, we cannot rule out that regions of skin located more distant to the knee may be involved in DJPS about the knee since we only reported the ineffectiveness of EMLA placed on skin localized directly adjacent to the knee joint. Altering sensory information from regions distal to the knee may be used to enhance proprioception at the knee.

5. CONCLUSION

Based on the animal literature and limited human literature (Burton et al., 1972; Ghaffarinejad et al., 2014; Mense, 1978; Sato, 1983), the researchers hypothesized that increased skin temperature to 38^{o}C would decrease DJPS about the knee. This thesis suggests that increasing the skin temperature of the knee does improve DJPS sense during knee extension, with no significant difference to DJPS during knee flexion. Although EMLA was effective at reducing cutaneous information in some individuals, the topical anesthetic did not alter DJPS about the knee. This finding would suggest that information from cutaneous receptors may be redundant to information from muscle spindles. However, due to the small area of the skin affected by the EMLA we cannot rule out that regions of skin over the anterior thigh located more distal to the knee may provide relevant information regarding knee joint position. DJPS does prove to be more accurate during passive knee flexion, over passive knee extension. Regardless of temperature, participants displayed greater accuracy during movements of knee flexion, over knee extension.

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APPENDIX A: GROUPS CATEGORIZED BY AE ACCURACY

Introduction

Accurate DJPS is reliant on the ability to integrate multiple sources of feedback within the central nervous system (CNS), including information from muscle spindles and cutaneous receptors. Previous work has shown that kinesthetic tape over the knee can improve JPS accuracy over functional ranges of motion for individuals with hereditary sensory and autonomic neuropathy type III (HSAN III) (Macefield et al., 2016). Additional work using patellar sports tape and textured panels have also been shown to alter JPS about the knee for individuals who displayed baseline JPS matching error >4-5^{o}, with no change for individuals with baseline JPS <4-5^{o} (Callaghan et al., 2002; Callaghan et al., 2008; Lamers & Reeves et al., 2018).

Purpose

Analysis of the two EMLA response groups showed that these two groups had significantly different baseline AE scores. Previous work (Lamers & Reeves et al., 2018) has found that proprioception is not uniformly altered across all individuals. When texture was placed over the knee, individuals with poor JPS at baseline (baseline JPS error >4^{o}) saw larger changes in proprioception when texture was placed over the skin of the knee. These findings are compared to participants in the study who were determined to have good JPS (baseline JPS error <4^{o}) and did not show the large change in JPS with texture. The purpose of the current work was to explore if this difference in DJPS at baseline could have affected individual responses to increase skin temperature at the knee.

Method of Analysis

Participants were divided based on their AE responses (Accurate AE < 4^{o}; Inaccurate AE > 4^{o}) during NoEMLA sessions at baseline skin temperature during knee extension (Brown Forsythe p= 0.62 Shapiro Wilks p= 0.01) and knee flexion (Brown Forsythe p 0.16; Shapiro Wilks p= 0.04). Both flexion and extension data were assessed using Friedman's Analysis by Ranks (Accuracy (2) x EMLA (2) x Temperature (2)).

Results

Skin sensitivity scores

Semmes-Weinstein monofilament scores for the Accurate group Pre-EMLA were 0.45 $\pm$ 0.69 g , which was only marginally higher than the Inaccurate group skin sensitivity threshold of 0.45 $\pm$ 0.34 g. Post-EMLA, the Inaccurate group displayed a large increase in skin sensitivity threshold (mean=8.47 $\pm$ 5.54 g), while the Accurate group skin sensitivity increased to 1.08 $\pm$ 3.4 g. Post-Heat skin sensitivity scores returned to baseline, with Accurate mean threshold= 0.53 $\pm$ 0.97 g, and Inaccurate mean threshold= 0.58 $\pm$ 0.42 g.

Accuracy and Temperature

The effect of temperature was not found to be statistically different between Inaccurate and Accurate groups during flexion (F value= 0.28; p= 0.598) (*Figure 11)*. However, temperature did significantly improve AE during extension for both groups (F value= 5.09; p=0.02) (*Figure 12)* with no significant interaction between group and temperature (F value= 0.10; p=0.75). During passive knee extension, both Accurate (n=5) and Inaccurate (n= 6) groups improved AE by 0.83^{o} and 1.58^{o} respectively. However, during movements of flexion, the Inaccurate group (n= 5) only

marginally improved AE from 4.79º to 4.61º. The Accurate group (n= 6) became worse with heat, increasing their AE from 2.33º to 3.44º.

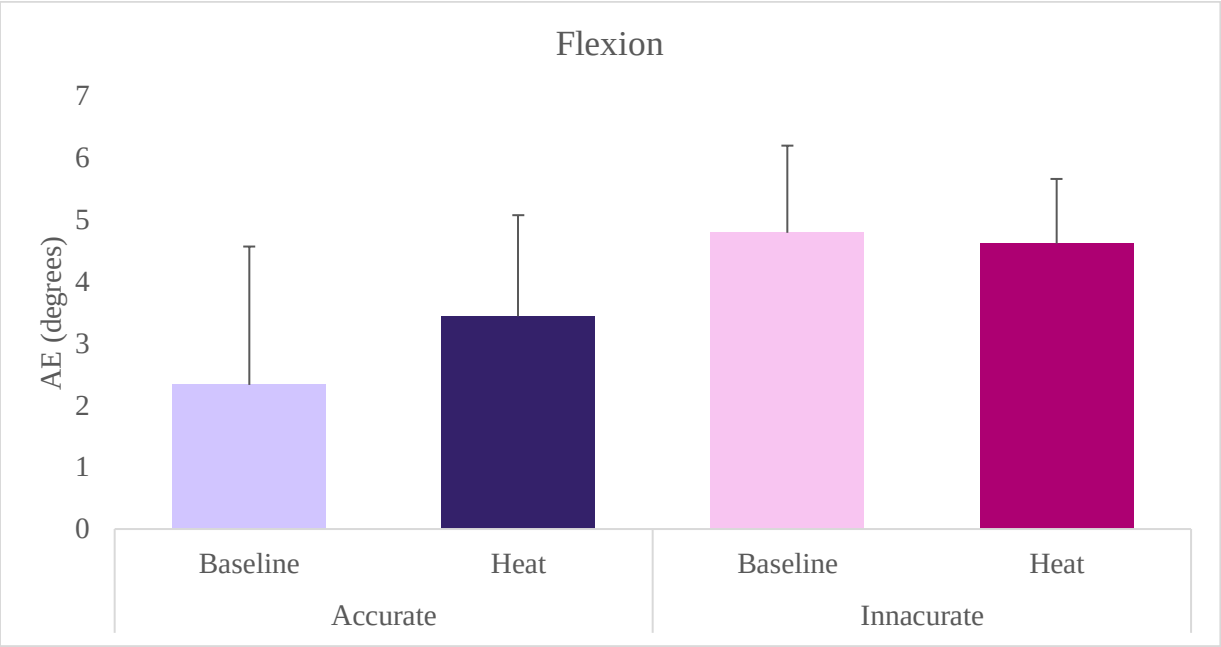

Figure 11: Absolute error (AE) during passive knee flexion, where Accurate AE (purple) during both baseline (light purple) and heated (dark purple) conditions were lower than Inaccurate AE (pink) during baseline (light pink) and heated (dark pink) conditions. Accurate individuals increased their AE with heat, while Inaccurate individuals marginally decreased their AE with heat. No changes in AE with temperature were found to be statistically significant.

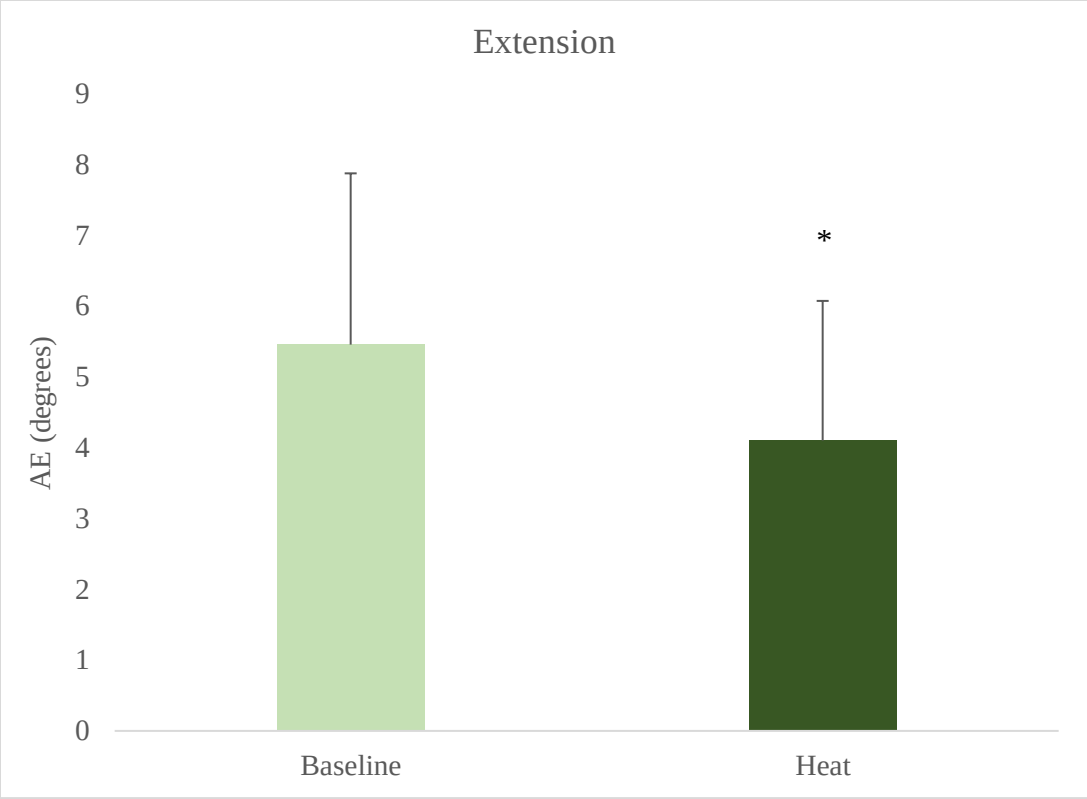

*Figure 12: AE during movements of passive knee extension for all participants. AE when the skin was at baseline temperature is represented by light green. AE when the skin was heated are represented by dark green. DJPS across all subjects, significantly improved with heat (*p=0.020) during movements of extension.*

Accuracy and EMLA

The interaction between participant accuracy and EMLA was significant during passive knee extension (F-value= 14.96; p< 0.001) (*Figure 13*). This interaction was driven by the large discrepancy between the two groups NoEMLA AE scores (p< 0.001) (Accurate AE= 2.94º; Inaccurate AE= 6.24º). Following the application of EMLA, the AE scores between the two groups were no longer significantly different (p= 0.975) (Accurate AE= 4.94º; Inaccurate AE= 4.72º). No significant interaction was found to exist between accuracy and EMLA during passive knee flexion (F-value= 3.01; p= 0.08).

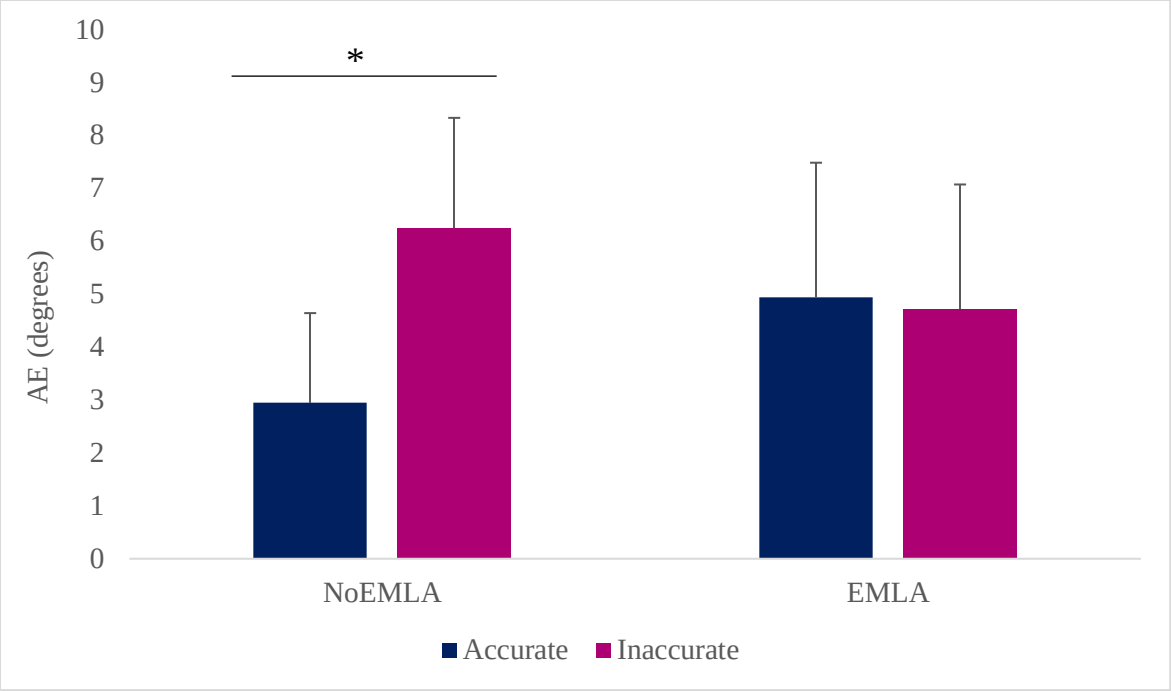

*Figure 13: The interaction between participant accuracy and EMLA during passive knee extension. EMLA reduced the difference between Accurate and Inaccurate AE scores Accurate participants are represented by the navy bars. Inaccurate participants are represented by the pink bars. Accurate and Inaccurate participants showed significantly different AE scores (*p< 0.001) during NoEMLA DJPS testing. The difference between the two groups' AE scores was not found during the EMLA conditions.*

Discussion

During movements of extension, increased skin temperature significantly decreased AE regardless of participant DJPS accuracy. Although there was no significant interaction between accuracy and temperature, there was a significant interaction between EMLA and accuracy during passive knee extension. This finding was largely driven by the difference between the groups AE during the NoEMLA protocol (Accurate AE= 2.94º; Inaccurate AE= 6.24º), because this is how the researchers defined the groups. Application of EMLA reduced Inaccurate AE (AE= 4.72º) and increased Accurate AE (AE= 4.93º). The Inaccurate group was predominantly comprised of Responders to EMLA (post-EMLA skin sensitivity > 4 g), while the Accurate group was predominantly Non-Responders to EMLA (post-EMLA skin sensitivity < 4 g). The

EMLA affected these two groups differently, such that Inaccurate individuals became better at the DJPS task, and Accurate individuals became worse. This finding suggests that not all individuals utilize information from skin receptors equally. Work by Macefield et al. (2016) found that individuals who lacked muscle spindle primary afferents, displayed large errors in passive joint matching (mean= 8.0 $\pm$ 0.8°). When kinesio tape was applied to the skin over the knee, this matching error was improved (mean= 5.4 $\pm$ 0.7°) (Macefield et al., 2016). However the healthy control group, which began with lower baseline matching error (mean= 3.0 $\pm$ 0.3°), did not show the same improvement in matching error with taping (mean= 3.0 $\pm$ 0.2°) (Macefield et al., 2016). Additionally, work by Lamers and Reeves (2018) used a textured sensory panel over one knee and a non-textured control panel on the contralateral knee. Individuals who displayed baseline JPS matching error > 4^{o} about 90^{o} became worse at the JPS matching task with enhanced cutaneous feedback, while no change to JPS matching occurred for individuals with baseline JPS < 4^{o}. Collectively this work suggests that there may be a threshold of JPS error, which altering cutaneous feedback may not be beneficial for enhancing DJPS. In the present research, reducing information from cutaneous afferents with EMLA affected AE differently between the two groups, such that individuals determined to be Accurate at baseline skin temperature became worse and individuals determined to be Inaccurate became better. Inaccurate individuals may not utilize information from cutaneous afferents effectively. However, the researchers propose that Accurate individuals, which were also Non-Responders (Non-Responders n= 4; Responders n= 1) were effectively utilizing information from cutaneous afferents. However, as described in Discussion section 4.3, EMLA can also affect skin hydration, which may alter deformation of cutaneous afferents. It is possible this deformation negatively affected DJPS in Accurate participants, because these individuals already had a high level of

DJPS accuracy. Alternatively, relative weighting may also explain the different effect of EMLA between Accurate and Inaccurate individuals. Although skin may provide information regarding proprioception, if EMLA decreased the reliability of cutaneous information by altering skin hydration it is possible that Inaccurate participants heavily weight cutaneous information and therefore show a greater change in AE. Conversely, AE for Accurate individuals, who may not place as large a relative weighting on skin afferent information, was less affected by EMLA.

Conclusion

The effect of increasing skin temperature on DJPS during knee extension was consistent, regardless of baseline accuracy. However, EMLA positively affected participants with inaccurate baseline DJPS by reducing their AE about a target 90^{o} reference angle, a change not seen in Accurate participants. Individuals regarded as Accurate increased AE about the target 90^{o} angle when EMLA was applied to the skin over their knee. This data suggests that information from cutaneous afferents are not utilized equally across all individuals, and there may be a sub-population of individuals who can benefit from augmenting cutaneous information.