Pain Perception and Physiological Responses to Thermal and Mechanical Experimental Pain: Foundation for Pain Studies in Dancers and Non-Dancers

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Statement of Authentication

I, **Sophie Madeleine Cornett,** declare that this thesis is original and based entirely on my own independent work except if acknowledged and referenced in the text. I declare that I have not submitted this material to gain qualification for this Master of Research, or any other degree at Western Sydney University, and it has not been submitted to any other academic institution.

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Abstract

Pain perception is a complex phenomenon comprised of the transmission of nociceptive signals and central neural processing to initiate responses to noxious stimuli. Great strides have been made in our understanding of the neurophysiological processes behind nociception, the role of psychosocial factors in modulating pain perception and how individuals respond physiologically to painful stimuli. However, there are still gaps in the literature regarding how individuals may respond to different types of experimental pain stimuli. This is particularly critical when looking at pain responses in populations who may experience a particular type of pain regularly. One such group is dancers. Due to the intensive physical and mental requirements of training and performance, dancers display high rates of mechanical pain associated with musculoskeletal injury and maladaptive injury management practices. It is hypothesised that when comparing two types of experimental pain - a cold pressor test (thermal) and hypertonic saline (HS) infusion into the tibialis anterior muscle (chemical) – the cold pressor test drives greater physiological responses that are associated with greater perceived pain. 12 cis female participants completed the two pain protocols while heart rate, blood pressure, respiratory rate and muscle sympathetic nerve activity (MSNA) were recorded continuously. The group included three dancers to pilot the pain models in this population and provide descriptive response patterns to inform future hypotheses. Based on the available literature, it is currently hypothesised that dancers report lower perceived pain than non-dancers, which is associated with greater increases in physiological responses. Participants in this study rated pain intensity during both pain protocols using a visual analogue scale (VAS; 0 – 10) and sensory affective pain characteristics using the short form McGill pain questionnaire. A significant effect of time was observed in the increased heart rate responses from baseline (73 ± 4 beats/min) during the first minute of the cold pressor test (85 ± 4 beats/min, $p = 0.006$). Blood pressure increased from the second minute of the cold pressor test and remained elevated throughout in contrast to the HS infusion. The significant interaction between time and pain model indicates greater responses to the cold pressor test in line with the hypothesis. Compared with the HS infusion, the cold pressor test was also associated with greater peak pain intensity (VAS 7 ± 0.5 vs. 6 ± 0.4, $p = 0.02$) and shorter time to pain onset (15 ± 3s vs 40 ± 10s, $p = 0.02$). There were no significant correlations between pain intensity and

physiological response to pain observed for either pain model, which does not align with the hypothesised response. Blood pressure response patterns during the cold pressor were comparable between dancer and non-dancer groups, whereas responses to hypertonic saline suggest reduced blood pressure changes in non-dancers and an opportunity to pursue potential differences in the dancer population with future research. Dancers peak pain was 6 ± 1 during the cold pressor, versus 8 ± 1 for the non-dancers. Peak pain during the hypertonic saline infusion was 5 ± 2 for dancers, and 6 ± 1 for non-dancers. The hypothesis of lower perceived pain in dancers will therefore be explored comprehensively in a future study. Although the cold pressor test is associated with greater peak pain and larger increases in heart rate and blood pressure, the responses are largely uniform amongst participants. Conversely, the hypertonic saline model provides an opportunity to investigate inter-individual and/or group differences in physiological responses and perceived pain, whilst more closely mimicking the type of pain experienced by dancers. Future studies involving the hypertonic pain model will be more reflective of the conditions under which dancers experience pain and can be used as the basis for understanding and managing pain in a dance context.

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Introduction

Pain has been a source of rigorous scientific investigation since the early 5th century BC (Chen, 2011). Despite the lengthy research history, the uniqueness of pain to the individual and the complex anatomical and physiological processes involved in pain perception mean that there are still gaps in our understanding of how different types of pain are experienced. When measuring physiological responses to experimental pain, there is significant disparity in how cardiovascular and respiratory function change in response to different types of noxious stimuli. A range of psychosocial factors such as emotion and memory play a role in how an individual experiences noxious stimuli. A combination of factors can also contribute to how pain perception and responses may differ between subsets of the population.

Dance has been critical to human culture for thousands of years as a form of communication and storytelling, a social exercise, an art form, and a sport. Significant focus on the development of athletic skill and strength through intense training means dancers are often described as a subset of the elite athlete population, with unique emphasis placed on meeting aesthetic requirements in performance settings. The intensity of training and performance in dance leads to a high rate of musculoskeletal injury, with 97% of Australian dancers reporting at least one serious injury throughout their career (Vassallo, 2017). Dancers also tend to continue dancing while injured and experiencing pain, resulting in complications or compensatory injuries (Vassallo, 2017). Despite these trends, limited research has investigated whether pain perception and responses to pain differ in dancers, potentially explaining maladaptive injury management behaviours. Prior studies on responses to experimental pain have had one common flaw, that the pain experience produced was not an accurate reflection of the type of pain typically experienced in a dance environment.

It is hypothesised that both cold pressor test and hypertonic saline (HS) infusion pain models are associated with significant increases in physiological responses, including heart rate, blood pressure and muscle sympathetic nerve activity (MSNA), but the cold pressor test is associated with greater perceived pain and physiological responses compared with HS

infusion. The primary aim for this project was to measure pain perception and physiological responses to two distinct types of experimental pain: a cold pressor test and a 5% HS infusion into the tibialis anterior muscle. This provides important insight into the accuracy of prior pain models in studying pain responses in an athletic population in which mechanical pain is experienced on a regular basis. It is hypothesised that dancers demonstrate greater physiological responses and lower perceived pain during the cold pressor test and HS infusion compared to non-dancers. Therefore, the secondary aim of this study was to pilot these protocols with groups of dancers and non-dancers to gain preliminary insights into the differences in pain perception and physiological responses as the basis for future studies.

Investigating whether there are significant differences between thermal and mechanical pain responses provides an important baseline for future studies in dancers and non-dancers. If differences are observed, this highlights the importance of employing clinically relevant methods of measuring pain perception and responses in this population to provide the most accurate insights into the difference between dancers and non-dancers. Measuring pain perception in dancers and non-dancers will offer important clinical insights into how pain may be experienced and should be managed in this athletic population. In addition, measuring physiological changes as a proxy for neural mechanisms of pain perception and modification will indicate whether there are differences in how dancers process pain compared to non-dancers. This understanding has implications for the development of dancer injury awareness and education in maintaining dancer health in the industry. As dancers are a subset of the elite athlete population, these results may also be applicable to athletes of other sports.

Literature Review

Anatomy and Physiology of Pain Perception:

Pain is a complex, multi-faceted phenomenon comprised of the anatomical mechanisms of nociception, the physiological responses to nociceptive signals and the psychosocial aspects of pain perception. The complexity of pain has prompted rigorous scientific enquiry into the phenomenon dating back as early as the 5th century BC (Chen, 2011). Pain is defined as "an unpleasant sensory and emotional experience, associated with or resembling that associated with, actual or potential tissue damage" (IASP, 2020). The definition incorporates the range of physical and psychological factors influencing an individual's unique pain perception and responses. In a clinical setting, pain was defined by Margo McCaffery, a pioneer in pain management nursing. She defined pain as "whatever the experiencing person says it is, existing whenever and wherever the person says it does" (McCaffery & University of California Los Angeles, 1968). This definition, while it does not integrate the physiological components of nociception, does emphasise the highly individual experience of pain. In turn, this understanding continues to highlight the importance of acknowledging and responding to the personal perception of pain.

Researching pain experience also includes developing an understanding of how different populations, such as dancers or elite athletes, may respond differently to painful stimuli. Minimal research has been conducted in the field of dancer pain experience. In a survey of Australian dancers, 97% of dancers identified experiencing at least one serious injury throughout their career (Vassallo, 2017), and yet little data exists on how dancers may experience or respond differently to pain. To interpret and critique prior studies in this field, an understanding of pain mechanisms is critical. The review below discusses the processes of peripheral nociception, pain processing in the central nervous system (CNS) and pain modulation pathways. In addition, the role of the autonomic nervous system (ANS) in physiological responses to pain and how experimental pain is induced and measured in a laboratory setting is discussed.

Peripheral Nociception

Noxious stimuli are extremes of temperature, mechanical stimulation or chemicals that cause or have the potential to cause tissue damage (Dubin & Patapoutian, 2010). These noxious stimuli are detected by specialised peripheral sensory neurons called nociceptors (Dubin & Patapoutian, 2010). Nociceptors can respond to a broad range of stimuli intensity both within and outside of the noxious range, however the receptor response rate tends to increase in the noxious range or when non-noxious stimulus is applied for long enough to become noxious. Nociceptors also demonstrate a high stimuli threshold compared to other sensory receptors (Dubin & Patapoutian, 2010).

Nociceptors are distributed through cutaneous structures, viscera, muscles and joints. The nociceptive innervation of visceral structures is complicated by the presence of low-threshold mechanosensory afferents (Robinson & Gebhart, 2008). These wide dynamic range afferents respond to both non-noxious distending pressures and noxious pressures. These fibre types do not fit the traditional definition of a nociceptor as a receptor that responds to tissue damage as they can also be activated by non-noxious stimuli. A non-noxious stimulus would not be perceived as noxious until the intensity increases (Robinson & Gebhart, 2008). Sleeping nociceptors are also present in visceral structures. Also referred to as silent nociceptors, these high threshold receptors will only respond to stimuli when sensitized by inflammatory chemicals (Robinson & Gebhart, 2008). Muscle and joints are innervated by both group III and group IV muscle afferents (Raja, Meyer & Campbell, 1988). Group III muscle afferents are thinly myelinated and respond to pressure applied to the muscle or tendon as opposed to stretch or contraction. Most of these fibres have high thresholds for activation, therefore only respond to noxious pressure stimuli. Some of these fibres are polymodal, also responding to noxious chemical and heat stimuli (Raja, Meyer & Campbell, 1988). Group IV fibres are unmyelinated afferents and respond similarly to cutaneous C fibres in that they tend to have higher mechanical thresholds than group III for activation and are readily excited by chemical and thermal stimuli (Raja, Meyer & Campbell, 1988).

Cutaneous nociceptors demonstrate extreme heterogeneity with regards to fibre type, transmission speed and stimuli responses. Majority of nociceptors have small, unmyelinated axons called C-fibres (Woolf & Ma, 2007). C-fibres have a conduction velocity of approximately 0.4 – 1.4m/s (Dubin & Patapoutian, 2010). C-fibres are most commonly polymodal, referring to their activation by a combination of noxious mechanical (M), hot (H), cold (C) and chemical stimuli (Raja, Meyer & Campbell, 1988; Van Hees & Gybels, 1981). Mechanically sensitive C fibres (C-MH and C-M) initiate a response to temperatures between 39˚C– 51˚C (C-MH) (Torebjork, LaMotte & Robinson, 1984), mechanical pressure (C-MH and C-M) (Koltzenburg & Handwerker, 1994) and chemical activators capsaicin (C-MH) (Schmidt et al., 1995) and allyl isothiocyanate (AITC) (C-MH and C-M) (Schmidt et al., 1995) via different ion channels. Mechanically insensitive C fibres (C-H and C-M_iH_i) respond to temperatures above 42˚C (C-H) (Weidner et al., 1999), chemical activators including capsaicin (C-H and C-M_iH_i), histamine, bradykinin and prostaglandin E2 (C-H) and AITC (C-M_iH_i) and are proposed to become mechanically or thermally sensitive following inflammation, typically associated with injury (Schmidt et al., 1995). A-fibre nociceptors have myelinated axons capable of conduction velocities of 5 – 30m/s (Djouhri & Lawson, 2004). A-fibres are predominately heat and mechanosensitive (A-MH I, A-MH II and A-M). Action potentials are associated with thermal stimuli between 43˚C – 47˚C (A-MH II), thermal stimuli greater than 53˚C (A-MH I), mechanical pressure (A-MH I, A-MH II and A-M) and capsaicin (A-MH II) (Djouhri & Lawson, 2004). The anatomical characteristics of nociceptors affecting the transmission speed and type of noxious stimuli information transmitted to the central systems emphasises the complexity of the peripheral nociception system. It in turn shapes the way individuals receive and can therefore respond to different types of pain.

Nociceptive signals are traditionally described as first (fast) or second (slow) pain (Dubin & Patapoutian, 2010). First pain is described as sharp or stabbing and are clearly localised, often transmitted by A-fibres (Dubin & Patapoutian, 2010). Meanwhile second pain is sustained and more dispersed, commonly associated with C-fibres (Dubin & Patapoutian, 2010). While this is a description that pervades pain research today, the classification of pain types is no longer viewed this simplistically. For example, thickly myelinated A-fibre high threshold mechanoreceptors have been reported, which are insensitive to light touch but act as high-speed transmissions pathways for noxious mechanical stimuli (Nagi et al., 2019).

Ion channels located on the nociceptor nerve endings act as pain transducers by opening in response to noxious stimulation and enabling generation of an action potential (Giniatullin, 2020). Table 1 provides a summary of the ion channels involved in pain transduction.

Table 1: *Ion channels involved in pain signal transduction.*

Ion channel	Description of role in pain transduction	Reference
P2X3	ATP sensitive ion channels, associated with inflammatory pain	Xiang et al., 2019
TRPV1	Heat and capsaicin sensitive, often co-expressed on nociceptors with TRPA1	Giniatullin, 2020
TRPA1	Cold and redox sensitive	Giniatullin, 2020
ASICs	Acid (H+ ions) sensitive	Giniatullin, 2020
Piezo	Piezo 1 and 2 are mechanosensitive ion channels	Coste et al., 2010
HCN2	Alterations may mediate thermal and mechanical hyperalgesia in chronic inflammatory pain states.	Jansen et al., 2021

The cold pressor task, involving immersion of the hand into ice water, acts as a cutaneous noxious cold stimulus. The cation channel TRPA1 is activated in response to noxious cold stimuli in this experimental stimulus and therefore is responsible for the generator potential that leads to cold pain transmission (Dubin & Patapoutian, 2010). In contrast, infusion of a hypertonic saline solution into the muscle belly acts as an important experimental model for muscle pain (Graven-Nielsen et al., 1997). While the HS infusion would be classified as a chemical stimulus based on the pathway of nerve activation, the quality of pain sensation generated closely resembles that of delayed onset muscle soreness (DOMS) which is a dull muscle ache that can follow exercise. It is proposed that pain associated with the HS infusion results from the increase in extracellular Na^+ ion concentration, causing direct depolarisation of nociceptors located in the muscle (Tegeder et al., 2002). When the ion channels open, an influx of positive ions into the nociceptor results in neuronal depolarization. This initial

event, called a generator potential, can activate the opening of specific voltage gated sodium channels which open to allow further influx of sodium cations and lead to a full action potential (**Figure 1)** (Dubin & Patapoutian, 2010). Sodium Nav1.8 and Nav1.9 are voltage gated sodium channels that are exclusively expressed on nociceptor neurons (Bennett et al., 2019). A strong enough noxious stimulus will initiate an action potential in the nociceptor, which is propagated along the afferent until it reaches the dorsal root ganglion of the spinal cord.

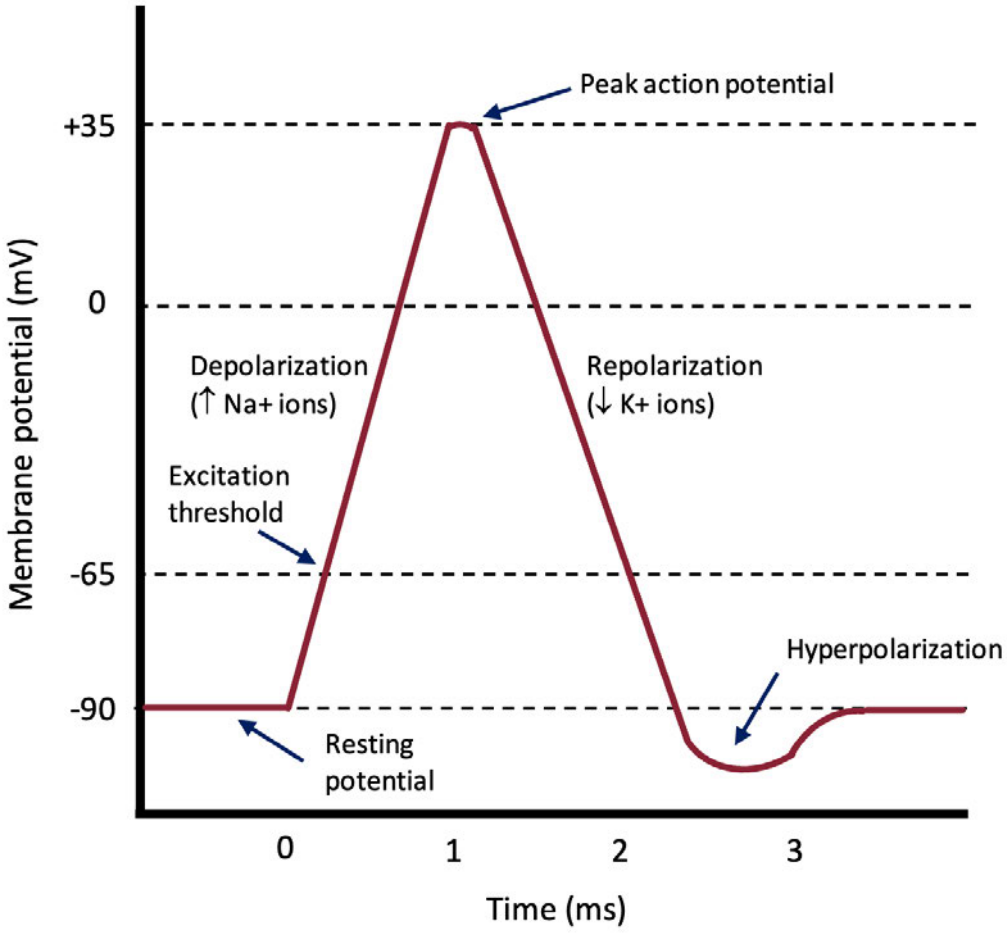

Figure 1: Action potential observed in nerve fibres. Nerve fibres have a resting membrane potential of -90mV. When stimuli are detected, Na+ ions enter the nerve cell. If enough Na+ enters (based on the intensity of the stimuli) to increase membrane potential to the excitation threshold (-65mV), a rapid influx of Na+ ions into the cell occurs (depolarization) (Dubin & Patapoutian, 2010). When membrane potential reaches peak (+35mV), K+ ions exit the nerve cell to restore the membrane potential to resting (depolarization) (Dubin & Patapoutian, 2010). The membrane potential may drop below the resting potential during

repolarization (hyperpolarization) before returning to resting potential. This action potential is propagated along nerve cells to transmit the signal through the CNS (Dubin & Patapoutian, 2010).

Central Mechanisms of Pain Perception

Following propagation of the action potential along the nociceptor axon, neurotransmitters are released which have the potential to excite second order neurons. The primary neurotransmitters involved in this process are glutamate and peptides such as substance P and calcitonin gene-related peptide (CGRP) (Basbaum et al., 2009). These neurotransmitters are considered excitatory, facilitating transmission of nociceptive signals to the spinal cord neurons. Glutamate is typically associated with the transmission of first or fast pain through the A fibres, while substance P is associated with slow pain transmission through C fibres (Dubin & Patapoutian, 2010). However, it is also hypothesised that substance P release assists in the uptake of glutamate through sensitization of the second order neurons (De Koninck & Henry, 1991). Substance P and CGRP are also released at the site of injury and contribute to the neurogenic inflammatory response (Zieglgänsberger, 2019). Peptide release at the injury site leads to degranulation of mast cells, vasodilation and chemotaxis of immune cells, creating an inflammatory immune response to assist with repair to the site (Zieglgänsberger, 2019). At cutaneous sites, this inflammatory response can lead to hyperalgesia, where an individual demonstrates increased responsiveness to noxious stimuli. Combined with allodynia, referring when nociceptors become responsive to normally non-noxious stimuli, these mechanisms trigger protective responses that minimise the risk of increased injury to an already injured site.

Release of substance P and glutamate from the presynaptic axon terminal of the nociceptors into the synaptic cleft located in the dorsal horn of the spinal cord can trigger activation of an action potential of a second order neuron, leading to transmission of the pain signal to the pain processing regions of the brain, or directly to the ventral horn of the spinal cord for reflex motor responses. Several monosynaptic pathways transmit nociceptive information from the dorsal horn of the spinal cord directly to cerebral structures. These pathways include the spinothalamic tract, spinoreticular tract, spino-mesencephalic tract,

spinoparabrachio-hypothalamic tract, spinohypothalamic (spinotelencephalic tract), spinocervical tract and the postsynaptic dorsal horn column (medial lemniscus) pathway **(Table 2)** (Millan, 1999). Each of these originate from laminae in the dorsal horn of the spinal cord where they synapse with nociceptors.

Table 2: Overview of key pathways of nociceptive transmission (Millan, 1999).

Tract	Laminae of origin	Tissue input	Principal targets
Spinothalamic	I, II, IV, V/VI, VII/VIII	Skin, viscera, joints/muscle	Thalamic nuclei
Spinoreticular	I, V/VI, VII/VIII	Skin, viscera, muscle	Reticular Formation of brainstem
Spino-mesencephalic	I-II, IV/V, VII, X	Skin, viscera, joints/muscle	Midbrain and peri-aqueductal gray
Spinoparabrachio-hypothalamic	I, II	Skin, viscera, joints/muscle	Parabrachial nuclei à hypothalamus
Spinoparabrachio-amygdaloid	I, II	Skin, viscera, joints/muscle	Parabrachial nuclei à amygdala
Spinohypothalamic (spinotelencephalic)	I, V, X	Skin, viscera	Hypothalamus and thalamus
Spinocervical	I, III/IV, V	Skin, joints/muscle	Relay through lateral cervical nuclei to thalamus and midbrain.
Postsynaptic dorsal column (medial lemniscus) pathway	III-V, VI, VII	Skin, viscera, joints/muscle	Relay through dorsal column nuclei to thalamus

The neuromatrix theory of pain states that multiple brain regions contribute to pain perception as opposed to a single region processing all inputs as in other sensations. This complexity contributes to the significant interindividual variability in pain perception and response and the psychosocial and emotional components of pain experience. **Figure 2** and

Table 3 demonstrate the key regions that have been implicated in pain processing and responses.

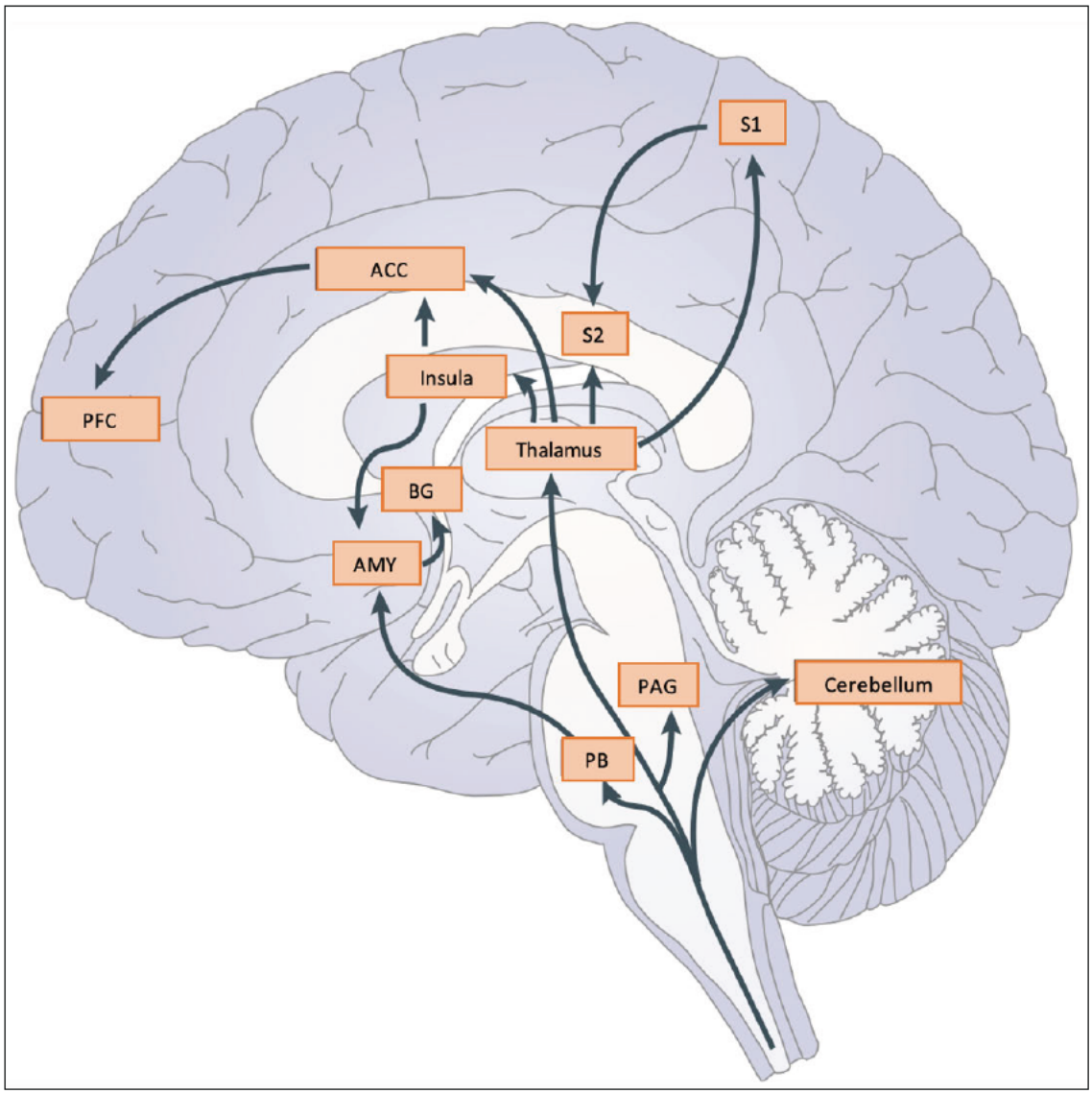

Figure 2: Diagram of brain regions and pathways involved in pain processing (Bushnell, Čeko & Low, 2013). Pain signals from the anterolateral spinal tracts pass through the brainstem, terminating in the cerebellum, periaqueductal grey (PAG), parabrachial nucleus (PB) or thalamus. Signals are transmitted from the thalamus to the primary and secondary somatosensory cortices (S1 and S2 respectively), anterior cingulate cortex (ACC) and insula. From PB, signals are transmitted to the amygdala (AMY), then on to the basal ganglia (BG). The prefrontal cortex (PFC) also receives signals from the ACC (Bushnell, Čeko & Low, 2013).

Table 3: Cerebral regions involved in pain function and innervation pathways (Bushnell, Čeko & Low, 2013; Saab & Willis, 2003).

Brain region	Function in pain	Innervation
Primary somatosensory cortex (S1)	Sensory features of pain (location and duration)	Spinothalamic pain pathways (nociceptive input from the thalamus)
Secondary somatosensory cortex (S2)	Sensory features of pain (location and duration)	Spinothalamic pain pathways (nociceptive input from the thalamus)
Anterior cingulate cortex (ACC)	Emotional and motivation aspects of pain	Spinothalamic pain pathways (nociceptive input from the thalamus)
Insula	Emotional and motivation aspects of pain	Spinothalamic pain pathways (nociceptive input from the thalamus)
Prefrontal cortex (PFC)	Cognitive aspects of pain	From ACC
Thalamus	Relay centre and processing of nociceptive information	Anterolateral pathways (spinothalamic, spinoreticular and spinomesencephalic), spinocervical, postsynaptic dorsal column (ML) pathway.
Hypothalamus	Endocrine responses to pain	Spinoparabrachio-hypothalamic and spinohypthalamic (spinotelencephalic) tracts
Basal ganglia	Sensory, affective and cognitive aspects of pain Modulation of nociceptive information	Spinoparabrachio-amygdaloid pathways (nociceptive input from the parabrachial nucleus sent to amygdala before the basal ganglia)
PAG	Modulation of nociceptive information, autonomic pain responses	Spino-mesencephalic tract
Cerebellum	Responds to pain stimuli however currently unclear specific role	

Pain Modulation

Numerous psychological and emotional aspects can influence pain perception. One aspect that has been significantly researched is the impact of attention. When distracted from pain by another stimulus, pain intensity is regularly reported as decreasing in participants (Villemure & Bushnell, 2002). Emotional state can also contribute directly to pain perception, with positive mood being associated with reduced pain perception under experimental conditions (Villemure & Bushnell, 2002). The role of mood is affecting pain attentional bias is also reported, with poor mood being associated with increased awareness of pain sensations (Villemure & Bushnell, 2002). Pain is also influenced by cognitive-behavioural processes involving learning about pain experience and the role of beliefs about pain in perception.

The CNS contains structures that form descending pain modulatory systems which assist with pain adaptation. This descending system can either be inhibitory or facilitatory, depending on the needs of the individual (Saccò et al., 2013). In the descending inhibitory pathway, neurons from the periaqueductal grey (PAG) and periventricular regions of the mesencephalon and upper pons send signals to the raphe Magnus nucleus (RMN), the thin midline nucleus in the lower pons and upper medulla and nucleus reticular paragigantocellularis located in the lateral medulla. From the nuclei, signals are transmitted down the dorsolateral columns to the pain inhibitory complex in the dorsal horn, blocking signals from reaching the brain (Saccò et al., 2013). This pathway is also called the periaqueductal grey-rostroventral medulla (PAG-RVM) pathway or the seratonergic pathway due to its release of serotonin as the primary transmitter. Serotonin is believed to have both inhibitory and excitatory effects associated with pain processing (Saccò et al., 2013).

Another descending pathway originates from the locus coeruleus and projects to the dorsal horn where norepinephrine release inhibits substance P and leads to reduced pain perception (Saccò et al., 2013). Inhibitory modulatory pathways enable pain to be blocked so that an individual can escape from the injury-causing event, therefore acting as a survival mechanism. However, once the acute danger has dissipated, facilitatory pathways enable

pain sensation to be retained as an indicator of damage to prevent injury and enable healing (Saccò et al., 2013). This pathway accesses the role of acute pain as a warning mechanism of damage to the body, initiating reflexes that promote protection of the damaged site and enable repair. The strong links between this network and brain regions such as the hypothalamus and limbic forebrain structures such as the amygdala, anterior cingulate cortex and anterior insula, indicate the strong correlations between pain processing and cognitive factors (Bushnell, Čeko & Low, 2013).

Conditioned pain modulation (CPM) is a clinical measurement of how efficient descending pain pathways are in both inhibiting and facilitating pain signal transmission. It is triggered and measured by application of a noxious conditioning stimulus which initiates an initial pain response (Ramaswamy & Wodehouse, 2021). A noxious test stimulus is applied before and after the conditioning stimulus to another region and the difference in pain intensity of that stimuli between the two time points reported (Ramaswamy & Wodehouse, 2021). If pain perception of the test stimulus decreases following the condition stimulus, the participant is perceived to demonstrate an anti-nociceptive profile, therefore the 'pain inhibits pain' role of the CPM is more active (Ramaswamy & Wodehouse, 2021). If pain perception of the test stimulus increases, then the participant is reported as having a less active CPM and is classified as pro-nociceptive. There are also proposed links between these descending pathways and the autonomic nervous system, which plays a key role in physiological responses to pain (Ramaswamy & Wodehouse, 2021).

Inducing and Measuring Responses to Experimental Pain

There are many different experimental pain protocols used to induce manageable pain in a laboratory setting. It is important to be able to evoke different pain responses to observe how different pain types are responded to and rated in intensity.

The cold pressor task involves submersing a limb (either the foot or hand) into ice water. The temperature and duration of the task can vary depending on the study. The cold pressor test serves as a stimulus for acute thermal pain by opening TRPA1 ion channels, which generates an action potential (Dubin & Patapoutian, 2010). This action potential is then transmitted

along A-fibre nociceptors. Another form of experimental pain protocol is a mild hypertonic saline (HS) infusion. A HS infusion causes a dull ache by activating C fibres through increased levels of extracellular sodium and can be injected either subcutaneously or into the muscle belly (Tegeder et al., 2002). The percentage of saline can vary depending on the study. There are also different approaches to infusion, including a bolus infusion of a specified volume or continuous infusion where the infusion rate is altered over time to induce a consistent pain rating (Burton, Fazalbhoy & Macefield, 2016).

Pain is an inherently subjective experience; however, tools have been developed to assist scientists in quantifying laboratory pain experiences. Participants are regularly asked to report the intensity of pain experiences verbally using a numerical rating scale or visually using a visual analogue scale (VAS). Typically pain intensity is rated on a scale of 0 to 10, with 0 being no pain and 10 being the worst pain imaginable. Pain threshold and tolerance can also be reported. Pain threshold is the minimum stimuli intensity required for pain whereas tolerance refers to the maximum amount of pain a subject can withstand (Paparizos et al. 2005; Tajet-Foxell & Rose, 1995). How these threshold and tolerance points are measured can vary depending on the pain protocol. For the cold pressor test, threshold is typically reflected as the time to pain onset and tolerance is the time when the participant needs to remove the limb from the ice water. Perceived pain intensity is also a common measurement used to reflect the intensity of a task overall with intensity rated between 0 (no pain) and 5 (excruciating).

The Short Form McGill Pain Questionnaire (SF-MPQ) is a common survey provided to participants. It consists of 15 adjectives and asks participants to rate on a scale of 0 (none) to 3 (severe) how each adjective describes the pain experienced. The first 11 adjectives on the list link to sensory measurement, or intensity, of the pain. The last 4 refer to the affective measures, or unpleasantness, of the pain stimuli. There are several psychological and emotional factors that can influence pain experience and questionnaires have also been designed to measure these factors (Melzack, 1987). The pain vigilance and awareness questionnaire measures attention to pain stimuli (McCracken, 1997). The pain catastrophizing scale measures 3 catastrophizing behaviours; rumination (can't stop thinking about the pain), magnification (concern over something serious occurring) and helplessness

(the pain is overwhelming). The pain anxiety symptoms scale is a tool used to measure fear avoidance behaviours associated with pain (Sullivan et al., 1995).

A specific survey associated with athletes' responses to different types of pain has also been developed, called the Sports Inventory of Pain. The survey measures how athletes respond to pain and injury across five pain response styles: coping through direct action, cognitively mediated coping, avoidance, catastrophizing, and somatic awareness (Meyers et al., 1992). The existence of this distinct survey suggests that athletes demonstrate distinct pain responses. Dancers, as a subset of the athletic population, would be similarly assumed to reflect these behaviours. Developing a stronger understanding of the nuances of these pain behaviours and the body's physiological responses to experimental pain is a critical contribution to the narrative that is dancers pain perception.

Pain Perception and the Autonomic Nervous System

The autonomic nervous system consists of two branches. The sympathetic nervous system controls 'fight or flight' responses to stress, including increased heart rate, respiratory rate, blood pressure, pupil dilation and sweat release. Meanwhile, activation of the parasympathetic nervous system is associated with 'rest or digest' responses including decreased heart rate, respiratory rate, blood pressure and increased digestive activity (Burton, Fazalbhoy & Macefield, 2016).

Acute pain is strongly correlated with an increase in sympathetic activation. In animal models, both mechanical and thermal noxious stimulation of the skin has been associated with activation of sympathetic responses, primarily those involved with vasoconstriction and consequently increased blood pressure (Horeyseck & Janig, 1974). The technique of microneurography enables the direct measurement of neural activity to muscle and skin in awake human subjects. Direct neural recordings have demonstrated that noxious stimulation including mechanical pressure to the skin (Schobel et al., 1996) and immersion of hand in ice water (cold pressor test) (Fagius, Karhuvaara & Sundlof, 1989) are associated with an increase in muscle sympathetic nerve activity (MSNA). The cold pressor test has been reported in several studies as also being associated with an increase in blood pressure

(Burton, Fazalbhoy & Macefield, 2016; Kakon et al., 2021; Mourot, Bouhaddi & Regnard, 2009; Saccò et al., 2013). This increase in blood pressure has been positively correlated with pain threshold and negatively associated with the perceived intensity of pain stimuli (Saccò et al., 2013). The CPM systems have been implicated in contributing to this negative correlation between physiological responses and pain sensitivity. One study observed that an increase in CPM activation, reflected in reduced pain intensity sensitivity and higher pain tolerance during a thermal noxious stimuli before and after application of the cold pressor test, was correlated with increases in heart rate and blood pressure (Chalaye et al., 2013). Anatomically, the solitary tract nucleus plays an important role in both the baroreceptor blood pressure response in the ANS and as a link with the vagus nerve and the dorsal horn of the spinal cord. Pain is proposed to activate the sympathetic nervous system, increasing blood pressure through the baroreceptor reflex which consecutively activates the descending inhibitory pathways (Saccò et al., 2013).

Some studies have reported that deep pain originating in structures such as joints and muscles may be associated with decreases in blood pressure (BP) and heart rate in awake human subjects. While deep short-lasting pain typically causes an increase in cardiac sympathetic drive, longer-lasting stimuli have been shown to result in both increases and decreases in BP, heart rate, and MSNA across participant groups (Fazalbhoy, Birznieks & Macefield, 2012). The reasons for these disparate responses have not been clearly established. Some studies suggest that the direction of the response is not correlated with anxiety or pain attitudes (Kobuch et al., 2016).

Heart rate responses have been less reliably reported. One study divided the responders into those whose heart rates increased and those whose heart rate decreased during the cold pressor test. The group with heart rate increase demonstrated an increase in heart rate during the second and third minute of the cold pressor test which was associated with increased sympathetic activity and decreased vagal outflow. In contrast, the group with heart rate decrease showed a significant decrease in heart rate after the second minute of the cold pressor test, which was associated with increased vagal outflow and decreased sympathetic activity (Mourot, Bouhaddi & Regnard, 2009). Another study observed a trend towards an increased heart rate during the cold pressor test which was significantly

correlated with the peak pain ratings of the cold pressor test and pain catastrophizing behaviours (Kakon et al., 2021). These findings suggest that heart rate responses to pain stimuli may be associated with pain intensity and cognitive responses to pain. However, the disparity of heart rate responses over time during pain stimuli requires further investigation in different participant groups.

Heart rate variability (HRV) measurements such as the low frequency (LF)/high frequency (HF) ratio aim to reflect the relative sympathetic and parasympathetic contributions to heart rate. An increase in LF HRV indicates an increase in sympathetic activation while HF is associated with increased parasympathetic activation (Koenig et al., 2014). One study observed that an increase in the LF/HF ratio followed intramuscular and subcutaneous injection of HS (Koenig et al., 2014). Therefore, increased sympathetic outflow was associated with both skin and muscle pain. The same trend was also observed for the cold pressor test (Koenig et al., 2014). The range of intensity of the cold pressor test were not significantly predicted by this ratio, but LF HRV was inversely associated with cold pressor test unpleasantness. This suggests a role of increased sympathetic activation in reducing pain perception (Koenig et al., 2014). In contrast, another study found that participants who had higher HF HRV at baseline were more likely to complete a 2-minute cold pressor test. This suggests that a higher pain tolerance may be associated with parasympathetic stimulation, which can have an analgesic effect via descending pain inhibition (Umeda & Okifuji, 2022). These findings suggest that parasympathetic activation may also play a role in modulating pain perception and tolerance, but more research is needed to fully understand the mechanisms involved.

When observing respiratory responses, one study observed no changes in respiratory rate during the cold pressor test (Apelt-Glitz et al., 2022). However, another study did observe an increase in tidal volume and minute ventilation during the cold pressor test (Mourot, Bouhaddi & Regnard, 2009). The disparity in reported physiological responses to different types of experimental pain and on a minute-by-minute basis throughout pain protocols indicates the important of further investigating the nature of physiological responses to experimental pain in different populations.

Pain Perception in Dancers:

Dance is mostly simply defined as rhythmic movement of the body typically set to music (Mackrell, 2020). However, dance as a performance art form is considered an intense form of physical activity. Dancers are consequently at high risk of musculoskeletal injury, defined clinically as damage to skeletal bones, tendons, joints, ligaments or skeletal muscle. Since 1990, the Australian Dance Council (AusDance) have investigated the prevalence and characteristics of injury in Australian dancers. The most recent survey in 2017 reported that 97% of dancers experience at least one significant injury during their career, an increase from the 89% reported in 1999 (Crookshanks, 1999; Vassallo, 2017). Dancers have reported dance culture as one of tolerance, perseverance and accepting or ignoring injury, leading to dancers continuing to dance through pain (Harrison & Ruddock-Hudson, 2017). It is this trend - similarly reported in other athletic populations - that prompts the question of whether dancers demonstrate an enhanced ability to withstand pain compared to non-dancers. Pain research in dancers has taken two distinct forms in previous year, divided into those measuring pain perception in response to experimental pain stimuli, and those employing pain questionnaires and surveys to understand dancers pain awareness over time.

Experimental Pain Perception Studies in Dancers

Despite the rise in injury rates, limited research has focused on pain perception and response to experimental pain in dancers. One two studies directly reported pain perception measurements in dancers compared to non-dancer populations (Paparizos et al. 2005; Tajet-Foxell & Rose, 1995). Both studies investigated potential psychological factors influencing pain perception differences between dancers and non-dancers. One study measured the influence of coping styles, extraversion/introversion and neuroticism (Tajet-Foxell & Rose, 1995). The other reported the influence of catastrophizing scales (Paparizos et al. 2005). Both studies employed the cold pressor test to determine the subject's pain threshold and pain tolerance (Paparizos et al. 2005; Tajet-Foxell & Rose, 1995). Participants also reported on sensory and affective pain characteristics by completing the SF-MPQ (Paparizos et al. 2005; Tajet-Foxell & Rose, 1995).

The cold pressor test employed in both studies is a viable and effective tool for inducing and measuring pain responses. However, the cold pressor test induces a thermal pain sensation. Dancers are exposed to mechanical and chemical pain more regularly in their sport, which is associated with musculoskeletal injury. Furthermore, the cold pressor test induces a cutaneous pain sensation while musculoskeletal injury is associated with muscular and joint pain. This leads to differences in nociceptor activation in different tissue structures. While important insights into the differences in pain responses can be gleaned from the use of a standard pain protocol, it is important to identify that the cold pressor test stimulus does not replicate real world pain experiences in dancers. To ensure that the results observed can be directly applied to understanding dancers' responses to pain, experimental stimuli that replicate the type of pain commonly experienced in a dance context are important to investigate.

Pain tolerance and pain threshold were reported as higher in dancers compared to non-dancers in 1995 (Tajet-Foxell & Rose, 1995). The same trend was observed in the 2005 paper for pain tolerance (Paparizos et al. 2005). One flaw in this comparison is that pain threshold scores was not reported in the 2005 paper, making direct comparison between the two results difficult. Initially, total pain score, sensory pain score and affective pain scores from the SF-MPQ were reported as significantly higher in dancers compared to non-dancers (Tajet-Foxell & Rose, 1995). This suggested that while dancers had a greater capacity to withstand pain, they experienced it more severely. However higher sensory and affective pain scores were not reported 10 years later. Researchers also observed that dance skill was not directly correlated with sensory and affective pain scores (Paparizos et al. 2005). The authors of the 2005 paper identified methodological limitations in comparing results across the two studies, including the potential difference in water temperature and time for the cold pressor test (Paparizos et al. 2005). The 1995 paper also studied professional ballet dancers, while the 2005 paper investigated recreational ballet dancers, therefore the possible effect of difference in dance experience on pain perception should be further investigated (Paparizos et al. 2005; Tajet-Foxell & Rose, 1995). Prior research has also reported athletes as demonstrating higher pain tolerance, however neither study attempted to account for non-dance related athleticism in their control or non-dancer population.

The first study reported neuroticism scores as slightly higher in dancers than non-dancers, though this did not align with the hypothesis that lower neuroticism would correlate with higher pain tolerance and threshold. No other psychological factors studied demonstrate a significant difference between the dancer and non-dancer populations (Tajet-Foxell & Rose, 1995). In 2005, correlation analysis between catastrophizing and pain scores suggested a relationship between the magnification sub scale and pain scores for the dancer population. A correlation was found between helplessness and total catastrophizing scores and pain for the controls (Paparizos et al. 2005). This suggested a difference between dancers and non-dancers with regards to the psychological influences on pain experience.

The influence of dance on pain thresholds was further investigated in a 2015 study. The investigation reported the pressure pain responses in a group of high school students who performed dance activities at different levels of exertion and movement in time with fellow students (synchrony) (Tarr, 2015). To measure pain threshold, a blood pressure cuff was inflated around the non-dominant arm until the pressure became uncomfortable. It was found that completing a dance of high exertion in sync with others elevated pain thresholds (Tarr, 2015). The pain threshold values were recorded as a proxy measurement for activity of the endogenous opioid system (EOS). When the EOS is activated, pain thresholds are increased, therefore future research could involve report EOS activity in trained dancers (Tarr, 2015). Subjects in this study were not directly applicable to a dancer cohort and further research is required to understand the role of dance training in pain perception.

Survey Based Injury and Pain Response Studies in Dancers

Survey-based studies conducted among dancer populations have requested participants to retrospectively report their pain experience, considering prior injuries or painful sites. These studies have sought to measure pain location, type and prevalence, severity of pain, sensory affective pain responses, and pain behaviour (Lampe et al., 2018).

A recurring theme throughout survey-based dancer studies is that dancers, like other athletes, tend to distinguish between ‘good’ and ‘bad’ pain. These pain terms are also

described as ‘performance pain’ and ‘injury pain’. One quantitative study of 20 current or retired professional dancers revealed that the personal definition of the two pain types can vary significantly between individuals. Performance pain is typically described by dancers as pain associated with physical exertion or performance. It is considered a ‘normal’ result of pushing one’s body during physical activity and often associated with fitness or improvement. Meanwhile bad pain was associated with injury, could require medical intervention and described by dancers as unmanageable (Harrison & Ruddock-Hudson, 2017). In another study, dancers described good and bad pain in regard to quantity over quality. Good pain was considered transient and something dancers did to themselves, while bad pain was recurring (Thomas & Tarr, 2009).

Distinguishing between pain associated with physical exertion and pain associated with injury is crucial in an athletic context. Failing to differentiate between the two types of pain can pose a significant risk to athletes. Recurring pain during exercise can be an early indicator of an underlying injury. Recognizing these warning signs can prompt pre-emptive medical intervention, which can prevent further and potentially career-ending damage (Harrison & Ruddock-Hudson, 2017). However, dancers across several studies reported feeling they were unable to clearly differentiate between the two (Harrison & Ruddock-Hudson, 2017; Lampe et al., 2018). One study compared dancers and dance teachers, finding that more dancers described experiencing pain as ‘harmless’ and as a ‘natural consequence’ of dance. Meanwhile more dance teachers reported that pain could be viewed as ‘questionable’ and as an ‘early warning sign’ of injury (Lampe et al., 2018). Similarly, dancers in another study reported being unaware that ongoing pain may be an injury sign, with low-grade pain that didn’t impinge on ability not being described as an injury. Those with more experience were more likely to report an awareness of chronic injuries and attend to chronic pain sites (Thomas & Tarr, 2009). This suggests that age, experience and potentially taking on leadership and guidance roles within the dance community can lead to greater awareness of pain experience and the different types of pain.

One recent study employed an online survey to gather pain experience data, including sensory, affective and motor components and the temporal (acute or chronic) characteristics of dance pain (Lampe et al., 2019a). The sample population consisted of female ballet and

jazz, modern, contemporary dancers. No difference between the two dance styles was reported with regards to the prevalence, temporal course and pain experience. However, the common injury sites differed with ballet dancers more commonly experiencing injuries in the lower limb (calf, forefoot and toes), while jazz, modern, contemporary dancers experience more upper body injuries (shoulders, elbows, wrists, neck and back) (Lampe et al., 2019a). In an Australian study, 73% of the surveyed population reported experience a dance-related injury in the 12 months preceding the survey. The ankle (26%), knee (11%) and hip (10%) being the most common injury sites (Vassallo, 2017). One other study reported in Latin American dancers, females reported more sites of injury (245 sites) compared to male dancers (109) (Wanke, Haenel & Groneberg, 2020). While these studies indicate the prevalence of injury and multitude of sites affected, it is important to consider the differences in injury and pain between dance styles and between different cohorts.

Dancers regularly report the ability to recognise the difference in pain experience and pain intensity both between dancers and non-dancers and between individual dancers themselves. One study reported on the pain appraisal of performance and injury pain, referring to how threatening the dancers reported the pain to be. There was no significant difference in the appraisal of performance compared to injury pain across the cohort. This reinforces the concern that dancers may be unable to accurately tell the difference between 'good' and 'bad' pain and react appropriately (Anderson & Hanrahan, 2008). The subjectivity of pain was acknowledged by majority of dancers in the study, with these dancers also describing they felt that had a greater understanding of pain compared to non-dancers due to the prevalence of pain in their profession (Harrison & Ruddock-Hudson, 2017). Pain intensity has been reported as changing with age in the dancer population. In one study, 11 out of 20 dancers reported they felt their pain threshold had decreased over time as their body became over sensitised and 'felt threatened' (Harrison & Ruddock-Hudson, 2017). Similarly dance teachers compared to dancers in one study reported significantly higher pain intensity when reporting the pain experienced in the most affected site within a 3-month period. In the same study, sensory and affective perception of pain was measured in dancers and dance teachers. Sensory measures demonstrated no significant differences between the two groups, however certain affective measures (tiring/exhausting, fearful and dreadful) were selected more by dance teachers than dancers (Lampe et al. 2019b). This supports the

importance of acknowledging inter individual differences in pain perception in dancers and the potential influence of age and experience or education on pain perception. Dancers are similar to other athletes in that they are reported to have high interceptive ability. This refers to their capability to interpret signals from their body. This high level interoceptive capability could also contribute to how dancers interpret and respond to pain signals from the body (Bellan et al., 2017).

Pain behaviour describes both noticeable and unnoticeable responses to a painful sensation. In a sport or dance context, this can include behaviours such as modifications to training and performance and seeking professional help. Dance culture has been described as a 'culture of risk', where pain is normalised, and dancers often push through or ignore pain in favour of continuing to rehearse and perform while experiencing pain. The majority (19/20) of dancers in one study reported feeling that pain had been normalised in the industry and that it was to be expected, managed and pushed through (Harrison & Ruddock-Hudson, 2017). While strides have been made to try and remove this element from dance culture, dancers have revealed maladaptive injury and pain behaviours throughout several studies. In one study focusing on male and female Latin American dancers, both genders ignored injuries and the resulting pain. The reasons provided for this behaviour were feelings of responsibility, not wanting to let down their dance team and passion for dance. The majority (78.8% of males and 76.9% of females) trained to the full extent, while others continued to train while protecting their injured site (Wanke, Haenel & Groneberg, 2020). In the study by Lampe et al., (2019b) dancers and dance teachers reported the same behaviours, however more dancers revealed they danced to the full extent while in pain while teachers were more likely to teach through pain and try to 'take it easy' (Lampe et al., 2019b). An Australian survey similarly revealed that while most dancers who experienced an injury in the 12 months before the study sought professional advice and treatment post-injury, 71% returned to dance training by modifying their practice and reported regularly dancing through injury pain (Vassallo, 2017). One study recorded modifications to dance training in correlation with reported pain perception, using sensors to detect duration of light intensity exercise, ground force during jumps and the quantity and angle of both front and side leg lifts. Increased self-reported pain correlated with greater levels of light activity, reduced duration and quantity of front leg lifts and greater side leg lift angles, proposed as a

compensatory measure. These modifications could be interpreted as either deliberate compensatory measures in response to injury or the result of reduced strength and endurance due to pain. However, either interpretation does indicate an alteration to physical behaviour resulting from pain in dancers and that dancers demonstrate a tendency to continue dancing through pain (Hendry et al. 2022).

Another study compared the coping styles of dancers at varying intensities of performance and injury pain. In this study, active coping, either pushing through or ignoring, was the dominant coping style during both high and low-level performance-based pain. As pain was considered more threatening, the dominant coping style shifted to avoidance (trying not to make it worse) and catastrophizing (dwelling on pain and associated emotions) (Anderson & Hanrahan, 2008). This trend aligns with passion for dance being a dominant factor in determining behaviours as being unable to rehearse or perform could become very anxiety inducing, particularly in a professional dance environment. These reasons also tend to be reflected when discussing accessing medical or therapeutic interventions for pain and injury in dance. In a group of Latin American dancers, male dancers consulted specialists and spoke to others about the pain experienced significantly less than females (Wanke, Haenel & Groneberg, 2020). In a comparison of dancers and dance teachers, dancers were far more likely to report they felt medical intervention was unnecessary, with dance teachers accessing medical and therapeutic assistance more regularly (Lampe et al., 2019b). This speaks to the impact of age and experience on pain behaviour. Molnar and Karin (2017) in an editorial on the complexities of dancers' pain, summarised these different pain behaviours into three distinct groups. The first group included dancers who perceive discomfort or 'pre-pain' as an indicator that something needs to be changed such as modifying warm-up or cool-down practices. The second are those that try to protect the site by limiting movement while continuing to perform normally. The final group are those that block or ignore pain signals, dancing with the same level of intensity. Only the first of these groups demonstrates an advantageous response to pain, as groups two and three put themselves at risk of further injury by promoting poor motor programs or limiting the self-awareness required for safe dance practice (Molnar & Karin, 2017).

The varying levels of pain perception and resulting pain behaviours make it critical to develop a greater understanding of how dancers respond to pain and encourage strong awareness of self and pain signals in safe dance practice. One flaw to be noted in using survey-based data is the influence of recall bias as participants are reporting on pain experiences retrospectively. Eliminating this recall bias and measuring pain responses in the moment provides more accurate insight into dancers' pain perception. For this reason, controlled experimental pain studies, particularly those that mimic the pain experienced in a dance environment as closely as possible, are critical in future research. As dancers are considered a subset of the athletic population, understanding dancer pain responses can support an understanding of pain responses in other sports and vice versa.

Pain Perception in Athletes:

The intense physical and mental training required of dancers classifies them as a unique subset of the elite athlete population. Prior research into differences in pain responses between athletes and non-athletic populations may therefore provide insight into whether dancers respond differently to pain compared to non-dancers.

Investigations into dancers' pain perception and behaviour has reported the effect of variables such as dance style and experience on pain characteristics. Similarly, studies on athletic populations have focused on the influence of certain factors on pain awareness. One study asked participants to rate the pain experienced by an athlete described in a written vignette to demonstrate the effect of gender, sport type (individual or team) and injury history of pain perception. It was found that the athlete's gender in the vignette did not significantly affect how legitimate the participant's rated the athlete's pain. However, female participants were more likely to rate the pain experienced by the athlete in the vignette as higher and more legitimate than males. This is suggested to be linked to attitudes within sporting culture and potential differences in how males and females are expected to feel and acknowledge pain (Wandner, Devlin & Chrisler, 2011). It was also observed that participants who played individual compared to team sports were more likely to perceive the athlete's pain as valid in the vignette (Wandner, Devlin & Chrisler, 2011). This study suggests that, like dancers, athletes may also have varying pain experiences when their team members depend on them. The study also found that participants with 11 to 15 years of experience in the sport rated the athlete's pain as higher in the vignette as compared to those with 1 to 5 years of experience (Wandner, Devlin & Chrisler, 2011). This ties in with the suggestion that athletes, including dancers, develop a greater awareness of pain perception with experience and age.

Another study looked at the role of athletic identity in pain experience. Those with a high athletic identity are those who primarily define themselves in terms of their athletic ability and place great significance on their success or failure in their chosen sport. In a study of 130 male and female recreational basketball players, those with high athletic identity across both genders were more likely to play through pain and injury (Weinberg, Vernau & Horn,

2013). This links to studies on dancers as passion for dance was often a reason cited for dancers to continue rehearsing and performing through pain or injury. In a cohort of soccer players, the fear of losing their roles, frustration about being unable to participate, and the desire to play in important games were identified as reasons for why athletes may continue to play through pain, despite the potential risks of further injury (Roderick, Waddington & Parker, 2000). Similar reasons were also reflected in dancers. The similarities between dancers and other athletes as to the awareness of pain and pain behaviours reinforces the classification of dancers as a subgroup of the athletic population and the relevance of athletic research to this demographic.

Previous research has suggested that athletes demonstrate altered pain thresholds and tolerance values with varying levels of consistency (Tesarz et al., 2012). Several studies report that athletes have greater pain tolerance compared to non-athletes. However, other reports failed to identify this difference (Tesarz et al., 2012). Furthermore, a review comparing the results of several studies into differences in pain perception between athletes and non-athletes found a significant sex difference effect was measured, with females consistently demonstrating a higher pain tolerance, which was not observed in males (Tesarz et al., 2012). A similar trend was observed with pain threshold studies, some showing statistically significant increases in pain thresholds in athletes, while others reported no significant differences (Tesarz et al., 2012). Previous research has also identified the influence of different types of sport on pain responses. One paper found strength athletes have significantly higher heat-pain thresholds compared to endurance athletes and controls, while endurance athletes demonstrated greater heat pain tolerance compared to strength athletes and controls (Assa et al., 2019). Competition athletes have also demonstrated a pattern of lower cold pressor pain ratings during competition compared to baseline levels taken before and after competition, a trend not demonstrated by control groups (Sternberg et al., 1998). This emphasises the complex role of psychological and emotional factors in pain responses and raises the question of whether competition or performance leads to a similar trend in dancers, which may explain their ability to continue dancing while in pain, similar to how elite athletes continue to compete and training while injured.

Reviews have determined that athletes more consistently report increased pain tolerance compared to non-athletes, rather than changes in pain threshold. It has been suggested that pain threshold remains consistent for an individual, while pain tolerance can fluctuate depending on psychosocial and psychological factors. More consistent pain tolerance readings may result from athletes developing stronger coping skills due to training and regular pain exposure compared to non-athletes (Tesarz et al., 2012). However, there are questions associated with whether athletes may develop higher pain thresholds and tolerances due to intense training and potential prolonged pain exposure, or if athletes with a disposition for higher pain tolerance and thresholds are more inclined to progress further in the sport. A similar debate regarding the delay in onset of menarche in young female athletes across sports such as gymnastics, tennis and swimming is observed in the literature (Malina et al., 2013). Therefore, it is worthwhile considering whether it is inherent, or training induced changes in pain pathways or psychological approaches to pain that influence athletes pain responses.

Previous research into pain perception in athletes has reported pain tolerance and threshold values using a range of pain induction methods, including the cold pressor test, pressure algometry, electrical stimulation, heat and ischemia. It is important to identify the potential differences in responses to different types of pain stimuli when comparing the pain response results of different investigations (Tesarz et al., 2012). When looking at pain responses researchers typically focus on reporting statistically significant values. However, this does not always directly translate into clinical significance, especially when looking to apply results to 'real-world' scenarios if they have not used a pain model reflective of the pain type athletes would typically experience (Tesarz et al., 2012).

There has also been significant evidence that individuals experience an episode of acute exercise-induced analgesia (inability to feel pain) following intense exercise. While the exact mechanism of this phenomenon is not understood, it has been suggested that this could be linked to endogenous pain-modulatory mechanisms such as conditioned pain modulation (CPM), where pain inhibits further pain. One study investigated the effects of the CPM system (induced using the cold pressor test) on responses to different types of experimental pain. Athletes demonstrated significantly less sensitivity to mechanical pain but increased

sensitivity to vibration, while no significant difference was found for heat, cold or pressure pain thresholds, or for temperature and mechanical detection thresholds between athletes and controls. Athletes also demonstrated less CPM activation, which the authors suggest may result from continuous activation of this system, leading to a truncated response to the cold pressor task (Tesarz et al., 2013). Another study reported higher than average pressure pain thresholds and reduced pain intensity ratings during the same CPM test. However, they demonstrated a conflicting result where athletes demonstrated higher CPM responses compared to non-athletes. The authors of this paper proposed several factors, including the experimental design or characteristics of the research population, that may have influenced these results. However, the clear disparity between findings in these studies emphasises the importance of refining our understanding of pain responses in athletes (Flood et al., 2017).

Athletes and clinical experts need to be aware of the different types of pain experiences. Pain can be classified according to duration (acute or chronic), location (localised or general) or origin (physiological and pathological), as well as either benign or harmful. Doctors and health care professionals such as physiotherapists must ensure they have a strong understanding of the different types of pain athletes experience. While the treatment and prevention of specific injuries is often considered separate to pain management in athletes, both must be understood to ensure the best outcomes for patients. Therefore, it is vital to fill the gap in knowledge of specific responses to pain in athletes (Hainline et al., 2017).

Project Aims and Hypotheses

The primary gaps in the literature centre around the inconsistencies in reported physiological responses to thermal and chemical experimental pain and the appropriateness of methods used to test dancers and non-dancers pain experience in a laboratory setting.

It is hypothesised that both the cold pressor test and hypertonic saline infusion pain protocols are associated with significant physiological responses, including increased heart rate, blood pressure and MSNA. However, it is hypothesised that the cold pressor test is associated with greater increases in these variables, and greater perceived pain compared with the hypertonic saline infusion. Dancers are hypothesised to demonstrate greater autonomic responses and lower perceived pain during the two pain protocols compared to non-dancers.

The primary aim for this project was therefore to measure pain perception and physiological responses to two distinct types of experimental pain, a cold pressor task and a 5% hypertonic saline infusion into the tibialis anterior muscle. The secondary aim of this study was to pilot these protocols with groups of dancers and non-dancers to gain preliminary insights into the differences in pain perception and physiological responses between the two groups.

Methods

Ethics:

This study was approved by the Western Sydney University Human Research Ethics Committee in accordance with the National Statement on Ethical Conduct in Human Research 2007 (Updated 2018) (H14838).

Pilot Study:

As part of the experimental design process, the hypertonic saline (HS) infusion was piloted as a pain protocol with a 1ml/min bolus infusion. This produced a moderate pain intensity rating in three participants (peak pain of between 4 and 6 out of 10), hence was selected as an appropriate model for mechanical pain in the cohort. This was initially compared to an ischaemia protocol, in which a blood pressure cuff was inflated around the lower leg. However, the ischaemia protocol did not produce as significant a pain response and therefore was not included in the final study design. While there was no direct trial of the cold pressor test in comparison with the HS infusion for physiological responses and pain perception, both protocols have produced a measurable response in prior studies (Burton et al., 2009; Fagius, Karhuvaara & Sundlof, 1989).

Participants:

12 healthy participants were recruited for this study. All participants were cis female, aged between 19 and 48 (29 ± 8 years). Of the 12 participants recruited, nine were classified as non-dancers and three as dancers. Dancers were classified as those who were completing at least one performance-based dance activity as part of their weekly exercise. They also needed to have been completing regular dance activity for at least one year prior to the experiment. Non-dancers were categorised as those not completing any dance-based activities on a regular basis and had not participated in regular dance classes since early childhood. All participants were defined as healthy, with no history of musculoskeletal or

neurological conditions. Additional information about the participant demographics can be found in the results section.

Surveys:

All participants completed two surveys prior to coming in for testing. The first eligibility questionnaire confirmed the participants sex, age, health status and dancer/non-dancer classification. Participants also completed a medical and health history questionnaire with questions regarding medical screening for conditions, medical history, medication use, exercise habits, dance experience (dancers only), dance injury (dancers only) and lifestyle. A complete question list can be found in **Appendix 1** and **2**.

Physiological Response Measurements:

Participants attended the neurophysiology laboratory located in the School of Medicine building on Campbelltown Campus, Western Sydney University for a single 3-hr session. They were asked to refrain from caffeine 12 hours prior to the experiment and alcohol and rigorous exercise 24 hours prior to the experiment. This is standard practice to avoid factors that can contribute to activation of the sympathetic nervous system or cause pain that will influence the experiment reliability (Corti et al., 2002). Upon arrival, participants signed the consent form and completed the appropriate surveys. Participant's weight, height and BMI were measured before being comfortably seated in a semi-reclined position.

Prior to setting up physiological measurement equipment, participants were tested for pre-existing muscle pain hypersensitivity as can be caused by delayed onset muscle soreness (DOMS) which is typically experienced in the days following rigorous exercise. Underlying pain sensitivity could influence their response to the experimental pain protocols (Finocchietti, Graven-Nielsen & Arendt-Nielsen, 2015). A mechanical algometer was applied at a force of 30N on 5 points across the belly of the tibias anterior muscle of the lower leg (**Figure 1**). This force should not cause any discomfort or pain (Finocchietti, Graven-Nielsen & Arendt-Nielsen, 2015). Therefore, if pain was reported by the participant, this indicates DOMS and must be taken into consideration when interpreting the pain response. The

presence of DOMS was not deemed an exclusion criterium for completing the protocol. Across all participants, none reported any pain or discomfort at any of the 5 tested sites suggesting no presence of DOMS.

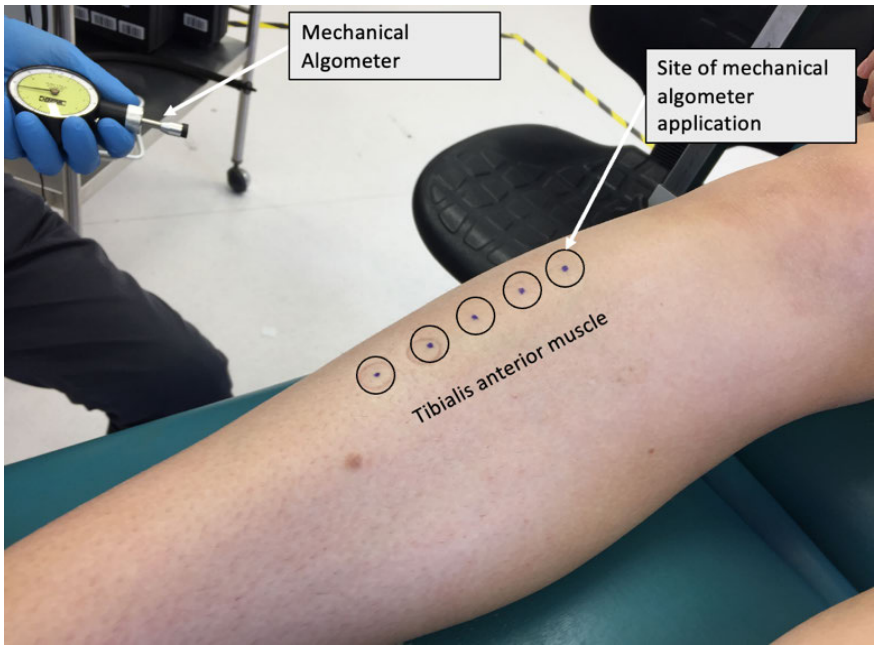

Figure 3: Sites of mechanical algometry application to the tibialis anterior muscle to test for DOMS. For baseline pain sensitivity testing, a mechanical algometer was applied at a pressure of 30N to 5 points across the tibialis anterior (TA) muscle. The TA is identified by palpation of the muscle belly. The 5 points identified were spread approximately 1cm apart across the muscle belly.

Cardiovascular, respiratory and MSNA responses were measured according to standard laboratory practices. These are described by Boulton et al. (2016) and a summary included here. A single lead (II) electrocardiogram (0.3 – 1 kHz) was recorded with Ag-AgCl surface electrodes (BioAmp, PowerLab, ADInstruments, Sydney, Australia) on the chest. Respiration was recorded using a strain-gauge transducer (DC-100 Hz; Pneumotrace II, UFI, Morro Bay, CA, USA) around the chest. Blood pressure was measured at the finger using height corrected continuous, non-invasive, beat-to-beat digital arterial plethysmography (Finometer Pro, Finapres Medical Systems, The Netherlands). The Finometer blood pressure measurement was calibrated during baseline using brachial blood pressure measurements

(Omron, Kyoto, Japan). Heart rate, respiratory rate and blood pressure act as indirect indicators of the activity of the nervous system (Boulton et al. 2016).

The technique of microneurography was employed to measure the activity of the sympathetic nervous system directly by recording electrical activity from the peripheral nerves that innervate smooth muscle in blood vessels supplying skeletal muscle. This nerve activity is called muscle sympathetic nerve activity (MSNA). The technique of microneurography, as described by Boulton et al. (2016) involves locating the common peroneal nerve at the fibular head using a 2 mm diameter probe delivering constant-current stimuli (0.2 ms pulses, 2 – 10 mA) at 1 Hz (Stimulus Isolator, ADInstruments, Sydney, Australia). A tungsten microelectrode (Frederick Haer and Co, Bowdoin, ME, USA) was inserted at a site overlying the common peroneal nerve. The site was decided based on where a muscle twitch could be elicited by application of external stimulation. The electrode was then advanced toward the nerve while delivering weak electrical stimuli (0.02 – 1 mA) through the microelectrode. An adjacent uninsulated microelectrode was inserted into the skin as a reference (Boulton et al. 2016). Twitches in the pretibial flexors at <20 μA indicates that the microelectrode was located in a muscle fascicle. Neural activity was amplified (gain 2×10^4) and filtered (bandpass 0.3 – 5.0 kHz) using an isolated amplifier and headstage (NeuroAmpEX, ADInstruments, Sydney, Australia), and stored on a computer (10 kHz sampling) using a PowerLab 16SP system (hardware) and LabChart 8 data acquisition system (software). The presence of activity due to muscle spindle activation when palpating or adjusting the muscle belly or tendon, absence of activity when the skin is lightly stroked was used to confirm the location of the microelectrode. The microelectrode tip was adjusted to record spontaneous bursts of MSNA (not triggered by muscle palpation) and maximize the signal to noise ratio of MSNA such that discrete negative-going spikes of MSNA were detected in an oligounitary recording in LabChart (Boulton et al. 2016). A calculation for root mean square was applied to the raw nerve signal to assist in clearly identifying MSNA spikes. Spikes were recognised through their distinct shape (downward going spikes on the raw nerve signal, distinct peaks on RMS channel) and sound (like ‘stepping on dried leaves’).

Experimental Protocol:

The protocol consisted of two 5-minute experimental pain tests, the cold pressor test and 5% hypertonic saline (HS) infusion. Each test was preceded by a stable baseline recording of at least 3 minutes and followed by a 3-minute recovery period. A summary of the full protocol can be found in **Figure 4**.

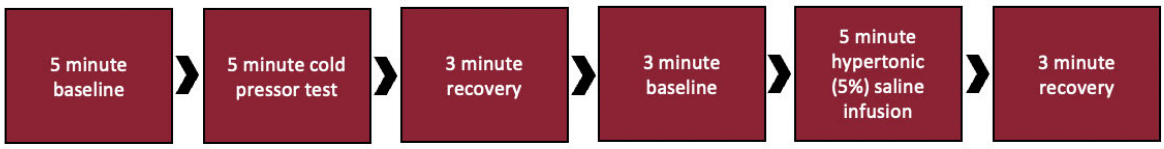

Figure 4: Representation of experimental protocol

A 5-minute baseline recording of all responses was first taken for participants. During this time, participants were asked to remain still, breathing quietly and avoid talking to ensure a clean recording. Following the baseline recording, the cold pressor test was conducted. When advised to do so, participants inserted their hand (up to the wrist) into a bucket of ice water (approx. 1°C, measured with standard thermometer). This was conducted in the contralateral arm to the arm being used to measure continuous blood pressure. The maximum time for the cold pressor test was 5 minutes. However, participants were not advised of this maximum time. Instead, they were asked to keep their hand in the ice water for as long as possible. However, if the sensation became unbearable, they could remove it. Following the cold pressor test, participants were advised to remain still once again, breathing quietly and avoid talking to record responses during a 3-minute recovery period. Additional recovery time was provided where required to ensure pain, heart rate and BP had returned to resting levels before commencing the rest period prior to the HS infusion.

A second 3-minute baseline was recorded prior to commencement of the HS infusion. Using the same leg as for the microneurography and DOMS testing, a sterile 5% HS solution was infused into the belly of the tibialis anterior muscle via a butterfly needle (Pump Elite 11; Harvard Instruments) (Smith et al. 2019). The HS was infused at a rate of 1mL/minute for the first minute only and turned off for the remaining 4 minutes of the test (5-minute total test

duration). Participants could advise if the pain became unbearable during the 1-minute infusion and the infusion would be stopped. After the 5-minute test, participants were instructed to remain still, breathe quietly, and refrain from talking for a 3-minute recovery period while recording their responses. After the 3-minute recovery period, the butterfly needle and all equipment used for physiological measurements were removed from the participants.

Pain Measurements

During and following both experimental pain protocols, participants were asked to report on the pain intensity and sensory and affective aspects of their pain experience. Participants were given a sliding visual analogue scale (VAS) and advised to rate their pain on a scale of 0 (no pain) to 10 (worst pain imaginable) consistently throughout the 5-minute cold pressor test and 5-minute HS infusion and recovery period afterwards. All pain intensity data is represented as a mean ± standard error. Following the 3-minute recovery for each pain protocol each participant was asked to complete the Short-Form McGill Pain Questionnaire (SF-MPQ) to rate the affective and sensory aspects of the pain experience. The full form can be found in **Appendix 3**. For each of the sensory and affective descriptors participants were asked to rate how well it described their experience of the pain on a scale from 0 (not applicable) to 3 (highly applicable). Participants also used this form to report on the overall perceived pain intensity on a scale of 0 (no pain) to 5 (excruciating) for the entire protocol.

Data Analysis

All data from the study were collated in password secured Excel spreadsheets for ease of representation and transferred to analysis software GraphPad Prism (GraphPad Prism 9; Dotmatics, Boston). The application of a password ensures the security of any participants personal information. Each participant was assigned a participant code for de-identification and only the primary researcher had access to the data.

Heart rate (beats/min), respiratory rate (breaths/min), respiratory height (relative change to baseline), systolic BP (mmHg), diastolic BP (mmHg), and mean arterial pressure (mmHg)

were calculated for all stages of the experimental protocol in the LabChart software. In LabChart, blood pressure was also calibrated to the brachial BP measurement taken during the baseline prior to the cold pressor and during the baseline prior to the HS infusion. All physiological responses were recorded for each one-min interval and the mean for each section (I.e., rest, pain and recovery periods). To address inter-individual variability in resting BP, data are also reported as percentage changes from baseline. Ensemble analysis software (Elucimed; Wellington, NZ) was employed to analyse the MSNA recordings in to determine MSNA burst frequency (bursts/min) and MSNA burst amplitude (au, relative to largest burst during baseline). Ensemble was used to calculate heart rate variability (HRV) using both time and frequency domains for baseline periods and during pain protocols. Specifically, high frequency HRV and the root mean square of successive differences between normal heartbeats (RMSSD) were determined as indicators of parasympathetic vagal modulation of heart rate.

For each participant, the mean pain intensity was determined for each minute of the pain protocols. The time to pain onset was noted in seconds from the start of the pain protocol. The peak VAS rating and the time taken to reach this peak (in seconds from the time of pain onset) were also recorded.

Statistical Analysis

All statistical analysis was conducted in Prism version 9 (GraphPad software, San Diego, CA). Two-way repeated measures ANOVAs were applied to the heart rate, BP and VAS data for all 12 participants. The analysis was conducted to determine whether there was a significant main effect of time (baseline and 1-min intervals during pain), main effect of pain model (cold pressor and HS infusion), and a significant interaction between time and pain model. Sidak's multiple comparisons test was used to compare each minute of the pain protocols against a 1-min baseline period. The 1-min period selected was three minutes prior to the start of the pain protocol to minimise the impact of anticipatory effects on physiological variables. Paired t-tests were used to compare the peak pain and time to pain onset data for the cold pressor test versus the HS infusion. For all tests, a probability level of $p < 0.05$ was regarded as significant. Data are represented as the mean ± standard error.

Correlational analysis was applied to determine any relationships between the maximum and average change in heart rate and BP from baseline and the peak pain intensity for the cold pressor test and HS infusion. Relationships were considered significant where $p < 0.05$. Strong associations were identified where the correlation co-efficient (r) was $0.5 < r < 1.0$ or $-1.0 < r < -0.5$.

Results

Physiological Responses:

Analysis of heart rate changes from baseline during the cold pressor test and HS infusion revealed a significant main effect of time ($p = 0.001$) and a significant interaction between time and pain model ($p = 0.05$). Heart rate during minute 1 of the cold pressor test (85 ± 4 beats/min) was significantly greater than baseline (73 ± 4 beats/min, $p = 0.006$, **Figure 5A**). Heart rate during minute 1 (71 ± 4 beats/min) and minute 5 of HS infusion (70 ± 3 beats/min) did not reach statistical significance from baseline (67 ± 3 beats/min, $p = 0.06$). Due to the inter-individual variability in baseline heart rate, changes in heart rate were also compared as percentage changes from baseline. The same main effects of time ($p = 0.0006$) and time and model interaction ($p = 0.04$) were observed.

There was a significant main effect of time on systolic BP ($p = 0.001$) and a significant interaction between time and pain model ($p = 0.0008$). Systolic BP was significantly greater than baseline (113 ± 2 mmHg) during minute 2 (127 ± 5 mmHg, $p = 0.01$), minute 3 (127 ± 5 mmHg, $p = 0.009$) and minute 4 (122 ± 4 mmHg, $p = 0.04$) of the cold pressor test (**Figure 5B**). Due to the inter-individual variability in baseline systolic BP, changes in systolic BP were also compared as percentage changes from baseline. The same main effects of time ($p = 0.0008$) and time and model interaction ($p = 0.0003$) were observed. However, a significant effect of the model on changes in systolic BP was also seen ($p = 0.004$), with greater increases in systolic BP during the cold pressor test compared with the HS infusion.

There was a significant main effect of time on diastolic BP ($p < 0.0001$) and a significant interaction between time and pain model ($p < 0.0001$). Diastolic BP was significantly elevated above baseline (72 ± 3 mmHg) during minute 2 (81 ± 4 mmHg, $p = 0.003$), minute 3 (81 ± 3 mmHg, $p = 0.003$), minute 4 (79 ± 4 mmHg, $p = 0.009$) and minute 5 (79 ± 4 mmHg, $p = 0.03$) of the cold pressor test (**Figure 5C**). Due to the inter-individual variability in baseline diastolic BP, changes in diastolic blood pressure were also compared as percentage changes from baseline. The same main effects of time ($p < 0.0001$) and time and model interaction (p

< 0.0001) were observed. However, a significant effect of the model on changes in diastolic BP was also seen (p = 0.0002), with greater increases in diastolic BP during the cold pressor test compared with the HS infusion.

Analysis of mean arterial blood pressure (MAP) revealed a significant main effect of time (p < 0.0001) and a significant interaction between time and pain model (p < 0.0001). MAP was significantly elevated above baseline (85 ± 2 mmHg) during minute 2 (97 ± 4 mmHg, p = 0.002), minute 3 (98 ± 4 mmHg, p = 0.001), minute 4 (95 ± 4 mmHg, p = 0.004) and minute 5 (95 ± 4 mmHg, p = 0.01) of the cold pressor test (**Figure 5D**). MAP was also significantly greater than baseline (91 ± 2 mmHg) during minute 5 of the HS infusion (92 ± 3 mmHg, p = 0.04). Due to the inter-individual variability in baseline MAP, changes were also compared as percentage changes from baseline. The same main effects of time (p < 0.0001) and time and model interaction (p < 0.0001) were observed. However, a significant effect of the model on changes in MAP was also seen (p = 0.0001), with greater increases in MAP during the cold pressor test compared with the HS infusion.

Analysis of high frequency heart rate variability (HF HRV) and RMSSD for HRV revealed no significant difference between baseline and pain, with no effect of pain model or time/model interaction (p > 0.05).

A paired t-test confirmed no significant differences in baseline measures of BP prior to the cold pressor test and the HS infusion (P > 0.05). However, a difference was observed in baseline heart rate, with heart rate being significantly higher during the cold pressor test baseline (73 ± 4 beats/min) than the HS infusion baseline (67 ± 3 beats/min, p = 0.01). A one-way repeated measures ANOVA including each minute of the cold pressor test baseline revealed a significant change in heart rate over the course of the baseline period, with heart rate rising slightly prior to the test (p = 0.03). Similar patterns were observed during the baseline period prior to the HS infusion baseline (p = 0.01), albeit at lower heart rates than cold pressor test. Specifically, heart rate three minutes prior to the start of the cold pressor test (73 ± 4 beats/min) was significantly higher than five minutes prior (70 ± 4 beats/min, p = 0.02). Heart rate in the minute prior to the HS infusion (70 ± 3 beats/min) was significantly higher than three minutes prior to the infusion (67 ± 3 beats/min, p = 0.03).

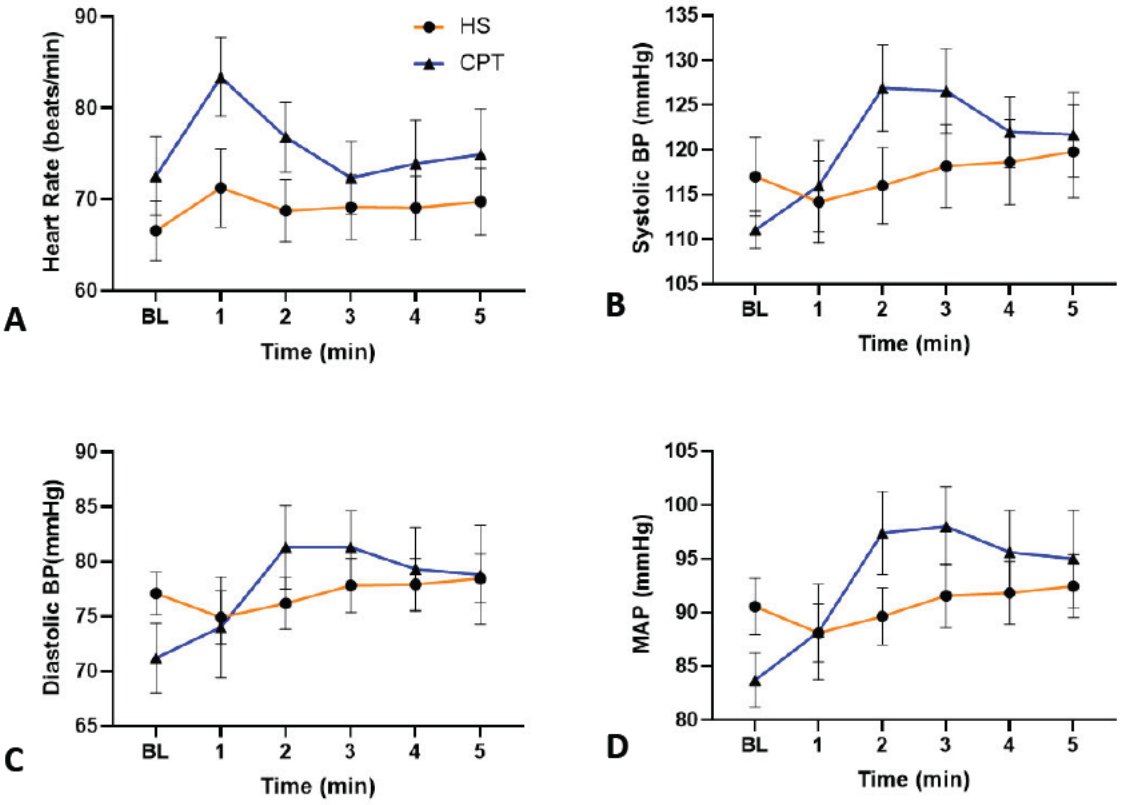

Figure 5: Physiological responses to cold pressor test and HS infusion. Changes during cold pressor test represented as triangles with blue line, changes during HS infusion represented as circles with orange line. All data represented as the mean ± standard error. A.) Heart rate responses (beats/minute), B.) Systolic blood pressure responses (mmHg), C.) Diastolic blood pressure responses (mmHg), D.) Mean arterial pressure responses (mmHg). BL, baseline.

Spontaneous MSNA data could only be collected in three of the 12 participants, therefore no statistical analysis was performed on these values. **Figure 6** displays the individual participant data for MSNA frequency (**6A and B**) and amplitude (**6C and D**).

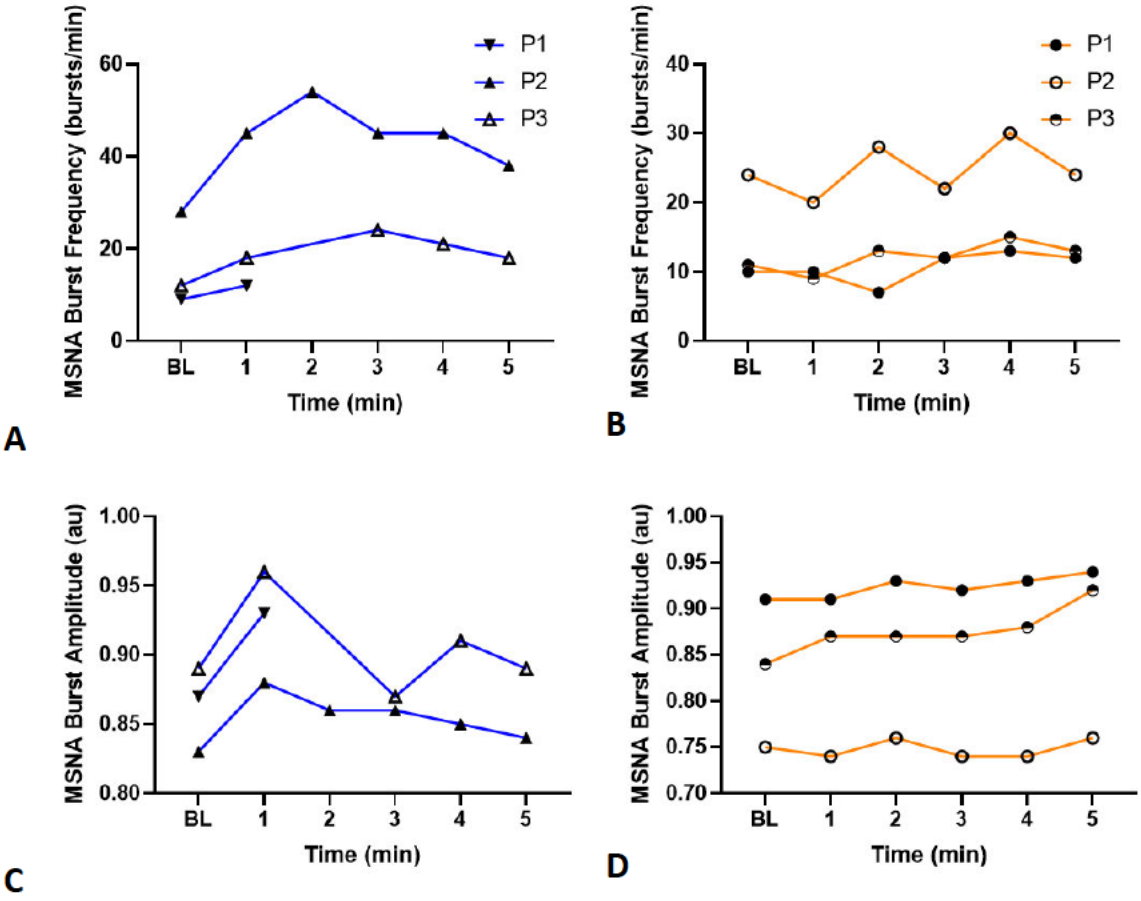

Figure 6: MSNA during the cold pressor test and HS infusion. A.) MSNA burst frequency (bursts/min) during the cold pressor test represented as triangles for each participant. B.) MSNA burst frequency (bursts/min) during the HS infusion represented as circles for each participant. C.) MSNA burst amplitude (μV, normalised to largest burst) during the cold pressor test represented as triangles for each participant. D.) MSNA burst amplitude (μV, corrected to largest burst) during the HS infusion represented as triangles for each participant. Participant 1 (P1) and 3 (P3) are dancers and participant 2 (P2) is a non-dancer. P1 was unable to complete more than one minute of the cold pressor test.

Pain Perception:

Statistical analysis of reported pain intensity revealed a significant effect of time ($p < 0.0001$). As illustrated in **Figure 7**, compared to minute 1 of the cold pressor test (3 ± 0 VAS), a significant increase in pain intensity was observed during minute 2 (5 ± 0 VAS, $p = 0.0004$), minute 3 (6 ± 0 VAS, $p = 0.003$), minute 4 (6 ± 0 VAS, $p = 0.003$) and minute 5 (6 ± 0 VAS, p =

0.005). Similarly, compared to minute 1 of the HS infusion (2 ± 0 VAS), a significant increase in pain intensity was observed during minute 2 (4 ± 1 VAS, p = 0.001), minute 3 (5 ± 1 VAS, p = 0.0009), minute 4 (5 ± 1 VAS, p = 0.0002) and minute 5 (4 ± 1 VAS, p = 0.0001).

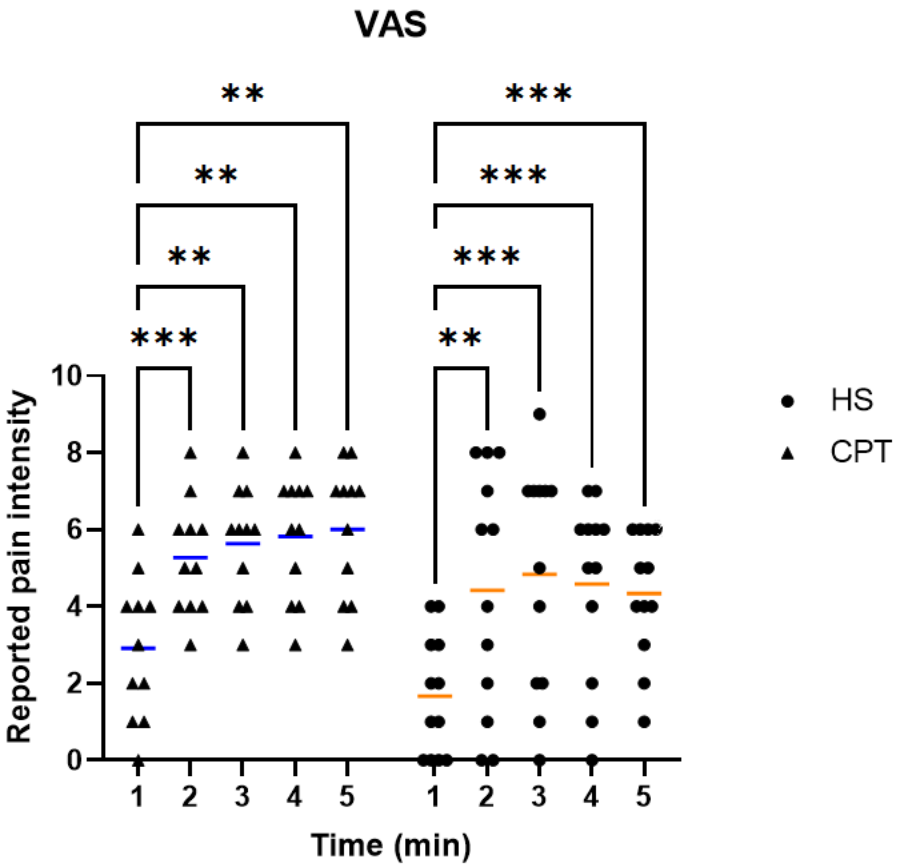

Figure 7: Reported pain intensity during the cold pressor test and HS infusion. Data shown as triangles for the cold pressor test and circles representing the HS. Blue lines represent the average pain intensity for the cold pressor test at each time point and orange line represents the average pain intensity for the HS infusion at each time point.

Analysis of the peak reported pain intensity revealed a significant difference between the peak pain during the cold pressor test (7 ± 0.5 VAS) compared with the HS infusion (6 ± 0.4 VAS, p = 0.02). There was also a significantly lower pain threshold (time to pain onset) for the cold pressor test (15 ± 3s) compared with the HS infusion (40 ± 10s, p = 0.02). The time to peak pain from pain onset did not demonstrate a significant difference between the cold pressor test (177 ± 40s) and the HS infusion (134 ± 23s).

The SF-MPQ enabled participants to report on the sensory and affective characteristics of the pain for each of the protocols. The most selected sensory characteristics for the cold pressor test were aching (n = 10), sharp (n = 10) and throbbing (n = 10) and for the HS infusion were aching (n = 10), throbbing (n = 9), sharp (n = 8) and heavy (n = 8). Tiring/exhausting (n = 4) and punishing/cruel (n = 4) were the most frequently selected affective characteristics for the cold pressor test, and tiring/exhausting (n = 4) was the most frequently selected for the HS infusion. 'Distressing' was the most selected perceived pain intensity descriptor (n = 6) for the cold pressor test, and 'discomforting' was the most selected for the HS infusion (n = 5).

Correlation between pain perception and physiological responses:

Correlational analysis between the peak pain intensity and peak changes in heart rate, systolic BP, diastolic BP and MAP from baseline revealed no significant relationship for either pain model ($p > 0.05$). No significant relationships were observed between the mean pain intensity and the mean changes in heart rate and BP for both the cold pressor test and HS infusion ($P > 0.05$).

Dancers and non-dancers:

From the participants recruited, three of 12 were classified as dancers. As the dancer and non-dancer groups consisted of an uneven number of participants, comparisons between the two may be considered unreliable. However, a descriptive presentation of the physiological responses and pain perception for the two groups is provided to support the generation of future hypotheses.

Dance history and injury

Dancer participants reported attending between two and four formal dance classes per week, between 180 - 360 minutes in total duration. Of the three dancers, only two reported also completing other types of physical activity, including walking, running, swimming, yoga, pilates, weightlifting and cycling. Dancers commenced between the ages of two and five,

with two of the three dancers taking no breaks from dancing from when they commenced to the time of the study. Styles of dance completed by the participants include ballet (n = 3), jazz (n = 3), tap (n = 3), lyrical/contemporary (n = 2), hip hop (n = 2), musical theatre (n = 3) and ballroom (n = 1). Only one of the three dancers reported participating in solo dance, but all three dancers also participate in group dance. In addition, all dancers reported dancing for recreation and enjoyment, but one also danced competitively and as part of their employment. All dancers reported warming up before dance class/rehearsal and performances. Only one reported warming up before other types of activity and cooling down after dance class/rehearsal, performances and other types of activity.

Only one participant reported experiencing a dance related injury within the 12 months prior to the study. However, two participants reported experiencing at least one serious injury (2-3 injuries) throughout their dance career. Serious injuries were described for the purpose of this study as those requiring medical intervention and/or prevented the participant from continuing dance or physical activity during recovery. The sites selected for these injuries were ankle (n = 1), knee (n = 2), foot (n = 1), shoulder (n = 2) and toe (n = 1). When describing the nature of the injury, one person identified that their injury comprised of torn ligaments due to repetitive dance related strain, and that this required surgery on both the knee and shoulder. The other participant reported a torn muscle in the foot and a dislocated shoulder due to a dance lift, both requiring physiotherapist intervention. When reporting on injury behaviour, both participants indicated they sought medical advice and continued to dance but modified their practices. Only one told members of their dance company about their injury.

Physiological responses

Figure 8A illustrates the heart rate responses to the cold pressor test in dancers and non-dancers. The peak change in heart rate from baseline was of 17 ± 8 beats/min in dancers and 12 ± 2 beats/min in non-dancers. Baseline heart rates prior to the cold pressor test were 85 ± 3 beats/min for dancers, and 70 ± 5 beats/min for non-dancers. Heart rate responses to the HS infusion are shown in **Figure 8B**. Peak changes in heart rate were 10 ± 3 beats/min in dancers and 8 ± 1 beats/min in non-dancers. Baseline heart rates prior to HS infusion were

69 ± 5 beats/min for dancers, and 66 ± 4 beats/min for non-dancers. Heart responses appear to have been skewed by one participant having a higher resting heart rate but smaller changes in heart rate response during the cold pressor test and HS infusion compared to the other two participants.

Figure 8 (C, E, G) depicts similar BP response patterns to the cold pressor test amongst dancers and non-dancers, with elevations in BP that are sustained during minutes two to five of the test. **Figure 8 (D, F, H)** suggests stable BP in non-dancers during HS infusion, with initial falls in BP in the dancers that warrant further investigation.

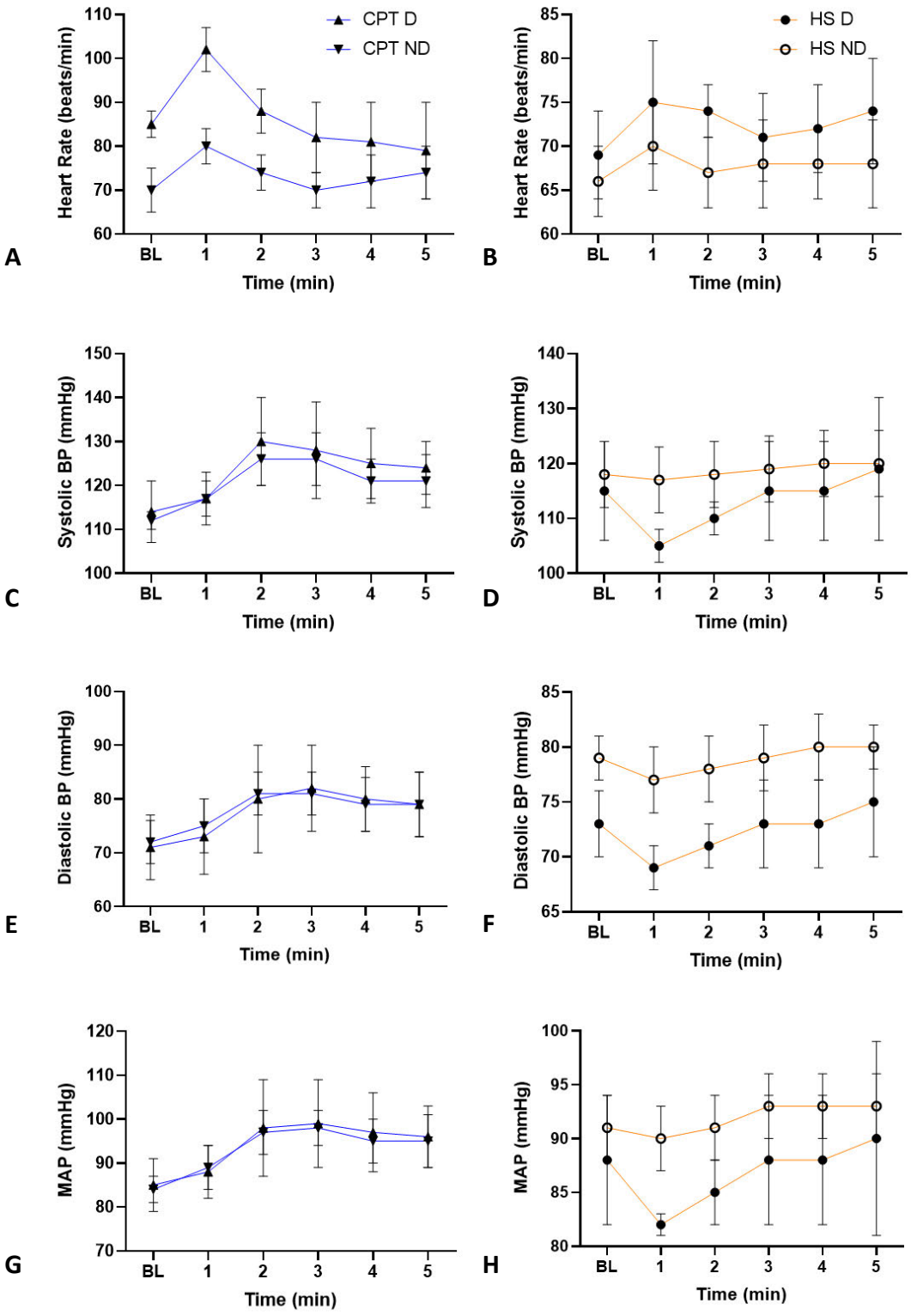

Figure 8: Physiological responses in dancers (n = 3) and non-dancers (n = 9) during the cold pressor test and HS infusion. Changes during cold pressor test represented as triangles with blue line, changes during HS infusion represented as circles with orange line. In cold pressor test data (**A, C, E, G**), dancers are represented with an upwards triangle, while non-dancers

are represented by a downwards triangle. In HS infusion data (**B, D, F, H**), dancers are represented with a filled circle while non-dancers are represented by an open circle. All data represented as the mean ± standard error. A, B.) Heart rate responses (beats/minute), C, D.) Systolic blood pressure responses (mmHg), E, F.) Diastolic blood pressure responses (mmHg), G, H.) Mean arterial pressure responses (mmHg).

Pain perception

During the cold pressor test, the mean pain intensity was rated as 4 ± 1 by the dancers, and 6 ± 0 by non-dancers. The mean pain intensity for the HS infusion was 4 ± 1 for both dancers and non-dancers (**Figure 9**). Dancer and non-dancers' peak pain, time to pain onset and time to peak pain are reported in **Table 4**.

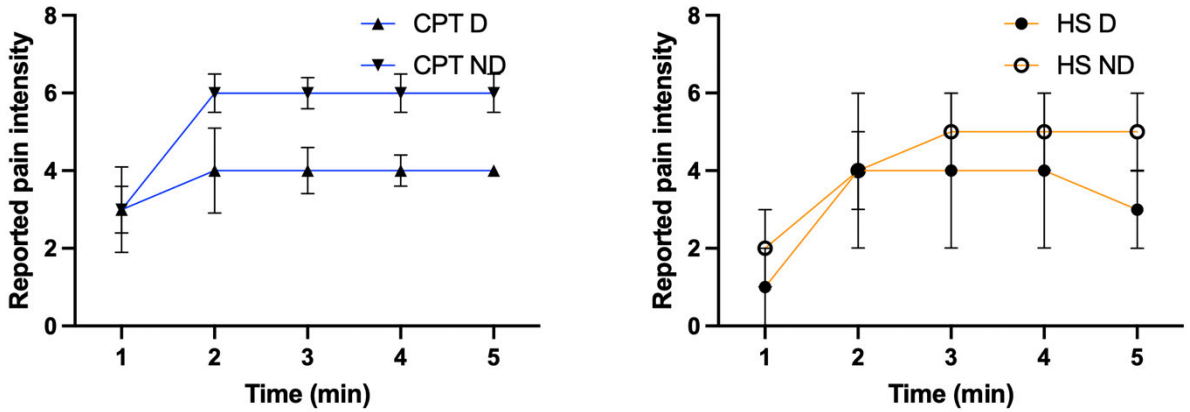

Figure 9: Reported pain intensity during the cold pressor test and HS infusion. Data reported as for both dancers (triangles and closed circles) and non-dancers (upside down triangles and open circles). Blue lines represent the average pain intensity for the cold pressor test at each time point and orange line represents the average pain intensity for the HS infusion at each time point.

Table 4: Dancer and non-dancer peak pain, time to pain onset and time to peak pain.

Pain variable	**Dancers (n=3)**	**Non-Dancers (n=9)**
Peak pain		
Cold pressor test	6 ± 1	8 ± 1
HS infusion	5 ± 2	6 ± 1
Time to pain onset (s)		
Cold pressor test	19 ± 12s	13 ± 2s
HS infusion	51 ± 27s	37 ± 11s
Time to peak pain (s)		
Cold pressor test	108 ± 72s	200 ± 50s
HS infusion	112 ± 50s	141 ± 37s

Discussion

In this thesis, physiological responses and pain perception were compared between two experimental pain protocols: the cold pressor test and hypertonic saline infusion. As hypothesised, the cold pressor test was associated with greater increases in blood pressure and heart rate, as well as greater perceived pain. Contrary to the hypothesis, physiological responses to pain were not correlated with reported levels of pain within the group, meaning that individuals reporting the highest levels of pain did not necessarily experience the greatest cardiovascular response for either pain model. The differences between the two pain models, which could reflect the specificity of responses based on pain type, emphasise the importance of considering the target population and research question when deciding on appropriate pain protocols.

Anticipatory responses:

Physiological responses to experimental pain can act as proxy indicators of nervous system activation. For this study, changes in heart rate, blood pressure and MSNA were analysed to develop insights into how participants respond to the two different types of experimental pain, thermal (cold pressor test) and chemical (HS infusion). Analysis of baseline data revealed significant higher heart rates prior to the cold pressor test compared with the HS infusion. Importantly, this is a critical indicator that there was no residual physiological effect of the cold pressor test that interfered with the responses to the HS infusion. When examining heart rate during the five minutes prior to the cold pressor test, it is revealed that heart rate began to steadily increase from minute 3 of this time period. This suggests a potential anticipatory response to the cold pressor test. Conversely, for the HS infusion, the needle is inserted well before the infusion commences and enough time was allowed for any responses to this to settle prior to starting the baseline recording. The minute of baseline that was three minutes prior to the start of each protocol was chosen a priori, specifically to avoid anticipatory effects. However, the evidence suggests that anticipatory responses prior to the cold pressor test may occur earlier and therefore measures could be considered in future studies to remove visual or auditory cues about when the test will start.

Early physiological responses:

No significant changes were observed in respiratory rate during each pain protocol. It is important during experimental pain protocols to instruct participants to breathe as consistently as possible, particularly at the start of the cold pressor test were there can be a tendency for a sharp intake of breath or for holding one's breath. This is associated with blood pressure changes and increased MSNA activity (Apelt-Glitz et al., 2022), and could therefore mask or exaggerate a physiological response to pain. The consistent respiratory rate in this study emphasises that the significant increases in blood pressure and heart rate are associated with the pain stimuli as opposed to changes in respiratory activity. Similar responses were recorded in a previous study where no significant changes were observed in the respiratory rate during the cold pressor test (Apelt-Glitz et al., 2022).

A statistically significant increase in heart rate was observed during the first minute of the cold pressor test. This increase was observed when analysing both the raw heart rate data and the percentage change compared to baseline. Representing the physiological responses as percentage changes from the corresponding baseline accounts for natural inter-individual variability in resting levels and enables more accurate comparison between participants. Heart rate changes have not been consistently reported as either increasing or decreasing during pain in prior literature. However, increases in heart rate associated with stronger activation of the sympathetic nervous system are typically associated with noxious stimulation. Kakon et al. (2021) found that, during the cold pressor test, heart rate showed an increase in some participants, but not in all. An earlier study investigating the correlation between heart rate and pain revealed a relationship present between the two characteristics in males but not females (Tousignant-Laflamme, Rainville & Marchand, 2005). The lack of relationship between heart rate response and pain in the current study, consisting solely of females, is consistent with this, although it is not currently clear why sex differences in such relationships may exist. Heart rate is the only characteristic in this study where every participant showed an increase during the first minute of the cold pressor test. Since the difference in heart rate between baseline and minute 1 of HS infusion did not reach statistical significance ($p = 0.06$), a greater sample size would be required to determine

whether similar response patterns exist for HS infusion, albeit involving smaller increases in heart rate. In contrast to heart rate, BP during the cold pressor test was still rising during the first minute, before sustained elevation from minutes 2 to 5.

Subsequent physiological responses:

In line with previous studies, there was a combination of participants who demonstrated a consistent increase in heart rate across the entire cold pressor test and those whose heart rate decreased after the first minute of the test. Mourot, Bouhaddi and Regnard (2009) separated participants into two groups according to their cold pressor test response: those whose heart rate increased and those whose heart rate decreased. It was found that heart rate was significantly higher in the second and third minute for the cold pressor test for the increasing group, and heart rate increased during the second minute and then decreased afterwards in the decreasing group. This was proposed to reflect increased sympathetic activity and reduced cardiac vagal outflow in response to the cold pressor test in the increasing group, and the opposite trend in the decreasing group (Mourot, Bouhaddi & Regnard, 2009).

A sustained elevation in blood pressure was observed from minute 2 of the cold pressor test. Blood pressure changes are directly correlated with MSNA which controls vasoconstriction of the muscle vasculature. Several studies report an increase in MSNA and consequently blood pressure during the cold pressor test (Burton, Fazalbhoy & Macefield, 2016; Coovadia et al., 2022; Kakon et al., 2021). Therefore, the blood pressure responses during the cold pressor test, alongside the small subset of MSNA burst frequency responses, are consistent with previous studies. No statistical analysis was performed on the MSNA data due to the limited number of participants in which MSNA was recorded. However, the patterns observed in MSNA burst frequency during the cold pressor test are in line with the blood pressure changes, in contrast to MSNA burst amplitude which demonstrates an early peak and warrants further investigation. Sacco et al. (2013) discuss the relationship between blood pressure and pain, and specifically the activity of an endogenous pain regulatory network in which the sympathetic nervous system plays an important role. According to Sacco et al. (2013), blood pressure changes correlate positively with pain threshold, meaning as blood pressure increases so does pain threshold. Meanwhile blood pressure correlates

negatively with perception of pain stimulus intensity (Sacco et al., 2013). As sympathetic activity causes an increase in blood pressure, this supports the idea that the increase in sympathetic activity may reflect a mechanism of managing or coping with pain.

In contrast to the cold pressor test, the physiological responses to the HS infusion failed to reach statistical significance, bar MAP during minute 5. Prior studies using the hypertonic saline infusion demonstrate divergent responses, with some individuals experiencing increases in heart rate, MSNA and blood pressure, and others experiencing decreases in these variables during the HS infusion (Burton, Fazalbhoy & Macefield, 2016). It is possible in the current study that the presence of both positive and negative responders may have neutralised the presence of any significant physiological responses to HS infusion. The physiological responses to the cold pressor test are, in comparison, more consistent between individuals. The chosen method of the HS infusion for this study was an infusion over 1 minute. However previous studies have used a continuous infusion over much longer time periods, which may result in different pain experiences (Burton et al., 2009; Fazalbhoy, Birznieks, & Macefield, 2012). These differences in pain experience could explain the differences in the observed changes in physiological responses between this study and prior work, and a longer infusion may have led to greater increases in BP.

According to previous studies, both the cold pressor test and HS infusion are associated with an increase in sympathetic activation and associated physiological responses. However, this study indicates that the physiological responses are greater and more uniform for the cold pressor test compared to the HS infusion, particularly for blood pressure. Although the consistent physiological responses to the cold pressor test may be beneficial for driving a predictable change in BP, the HS infusion may provide more opportunities for investigating inter-individual variability in perceived pain and physiological responses. Furthermore, choosing an appropriate pain model is critical as this study demonstrates that different models instigate different physiological responses. For results to be applicable to the target population, a pain model that accurately reflects the type of pain experienced in that group should be selected. For example, in a dancer cohort, as musculoskeletal pain is the most common pain type, experimental protocols that mimic this type of pain, such as the HS infusion, will induce responses that more accurately reflect their responses to pain on a day-

to-day basis in the industry. Prior studies of responses to experimental pain in dancers have used only the cold pressor test as a pain stimulus (Paparizos et al. 2005, Tajet-Foxell et al. 1995). However, temperature related noxious stimuli are not an accurate reflection of the type of pain typically experienced by dancers. In addition, pilot studies should be conducted to test the different methods of HS infusion and identify the type of protocol that most accurately reflects the type of pain experienced by dancers.

Pain perception:

Responses to pain were measured according to pain intensity and sensory affective characteristics. The average pain intensity was generally higher during the cold pressor test compared to the HS infusion. However, for both pain models, pain increased over the first minute and remained elevated for minutes 2 to 5 of the test. The peak pain was significantly higher during the cold pressor test compared to the HS infusion and as expected, the pain onset was significantly later during the HS infusion compared to the cold pressor test. As the participants hand was immersed in the ice water for the entire duration of the cold pressor test, the sustained pain intensity aligns with the anticipated pain response. The onset of pain was anticipated to commence later for the HS infusion protocol due to the full bolus infusion occurring over the first minute. However, the sustained pain levels throughout the 5-minute protocol suggests that this model may be useful for longer-term models that emulate the mechanical pain experienced by athletic populations. Therefore, trialling different types of the HS infusion protocol, whether a bolus infusion or continuous infusion, to create the best mimic of pain experienced by dancers is important to ensure that the responses to experimental pain are clinically relevant.

The most selected sensory descriptors for the pain during the cold pressor test were aching, sharp and throbbing, compared to just aching for the HS infusion. The difference in the sensory descriptions reinforces the difference in how the type of pain affects how the pain is perceived. In comparison, the affective characteristics were more similar across the cold pressor test and HS infusion indicating both were unpleasant. Perception of pain is not uniform for an individual across all pain types. Therefore, future studies need to use appropriate pain models to accurately reflect how a group of participants may perceive

contextually relevant pain. It is possible that differences in pain perception between models in this study is the effect of not randomizing the protocol. The longer-lasting effects of the HS infusion meant that this protocol was always completed after the cold pressor test. The pain perception measurements used in this study asked participants to rate the pain intensity compared to their worst pain imaginable. By having the cold pressor test task first, this acts as a recent comparison point for rating the intensity and unpleasantness of the HS infusion. Participant interpretation of whether the HS infusion was more or less unpleasant compared to the cold pressor test could therefore be reflected in the results, as opposed to their perception of it in the context of all their pain experiences.

No strong correlations were observed between the perceived pain intensity and the changes in physiological responses during each pain protocol, which may be related to the power of the study. In the past, increased physiological responses were associated with decreased pain intensity rating (Saccò et al., 2013). However, the findings of other studies indicate that increases in heart rate are positively correlated with pain intensity during the cold pressor test (Kakon et al., 2021). The differences in this study could be attributed to the smaller sample population for this study as well as the potential sex differences contributing to results in the earlier study.

Cold pressor test compared to HS infusion as an experimental pain model:

Based on the significant changes in physiological responses and pain perception measurements, both the cold pressor test and HS infusion act as effective pain models to induce both a physiological response and rateable pain. However, there are clear differences in the blood pressure and heart rate responses between the two tests as well as the peak pain and pain threshold. Therefore, researchers need to be mindful of selecting an appropriate pain model for the research question to ensure the results reported are clinically relevant.

In addition, the cold pressor test involves a thermal stimulus, and therefore may also be associated with changes in vasoconstriction at the surface and associated blood pressure changes to regulate temperature. The vasoconstriction of surface blood vessels could be

linked to changes in blood pressure. Because of this confounding factor, physiological responses need to be carefully interpreted during the cold pressor test as they may not solely be a reflect of the pain stimuli, but the body's attempt at restoring homeostasis (Fagius, Karhuvaara & Sundlof, 1989). Peckerman et al., (1994) introduced this concept when investigating the cold pressor response, determining that pain related responses were associated with increases in cardiac output and total peripheral resistance while non-pain related cold pressor responses were only linked to peripheral resistance changes. It is important when selecting and trialling experimental pain protocols that they not only reflect the type of pain typically experienced by a cohort but also that the confounding factors that could influence physiological responses such as vasodilation or respiratory changes are minimised.

Dancers and non-dancers' physiological responses:

Preliminary analysis of the dancer and non-dancers' responses to the cold pressor test and HS infusion provided some insights into potential differences between the two groups. Based on the patterns in the current study, it is worth exploring further whether dancers consistently experience greater heart rate responses during both pain protocols compared to non-dancers. In doing so, it could be confirmed whether blood pressure responses during the cold pressor test are indeed consistent between the two groups . The pooled participants in this study did not demonstrate any correlations between pain intensity and physiological responses. However, the idea that the sympathetic nervous system plays a role in modulating pain perception, could still be explored in dancer and non-dancer cohorts separately, given the differences in their lived experience of pain.

Due to the significant disparity in the number of dancer and non-dancer participants, no claims about the differences in physiological responses between the groups can be made with certainty. However, the preliminary insights suggest there could be differences in pain perception and physiological responses to explore, thus emphasising the importance of continuing to perform research in this field. In particular, the known association between sympathetic activity and reduced pain intensity rating in the general population (Sacco et al.,

2013) would be important to investigate to see if dancers have altered sympathetic reactivity that could contribute to how they manage pain and injury.

Dancers and non-dancers pain perception:

The preliminary results indicate that there is a potential difference between dancers and non-dancers rating of the pain intensity that warrants further in investigation. The apparent tendency for dancers to rate the pain intensity lower than non-dancers for both the cold pressor test and the HS infusion could be examined with a larger sample size. Such a difference could point to a greater pain tolerance in dancers, which does align with previous studies investigating pain perception in dancers during the cold pressor test (Paparizos et al. 2005, Tajet-Foxell et al. 1995). However, it must be noted that one of the dancers did not complete the cold pressor test beyond 40 seconds, which does not align with this theory. Prior exposure to particular types of pain should be taken into account and given that the cold pressor test is not reflective of the type of pain typically experienced in a dancer population, the responses to this pain protocol may not accurately reflect the overall pain sensitivity of dancers in a dance context. The hypertonic saline infusion to our knowledge has not been used previously as a form of pain stressor in this population, and expanding this work will therefore contribute new knowledge of how dancers respond to experimental pain aiming to mimic the pain experienced in a dance environment. While not assessed for statistical significance, the patterns observed in the pain responses suggest that the time course of pain should be explored between dancer and non-dancer groups, with the hypothesis that pain intensity increases later in the cold pressor test and hypertonic saline protocol compared to non-dancers. A future aim could be to determine whether dancers demonstrate a higher pain tolerance compared to non-dancers regardless of the type of pain, or whether it is specific to a particular pain stimulus Finally, the pilot data highlight the importance of investigating dancers' recovery during both the protocols, which preliminary response patterns indicate could commence sooner than the non-dancers, signifying a greater pain resilience or differences in coping mechanisms that enable faster reduction of pain intensity in dancers.

When reviewing the SF-MPQ responses, dancers tended to report lower values for both sensory and affective measures compared to the non-dancers. Future studies will test the hypothesis that dancers to not feel the intensity and unpleasantness of pain sensations as strongly as non-dancers. Previous studies have reported mixed results with regards to these pain perception measures during the cold pressor test (Paparizos et al. 2005, Tajet-Foxell et al. 1995). While this study does seem to initially support dancers demonstrating reduced pain sensitivity, these results must be interpreted cautiously due to the small and uneven numbers of dancers compared to non-dancers.

Preliminary insights into dancers and non-dancers pain responses:

Based on prior literature, we would anticipate that dancers could demonstrate increased physiological responses compared to non-dancers as a mechanism of reducing pain perception. This would correlate with their reported reduced pain sensitivity and the tendency for dancers to continue dancing through injury. Further investigation is required to report with certainty whether this may be the case. In particular, this needs to be reported based on relevant pain protocols that mimic the type of pain experienced by dancers, such as the HS infusion. The insight into the potential mechanisms behind how dancers' perception of pain intensity is reduced would provide important information for dancers and clinical experts that will enable to them to better understand and manage injury pain.

Methodological considerations:

Two distinct experimental pain protocols formed this study, each resulting in a distinct type of pain sensation. One potential limitation of the protocol is that the order of these two tests was not randomised, with all participants first completing the cold pressor test and then the HS infusion. It was decided that the order of the experimental pain protocols would not be randomised due to the different and observably inconsistent recovery times of the two pain protocols. Typically, participants recover quicker from the cold pressor test (a form of acute pain), while the HS (as a longer-lasting pain) can cause dull muscle aches for up to 24 hours following the protocol (Smith et al., 2019). Therefore, to minimise potential overlap in physiological or pain responses between the two tests, the cold pressor test was always

conducted first. Participants were also asked whether their pain had completely dissipated from the cold pressor test prior to commencing the baseline recording for the HS infusion. The butterfly needle for the HS infusion was also inserted and time allowed for any physiological responses to the needle insertion to dissipate prior to starting the HS infusion. However, one flaw lies in the subjective nature of pain experience. When rating the intensity or unpleasantness of the pain, participants may have been inclined to report the pain experience of the HS in comparison to the cold pressor test, as opposed to their usual pain baseline. However, what has been identified throughout reviews of previous literature and this study is that the cold pressor test causes a pain type that is not typical of the pain experienced in a dance environment. Therefore, the cold pressor test may not need to be included for future studies. Instead, other activities known to activate the SNS such as breath holds can be used to test for sympathetic activation or those related to physical activity such as a hand grip, could be integrated into the study.

Another potential area for amendment is how the HS protocol is conducted. The HS can be infused as either a bolus injection of a certain volume, as was used in this study, or as a continuous infusion. The bolus injection was chosen in order to provide some levels of consistency with the duration of the cold pressor test, which is unlikely to have been tolerated for much longer than five minutes in many participants. The benefit of a continuous infusion is that the infusion rate can be modified to achieve a consistent level of pain between participants, as well as potentially simulate a longer lasting pain type. This longer lasting pain may be more consistent with the duration of pain experienced by dancers. Therefore, for future studies, trialling different methods for saline infusion to identify how to simulate dance related pain most accurately would be beneficial. If male participants are also included in future studies, the potential role of HS dose also needs to be considered in the experimental design. As men can have a higher muscle mass, the dose levels of HS infusion may need to be tailored to male and female participants to provide a more equitable comparison between the two groups. This has been observed in prior studies, where providing different doses in males and females led to similar perception of pain intensity (Yekkalam et al., 2019).

The final number of participants consisted of an uneven number of dancers and non-dancers, with under-representation of dancers. In addition, not all physiological responses were able to be obtained for every participant recruited. This may limit the reliability of the statistical analysis as all results are based on lower participant numbers. In order to trust that the potential differences between dancers and non-dancers are accurate, a greater number of dancers would need to be recruited in future studies. One piece of feedback received about the recruitment process was that the duration of the protocol was too long a commitment for some interested participants, therefore difficult to schedule amongst work and other commitments. In addition, the nature of the protocol was that it did not obviously offer any direct insights that may be useful to dancers and assist them in better managing or understanding their pain experience. Therefore, the protocol could be adjusted for future studies by adding elements that directly relate to dancers, such as asking them to complete the sports inventory of pain questionnaire or integrating tests that require balance or stretching of dance related muscles. Future studies could also be supported through directed industry connections with relevant dance companies that would support further advertisement of the study and recruitment of its dancers.

Due to the high representation of females in the dance industry, only female participants were recruited for this initial study. However, the role of sex in pain perception cannot be overlooked. Studies have reported mixed findings in the past, however there is a general tendency for females to report greater pain sensitivity in both clinical and experimental pain settings compared to men (Bartley & Fillingim, 2013). The potential role of hormones should also not be overlooked in female cohorts, as prior studies have reported that women experience greater pain during the menstrual and pre-menstrual phases compared to the mid-menstrual and ovulatory phases (Hellstrom & Anderberg, 2003). Menstrual cycle phase was reported, but not controlled for in this study, and therefore may have contributed to the differences in pain perception between participants and limited the statistical reliability of results. To ensure that pain perception and response information that is clinically relevant to both men and women is obtained, future studies should incorporate both male and female participants and either control for or analyse the influence of menstrual cycle phase on pain perception and responses.

Future Directions:

This study has provided a foundation with which to develop specific hypotheses pertaining to between dancers and non-dancers' responses to experimental pain. Future studies should focus on recruiting more dancers and particularly those of a higher professional skill level to determine whether dancers demonstrate differences in pain perception in experimental settings. In particular, these studies should prioritise testing responses to pain that is typical of a dance setting. Although this study has focused on the difference between dancers and non-dancers, it has been observed that the broader category of athletes demonstrates a tendency for reduced pain perception. Therefore, future work should also focus on directly comparing dancers to other categories of athletes to identify if there are any significantly different responses. Recognising dancers as a distinct subset of the athletic population supports the development of interventions and programs that are specifically tailored to their injury types and needs. This would also be of significance in a clinical setting, where a greater awareness of dance pain nuances would promote support that enables them to continue dancing for longer.

Understanding sympathetic responses to pain in dancers may be beneficial in supporting the development of education and training programs regarding pain management in the dance industry. If it can be reasonably observed that in dancers, there is greater activation of the sympathetic nervous system as a potential mechanism for reducing pain perception, then this understanding could highlight the importance of high self-awareness in managing injuries in dancers. Dancers being made aware if there is a notable tendency for them to experience pain less severely would enable them to understand the importance of recognising early warning signs and taking preventative measures before pain reaches the point of irreversible injury.

A future focus area could also involve the use of brain imaging during painful stimuli to identify if there are differences in the activation of central nervous system, particularly focusing on the areas relating to pain perception and management. This could also involve conducting longitudinal studies following dancers throughout their career to observe if there are any noted neuroplastic changes over time in pain or sensory pathways. This would also

support further understanding of whether dancers could build up a pain tolerance or altered physiological responses over time due to dance training or if those who naturally have reduced pain perception progress further in a dance career.

Conclusion

The primary findings of this study indicate that there is a significant difference in how female populations respond to noxious cold compared to noxious chemical stimuli with reference to both physiological responses and perceived pain intensity. The disparity in these responses emphasises the highly nuanced nature of pain perception which needs to be considered by researchers when designing experimental protocols. If pain models that don't accurately reflect the pain type that regularly afflicts a sample population are chosen, then the reported physiological responses or pain perception ratings cannot be seen as immediately transferrable to clinical understanding.

The absence of prior research into physiological responses to experimental pain in dancers, particularly during pain models that mimic the experience of musculoskeletal injury, has limited our awareness of the potential differences in pain modulation pathways and pain perception between dancers and non-dancers. On the basis of the preliminary results from this study, future research in this field is necessary to confirm the hypothesis that dancers demonstrate increased heart rate but reduced blood pressure responses in correlation with reduced pain sensitivity in industry relevant experimental pain models. Limitations in this study associated with participant recruitment numbers, HS infusion protocol and lack of insights into sex differences should be the focus of future research design.

By prioritising research into how dancers may differ from non-dancers in their pain perception and responses, researchers can provide important insights to dance educators and clinicians to support dancer health and career prolongment.

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Appendix

Appendix 1: Question List: Eligibility Questionnaire

Section 1: General information

1. Full name
    a. Insert answer
2. Age (years)
    a. Insert answer
3. Biological sex
    a. Male
    b. Female
4. Contact email address
    a. Insert answer

Section 2: Eligibility criteria

1. Would you describe yourself as healthy, with no history of musculoskeletal or neurological disorders?
    a. Yes
    b. No
    c. Unsure
2. Do you attend at least one formal dance class (with a studio or dance instructor) a week, and have been doing so for at least the last 3 months?
    a. Yes
    b. No
3. Have you ever attended a formal dance class (with a studio or dance instructor)? If so, please briefly describe the details below:
    a. Insert answer
4. Are you a paid dance professional?
    a. Yes
    b. No
5. Do you describe yourself as a dancer?
    a. Yes
    b. No
    c. Unsure
6. Do you describe yourself as an elite/competitive athlete?
    a. Yes
    b. No
    c. Unsure
7. If you answered Yes to question 6 above, please briefly describe your sport participation below:
    a. Insert answer
8. Do you consent to be asked follow up questions to clarify any of the information described above?

a. Yes
b. No
c. Unsure

Appendix 2: Question List: Medical and Health History Questionnaire

Section 1: General information

1. Age (years)
    a. Insert answer
2. Biological sex
    a. Male
    b. Female

Section 2: Medical Screening

1. Select the options below that apply to you:
    a. Do you have any personal history of heart disease?
    b. Any personal history of thyroid, renal or liver disease?
    c. Have you had diabetes for less than 15 years?
    d. Have you had diabetes for 15 years or more?
    e. Have you experiences pain or discomfort in your chest apparently due to blood flow deficiency?
    f. Any unaccustomed shortness of breath (perhaps during light exercise)?
    g. Have you had any problems with dizziness or fainting?
    h. Do you have difficulty breathing while standing or sudden breathing problems at night?
    i. Do you suffer from ankle oedema (swelling of the ankles)?
    j. Have you experienced a rapid throbbing or fluttering of the heart?
    k. Have you experienced severe pain in leg muscles during walking?
    l. Do you have a known heart murmur?
    m. Do you have any family history of cardiac or pulmonary disease prior to age 55?
    n. Have you been assessed as hypertensive on at least 2 occasions?
    o. Have you been told your blood cholesterol is too high?
    p. Are you a cigarette smoker?
    q. Would you characterise your lifestyle as "sedentary"?
    r. If you are female, has menses been absent for at least 3 months?

Section 3: Medical History

1. Are you currently being treated for high blood pressure? If you know your average blood pressure, please enter:
    a. Insert answer
2. Has a doctor ever found: (please check all that apply)
    a. Abnormal ECG?
    b. Abnormal Chest X-Ray?
    c. Rheumatic Fever?
    d. Low Blood Pressure?
    e. Asthma?
    f. Bronchitis?

    g. Emphysema?
    h. Other lung problems?
    i. Arthritis?
    j. Bursitis?
    k. Swollen or Painful Joints?
    l. Foot Problems?
    m. Knee Problems?
    n. Shoulder Problems?
    o. Recently Broken Bones?
    p. Limited Joint Range of Motion?
    q. Epilepsy or Seizures?
    r. Chronic Migraine/Headaches?
    s. Persistent Fatigue?
    t. Stomach Problems?
    u. Hernia?
    v. Anemia?
    w. Stroke?
3. Are you pregnant?
    a. Yes
    b. No
    c. Unsure
4. When was your last menstrual period?
    a. Insert answer
5. What is the average duration of your menstrual cycle?
    a. Insert answer
6. Has a doctor imposed any activity restrictions? Yes/No. If so, please describe:
    a. Insert answer

Section 4: Medications

1. Please Select Any Medications You Are Currently Using
    a. Diuretics
    b. Beta Blockers
    c. Vasodilators
    d. Alpha Blockers
    e. Calcium Channel Blockers
    f. Other Cardiovascular
    g. Anti-Inflammatories (Motrin, Advil)
    h. Diabetes/Insulin
    i. Lipid Lowering (Statins)
2. Other drugs (list below)
    a. Insert answer
3. Please list the specific medications that you currently take, including contraceptive medication:
    a. Insert answer

Section 5: Exercise (Dancers please skip the section and complete section 6)

1. On average, how many times do you exercise per week?
    a. Insert answer
2. On average, how long do you exercise?
    a. Insert answer
3. On a scale from 1 (low) to 10 (high), how intense is your typical workout?
    a. Scale 1-10
4. Please select the activity types you typically participate in
    a. Running/jogging
    b. Walking
    c. Stair climbing
    d. Bicycle/spinning
    e. Weight training
    f. Aerobics classes
    g. Swimming
    h. Racquet sports
    i. Skiing/boarding
    j. Yoga/Martial Arts
    k. Dance/gymnastics
    l. Other (please specify)
5. Do you currently participate in sport at a competitive level?
    a. Yes
    b. No
6. If you answered yes to question 5 above, list the sports you compete in below:
    a. Insert answer
7. If you answered yes to question 5 above, describe how many times per week and for how long (minutes) you train for that sport below:
    a. Insert answer
8. If you answered yes to question 5 above, would you describe yourself as an elite athlete?
    a. Yes
    b. No
    c. Unsure

Section 6: Dance Experience (only complete this section if you classify as a dancer)

1. How many times per week do you attend formal dance classes (at a dance studio with an instructor)?
    a. Insert answer
2. How long do you spend at dance classes/training each week (minutes)?
    a. Insert answer
3. How long do you spend completing other types of training/physical activity each week (minutes)?
    a. Insert answer
4. Describe the types of physical activity you participate in outside of dance classes (e.g., running, weightlifting, etc.)
    a. Insert answer

5. How many years have you been dancing for? If you have taken breaks from dancing, please specify these below (e.g., danced from ages 1-5, took a break, resumed dancing at age 12 and have continued to dance since this time).
    a. Insert answer
6. Which styles of dance have you practiced?
    a. Ballet
    b. Jazz
    c. Tap
    d. Lyrical/contemporary
    e. Hip Hop
    f. Musical theatre
    g. Indigenous/cultural
    h. Ballroom
    i. Other (please specify)
7. For the dance styles selected in question 4, please describe below how long you practiced each dance style)
    a. Insert answer
8. Do you practice solo dance styles or partner/group dance styles?
    a. Solo
    b. Partner/Group
    c. Both
9. Which of the adjectives below would most accurately describe your involvement in dance?
    a. Recreational/enjoyment
    b. Competitive
    c. Performance
    d. Employment (as a professional dancer)
    e. Employment (as a dance teacher)
    f. Other
10. Do you participate in the following (select all that apply)?
    a. Warm up before dance class/rehearsal
    b. Warm up before performance/competition
    c. Warm up before other types of physical activity (outside dance)
    d. Cool down after dance class/rehearsal
    e. Cool down after performance/competition
    f. Cool down after other types of physical activity (outside dance).

Section 7: Dance Injury (only complete this section if you classify as a dancer)

1. In the past 12 months, have you experienced any dance-related injuries? If so, how many?
    a. 0
    b. 1
    c. 2
    d. 3
    e. More than 3 (please specify)

2. Throughout your dance history, have you experienced any serious dance-related injuries have you experienced? Serious injuries are described here as those requiring medical intervention and/or prevented you continuing dance or physical activity during recovery. If so, how many?
    a. 0
    b. 1
    c. 2
    d. 3
    e. More than 3 (please specify)
3. If you have experienced dance-related injuries, which body region/s have you experienced injuries to? Please select all that apply:
    a. Ankle
    b. Knee
    c. Hip
    d. Foot
    e. Lower leg (shin/calf)
    f. Back
    g. Shoulder
    h. Neck
    i. Hamstring
    j. Toe
    k. Head
    l. Other (please specify)
4. For any of the serious dance-related injuries (reported in question 2), please describe below the details of the injury (including duration of injury, the type of injury, when the injury occurred, whether medical intervention was required, the site of injury and whether it is an ongoing injury).
    a. Insert answer
5. Which of the phrases below best describes your approach to managing your dance-related injury (select all that apply)?
    a. When injured, I sought medical advice.
    b. When injured, I did not seek medical advice and managed the injury myself.
    c. I told members of my dance studio/dance company about my injury.
    d. I did not tell members of my dance studio/dance company about my injury
    e. I continued to dance while injured without modifying my practices.
    f. I continued to dance while injured but modified my practices.
    g. I did not continue to dance while injured.
6. Have you experienced any serious non-dance related injuries?
    a. Yes
    b. No
    c. Unsure
7. If you answered yes to question 6 above, did this impact upon your dancing? If so, describe how below:
    a. Insert answer

Section 8: Lifestyle

1. Are you a cigarette smoker? If so, how many per day?
    a. Insert answer
2. Were you previously a cigarette smoker? If so, when did you quit?
    a. Insert answer
3. How many years have you smoked or did you smoke before quitting?
    a. Insert answer
4. Do you/did you smoke:
    a. Cigarettes
    b. Cigars
    c. Pipe
    d. Other (please specify)
5. Please Rate Your Daily Stress Levels (Select one)
    a. Low
    b. Moderate
    c. High: often difficult to handle
    d. High: sometimes difficult to handle
    e. High: I enjoy the challenge
6. Do you drink alcoholic beverages?
    a. Yes
    b. No
7. How frequently do you drink alcohol (per week)?
    a. Insert answer
8. How many drinks in a sitting?
    a. Insert answer
9. Dietary habits. Please Select All That Apply:
    a. I seldom consume red or high fat meats
    b. I pursue a low-fat diet
    c. I eat at least 5 servings of fruit/vegetables per day
    d. I almost always eat a full, healthy breakfast
    e. My diet includes many high-fibre foods
    f. I rarely eat sugar or high-fat desserts

Section 9: Other

1. As far as you are aware, is there anything that might prevent you from successfully completing the tests that have been outlined to you?
    a. Insert answer
2. Do you consent to be asked follow up questions to clarify any of the information described above?
    a. Yes
    b. No
    c. Unsure

Appendix 3: Short Form McGill Pain Questionnaire

Short Form McGill Pain Questionnaire – Cold Pressor Task/ HS Infusion

	None (0)	Mild (1)	Moderate (2)	Severe (3)
THROBBING				
SHOOTING				
STABBING				
SHARP				
CRAMPING				
GNAWING				
HOT/BURNING				
ACHING				
HEAVY				
TENDER				
SPLITTING				
TIRING/EXHAUSTING				
SICKENING				
FEARFUL				
PUNISHING/CRUEL				

VAS No Pain Worst Possible Pain

PPI

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

The short-form McGill Pain Questionnaire (SF-MPQ). Descriptors 1-11 represent the sensory dimension of pain experience and 12-15 represent the affective dimension. Each descriptor is ranked on an intensity scale of 0 = none, 1 = mild, 2 = moderate, 3 = severe. The Present Pain Intensity (PPI) of the standard long-form McGill Pain Questionnaire (LF-MPQ) and the visual analogue scale (VAS) are also included to provide overall intensity scores.