

Factors Influencing how Electrotactile Stimuli are Consciously Perceived

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(ABSTRACT)

Tactile, or touch-related, perception is critical to successfully perform activities of daily living, such as holding a cup, hugging a loved one, or learning a new skill. However, approximately 30% of individuals in the United States experience tactile perceptual impairments, or difficulty/inability detecting and interpreting tactile stimuli. In clinical settings, tactile perceptual assessments are commonly used to diagnose impairments and somatosensory function (e.g., intact dermatomes following spinal cord injury). However, these existing examination methods that focus on tactile perception can be insufficient depending on the patient population targeted. One reason why tactile examinations may be insufficient is the large number of factors that may influence intact perception are not considered and, in turn, captured. Consequently, exploring the various factors that influence intact tactile perception is of significant interest. Current literature suggest that factors which can impact intact tactile perception include arm dominance, nerve stimulated, anatomical location of stimulation, biological sex, age, and cognitive-perceptual load. In this dissertation, I provide a comprehensive examination of the factors influencing tactile perception, and how they interact, in young and older adults who are neurologically intact. By gaining a deeper understanding of the various factors that influence tactile perception, and their interactions, in individuals who are neurotypical, clinicians can more effectively examine and interpret when and why tactile impairments arise in different populations.

This work initially examines factors influencing tactile perception, and and a subset of their

interactions, by having participants detect electrotactile stimuli applied at their upper limb. Findings from this body of work indicate that factors such as the nerve stimulated, anatomical location of stimulation, sex, age, and a subset of their interactions can impact tactile perception. A novel finding from this work is the significant interaction between age and anatomical location in shaping tactile perception. While prior studies have often examined age-related or location-based differences independently, this dissertation demonstrates how the combined influence of these factors can differentially affect sensory processing. These findings suggest that aging may alter tactile perception in a location-specific manner, with important implications for sensorimotor rehabilitation strategies and age-tailored sensory assessments. However, contrary to our preliminary findings and select literature, this work did not find a consistent effect of arm dominance, highlighting the need for further research into the conditions under which dominance of the arm stimulated influences tactile perception. Combined, this work suggests that when assessing intact tactile perception, various factors and their interactions should be considered.

Next, this work explores whether the cognitive resources allocated to perceiving tactile stimuli influence tactile perception in younger adults. Participants were introduced to an additional sensory load, through auditory stimuli, during which they were instructed to complete two tasks concurrently (i.e., tactile task and auditory task). Additionally, this body of work explored whether the nature of the electrotactile stimulus (i.e., detection versus discrimination) impacted how electrotactile stimuli were perceived. Findings indicate that arm dominance significantly influenced both the accuracy of detection and discrimination of electrotactile stimuli. While performing a concurrent auditory discrimination task significantly impacted precision during tactile detection, it primarily affected accuracy during tactile discrimination. Additionally, a significant interaction between participant sex and stimulation location was observed during detection but not discrimination of the stimuli. Notably, small effect sizes were observed alongside significant p-values, raising the possibility that statistical

effects may not fully reflect meaningful physiological differences. These findings indicate the importance of interpreting both statistical and physiological significance when examining the factors that influence tactile perception.

Lastly, this work explores whether the cognitive resources allocated to perceiving tactile stimuli influence tactile perception in older adults. Participants were introduced to an additional sensory load, through auditory stimuli, during which they were instructed to complete two tasks concurrently (i.e., tactile task and auditory task). Additionally, this body of work explored whether the nature of the auditory task (i.e., detection versus discrimination) and the nature of the electrotactile task (i.e., detection versus discrimination) impacted how electrotactile stimuli were perceived. This work suggests that concurrent auditory stimuli influenced participants' ability to accurately detect electrotactile stimuli when the auditory stimulus demanded greater cognitive resources (i.e., discrimination task). Furthermore, results indicate that concurrent auditory stimuli contributed to greater variability in perceiving the electrotactile stimuli when the auditory stimulus demanded less cognitive resources (i.e., detection). These results suggest that as cognitive-perceptual load increases, tactile perceptual outcomes may become impaired, particularly in older adults.

Overall, this dissertation emphasizes the importance of considering multiple contributing factors, and their interactions, when evaluating tactile perception. The results highlight that factors such as age, the anatomical location of stimulation, nerve, associated cognitive-perceptual load, and a subset of their interactions can significantly influence how tactile stimuli are perceived in young and older adults. These findings have implications for enhancing tactile assessments, particularly in clinical settings where precise measurements are crucial for accurate diagnoses and interventions. By incorporating these factors into evaluations for tactile perception, clinicians can provide more individualized assessments, ultimately leading to more effective and personalized treatments for those with tactile impairments.

Factors Influencing how Electrotactile Stimuli are Consciously Perceived

Emily Margaret Tirrell

(GENERAL AUDIENCE ABSTRACT)

Accurately perceiving the physical interactions with objects, or touch, is critical to successfully perform daily physical activities, like holding a cup, hugging a loved one, or learning new skills such as playing a musical instrument. However, roughly 30% of individuals in the United States experience difficulty or inability in detecting and interpreting touch-related stimuli, which can lead to a decrease in quality of life and performance in everyday tasks. Consequently, understanding the various factors that influence intact touch perception is of significant interest. These factors include arm dominance, nerve stimulated, location of stimulation, biological sex, age of a participant, mental effort associated with the task, and how these all interact. In clinical settings, assessments of touch-related perception are commonly used to diagnose impairments. However, existing assessment methods often inadequately consider the various factors that influence intact perception. As a result, recent investigations suggest that these assessments are insufficient. Here, we further explore the different factors that can influence touch perception in typical populations, namely young and older adults. If we can more greatly understand the different factors that influence touch perception in individuals who are typical, then we can better identify when and why impairments occur in clinically-relevant populations.

This work first examines the various factors that influence touch perception, and how they interact. Participants were asked to report whether they could perceive an externally applied stimulus (touch-related task) while at rest. This approach utilized electrical stimulation to

assess touch perception, which is easily manipulated and controlled. Utilizing this protocol in both younger and older adults, this work suggests that factors such as the nerve stimulated, location of stimulation, participant sex, and their interactions could impact touch-related perception in young adults. Additionally, this body of work suggests that in older adults factors such as age, location, nerve, and their interactions could influence touch perception. However, contrary to our preliminary findings and existing literature, no effect of arm dominance was observed. Combined, this work suggests that when assessing intact touch perception while at rest, factors such as nerve, location, age, sex, and their interactions should be considered.

This work next explores whether the mental resources allocated to perceiving touch influence touch-related perception in younger adults. Participants were asked to complete two tasks at the same time (one touch-related and one sound-related) to determine if performing both tasks at once would affect their ability to detect or differentiate between touch-related stimuli. This approach also examined whether the type of touch task (detection versus discrimination) influenced outcomes. Findings from this body of work suggest that factors such as the nerve stimulated and arm used can impact touch-related perception. However, performing the auditory task at the same time did not influence touch perception in younger adults. Notably, small impacts were observed, raising the possibility that observed effects may not fully reflect meaningful physiological differences. These findings highlight the importance of evaluating both statistical and physiological significance when interpreting results related to touch perception.

Lastly, this work explores whether the mental resources allocated to perceiving touch influence touch-related perception in older adults. Participants were asked to complete two tasks at the same time (one touch-related and one sound-related) to determine if performing both tasks at once would affect their ability to detect or differentiate between touch-related stimuli. This approach also examined whether the type of auditory task (i.e., detection versus

discrimination) and the type of touch task (i.e., detection versus discrimination) influenced outcomes. Findings from this body of work suggest that performing a more mentally demanding task (discrimination) made it harder for older adults to accurately detect touch stimuli. When the task was less demanding (detection), participants had greater variability in detecting touch stimuli. These findings suggest that as mental demands increase, touch-related perception may become less accurate or more varied in older adults.

Overall, this work emphasizes the importance of considering multiple factors when performing touch-related examinations. The findings demonstrate that characteristics such as age, location and nerve stimulated, mental demands, and their interactions can meaningfully shape how touch is experienced in both younger and older adults. These findings have implications for enhancing tactile assessments, particularly in clinical settings where precise measurements are crucial for accurate diagnoses and interventions. By incorporating these factors into evaluations for tactile perception, clinicians can provide more individualized assessments, ultimately leading to more effective and personalized treatments for those with tactile impairments.

Dedication

*In memory of my cousin, Ryan Johnson, Ph.D., who pursued his passions and inspired me
to do the same.*

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List of Abbreviations

CNS Central Nervous System

PNS Peripheral Nervous System

The CNS refers to the Central Nervous System, or the brain and spinal cord.

The PNS refers to the Peripheral Nervous System, or the nerves and ganglia outside of the Central Nervous System.

Chapter 1

Introduction

1.1 Problem Statement

Intact tactile perception, or the ability to perceive touch-related stimuli, is critical to successfully interact with, and respond to, the physical environment [36]. Whether hugging a loved one, learning a new skill, writing a doctoral dissertation, or holding a cup of coffee, intact tactile perception is required to detect and interpret external stimuli. For those with tactile impairments, or difficulty/inability perceiving tactile stimuli, movement deficits can arise that result in physical disability [36].

Tactile perception is shaped by multiple physiological and anatomical factors. Even so, current assessment methods often do not capture their impact for reasons including an insufficient understanding of their role and how they interact with other factors [118, 165]. Among these, arm dominance, or the preferential use of one arm over the other, is known to influence volitional motor control [130, 131, 132, 133], though its role in tactile perception remains debated [14, 23, 62, 156, 181]. Additional factors, such as nerve, anatomical stimulation location, and biological sex may also play critical roles in shaping tactile perceptual outcomes [28, 54, 152, 162, 170]. Despite the potential impact of each and their interactions, these variables are often overlooked in traditional assessment methods [118, 165].

Another important consideration is that tactile perception does not occur in isolation but,

rather, is modulated by executive function and cognitive-perceptual loads [52, 84]. The extent of a cognitive-perceptual load depends on the complexity and demands of the task performed, with corresponding cognitive and sensory resources utilized to process information and respond effectively [68, 161]. A higher cognitive-perceptual load occurs when tasks demand greater attention, working memory, and executive function, potentially limiting an individual’s ability to effectively process information (e.g., sensory stimuli) or perform tasks concurrently [118, 156].

A more comprehensive understanding of the factors that influence tactile perception, and their potential interactions, is critical for improving both clinical assessments and neurorehabilitation strategies for individuals with tactile impairments. Current assessments often do not replicate the complex, cross-modal nature of real-world sensory experiences, potentially leading to gaps in diagnosis and treatment depending on the condition [118, 165]. By examining factors such as arm dominance, nerve, anatomical location, biological sex, cognitive-perceptual load, and their interactions, researchers and clinicians can develop more precise approaches for evaluating tactile impairments in various populations and, in turn, individualized treatment plans.

1.2 Research Goals and Aims

The overarching goal of this dissertation is to advance the understanding of the factors that influence intact tactile perception. This dissertation relies on psychophysics and human subject testing to quantify tactile perception and explore the factors that shape conscious tactile perception. By examining typical outcomes during intact tactile perception, this work can inform future studies that then consider when and why tactile impairments arise in more complex patient populations (e.g., following a brain injury).

The research goal was investigated through the completion of the following aims:

1. Investigate the influence of arm dominance, nerve, anatomical stimulation location, biological sex, and their interactions on the conscious detection of electrotactile stimuli.
2. Investigate the impact of an auditory load, aging, and their interaction on detecting electrotactile stimuli.
3. Investigate the impact of an auditory load, aging, and their interaction on discriminating electrotactile stimuli.

1.3 Dissertation Outline

Chapter 2 provides background information on the differing factors explored in this body of work, namely arm dominance, nerve, anatomical location stimulated, biological sex, cognitive-perpetual load, and their interactions. This review introduces the need for continued exploration of the factors that influence tactile perception.

Chapter 3 examines various considerations for tactile perceptual assessments, specifically the effect of arm dominance, nerve, anatomical stimulation location, participant biological sex, and their interactions on electrotactile detection.

Chapters 4 and 5 explore the effect of an auditory load, aging, and their interaction on tactile perception. These chapters focus on whether a detection versus discrimination task differentially affects how tactile stimuli are perceived.

Chapter 2

Background

2.1 Neuromechanisms for the Perception of Tactile Stimuli

Tactile perception is mediated by a three-neuron relay system that transmits sensory information from cutaneous mechanoreceptors to the primary somatosensory cortex (S1). This process is facilitated by the dorsal column-medial lemniscus (DCML) pathway, which is responsible for conveying fine touch, vibration, and proprioceptive signals from one side of the body to the contralateral hemisphere of the brain (see Figure 2.1). Sensory nerve fibers originating from the dorsal root ganglia enter the spinal cord via the dorsal roots and ascend within the dorsal column. These sensory nerve fibers can be classified by size and innervation, with alpha-beta ($A\beta$) fibers of relevance to this body of work. $A\beta$ fibers, which are fast-conducting, large-diameter afferent fibers, innervate cutaneous mechanoreceptors and are responsible for transmitting signals related to tactile perception. Signals from the upper limbs travel through the fasciculus cuneatus and synapse onto second-order neurons in the nucleus cuneatus of the medulla, whereas signals from the lower limbs are transmitted via the fasciculus gracilis to the nucleus gracilis. Second-order neurons decussate (cross) at the level of the medulla and project to the ventral posterolateral nucleus (VPL) of the thalamus, where they synapse onto third-order neurons that subsequently relay tactile information to

S1 for processing and conscious perception [123].

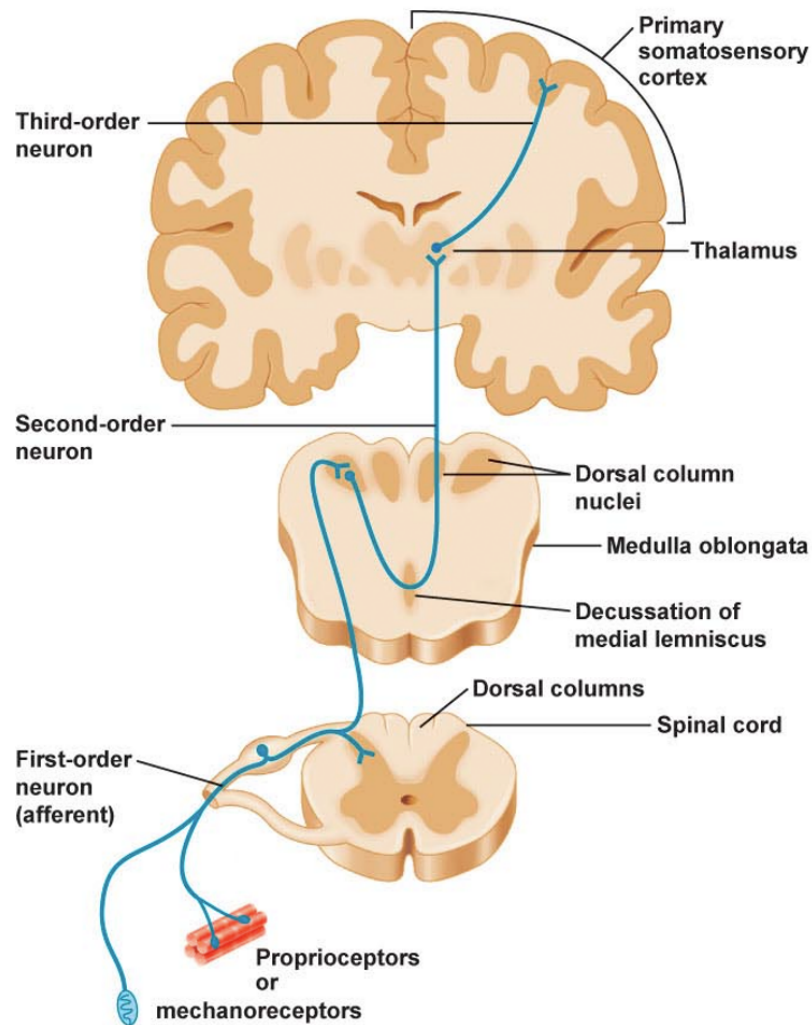


Figure 2.1: **The Dorsal Column-Medial Lemniscal Pathway.** This figure illustrates the primary afferents carrying tactile information. The afferents first synapse in the dorsal column nuclei of the ipsilateral medulla. The axon of second order sensory neurons cross the midline and ascend to the ventral posterolateral nucleus (VPL) nucleus of the thalamus. The third-order neurons then project their axon to the somatosensory cortex (S1). *This figure was adapted from Kandel, Shwartz, and Jessel 2000.*

Human skin contains specialized mechanoreceptors to detect tactile information, including Merkel cells, Meissner corpuscles, Ruffini endings, and Pacinian corpuscles. These mechanoreceptors differ in structure, function, and response properties, enabling percep-

tion of fine touch, vibration, pressure, and texture [80, 81, 82]. In contrast to tactile stimuli, perception of electrotactile stimuli involves detecting electrical currents applied to the skin. These electrical currents stimulate afferent nerve fibers in the absence of mechanical deformations [24, 179]. This sensory information is relayed through the spinal nerves, which correspond to specific dermatomes. Dermatomes, defined as regions of the skin innervated by a single spinal nerve, play a crucial role in organizing and mapping tactile perception, reflecting the segmental distribution of sensory fibers that relay information from mechanoreceptors to the brain [98].

These dermatomal regions follow a segmental pattern across the body, reflecting both embryological origins and the distribution of spinal nerves. Each spinal nerve, except for C1, is associated with a dermatome that covers different body areas from the head to the lower limbs. The formation of dermatomes occurs during embryonic development as somites (paired segments of mesoderm) and give rise to both muscles (myotomes) and skin (dermatomes). As spinal nerves emerge from the spinal cord, they establish connections with specific regions of developing skin, leading to the characteristic striped distribution of dermatomes across the body. During early development, somites form along the neural tube, and each somite is linked to a specific spinal nerve. These nerves grow into the corresponding regions of the skin, where sensory neurons from the neural crest project, creating a clear dermatome map across the skin. This segmentation of the body is mirrored in the dermatome distribution, with sensory fibers innervating the cervical, thoracic, lumbar, and sacral regions [98].

- **Cervical Dermatomes (C2-C8):** Correspond to the head, neck, shoulders, and upper arms.
- **Thoracic Dermatomes (T1-T12):** Correspond to the chest, back, and parts of the upper abdomen.

- **Lumbar Dermatomes (L1-L5):** Correspond to the lower back, hips, thighs, and part of the lower legs.
- **Sacral Dermatomes (S1-S5):** Correspond to the buttocks, posterior legs, and perineal region.

As spinal nerves grow and extend into their respective dermatomal regions, the boundaries between dermatomes become distinct, contributing to the clear segmental organization evident in the adult body. This organization is crucial for the accurate localization of sensory stimuli and plays a key role in tactile perceptual assessments, as specific dermatomes can be affected by injury or disease processes at particular spinal levels.

2.2 The Differing Factors Influencing Conscious Tactile Perception

Due to the importance of tactile perception on functional outcomes [15, 36], the differing factors that influence intact tactile perception are of interest. This body of work focuses on factors found within the literature, specifically the roles of arm dominance, nerve, location, sex, cognitive-perceptual load, and their interaction on conscious perception of tactile stimuli.

2.2.1 The Role of Arm Dominance on Perception of Tactile Stimuli

Arm dominance, defined as the preferential use of one limb over the other, is a well-established phenomenon in human sensorimotor function. It is typically characterized by greater strength, dexterity, and motor precision in the dominant limb, resulting from both experience-dependent neural plasticity and underlying hemispheric lateralization [168]. This

lateralization contributes to the division of labor during bimanual tasks, where the dominant and non-dominant arms perform distinct, yet complementary, roles [21, 35, 132, 138]. For example, during the act of cutting a loaf of bread, the dominant arm executes the cutting motion, a task requiring fine motor control and precise coordination to ensure smooth and accurate slicing. Simultaneously, the non-dominant arm stabilizes the loaf, providing structural support and maintaining balance. This functional specialization reflects the broader role differentiation between the dominant and non-dominant limbs, shaped by task-specific experience and hemispheric lateralization [45, 130, 131, 133]. However, when considering tactile perception, literature remains mixed, with some literature suggesting that there is a role of arm dominance on tactile perception [14, 23, 57, 181], while others suggesting that there is not [54, 62].

Examination of the relationship between arm dominance and tactile perception dates back to the 1960s, when Semmes, Weinstein, Ghent, and Tuber first investigated tactile perception at digit 1 in right-arm dominant participants [57]. This work sparked greater interest and further research into how arm dominance might influence tactile perception, which has continued to this day. Similar to their initial findings, some literature suggests that there is a role of arm dominance on intact tactile perception, namely, that tactile perception may be better at the non-dominant arm when compared to the dominant arm. These examinations include tasks that involve higher cognitive processing, including pressure, sharpness, and roughness discrimination tasks [14, 181].

Conversely, not all literature supports the notion that arm dominance plays a significant role in conscious tactile perception. Some studies, particularly those involving participants at rest or performing simple detection tasks, fail to observe any substantial difference between the dominant and non-dominant limbs [54, 62]. Overall, these findings may suggest that differences in tactile perception between arms may not be significant in tasks that do

not require complex cognitive or motor involvement, challenging the hypothesis that arm dominance consistently affects tactile perception.

Combined, the existing literature presents mixed evidence regarding the influence of arm dominance on tactile perception. These discrepancies may be attributed to differences in task complexity, experimental methodology, and the type of sensory stimuli used [14, 23, 91, 100, 140]. Overall, the relationship between arm dominance and tactile perception appears to be context-dependent, with the effects potentially varying based on the nature of the task and the cognitive load involved. Further research is needed to determine under what conditions arm dominance might significantly influence tactile perception.

2.2.2 The Role of Nerve Stimulated on Perception of Tactile Stimuli

The arm is primarily innervated by five main nerves that originate from the brachial plexus, a network of nerves formed by the ventral rami of the lower cervical and upper thoracic spinal nerves. These five nerves (median, ulnar, radial, musculocutaneous, axillary) play essential roles in both motor control and perception throughout the upper limb. The median, ulnar, and radial nerves are most relevant for this body of work, with each nerve innervating distinct regions of the hand. The median nerve innervates the palmar aspect of the hand and innervates digit 1 (thumb), digit 2 (index finger), digit 3 (middle finger), and part of digit 4 (ring finger). The ulnar nerve also innervates the hand, providing sensory innervation to digit 5 (pinky finger) and half of digit 4 (ring finger). The radial nerve covers the dorsal aspect of the hand, primarily supplying sensation to the back of digit 1 (thumb) and digit 2 (index finger). These nerves send signals up the dorsal column medial lemniscal (DCML) pathway to the brain, where tactile information is processed [117].

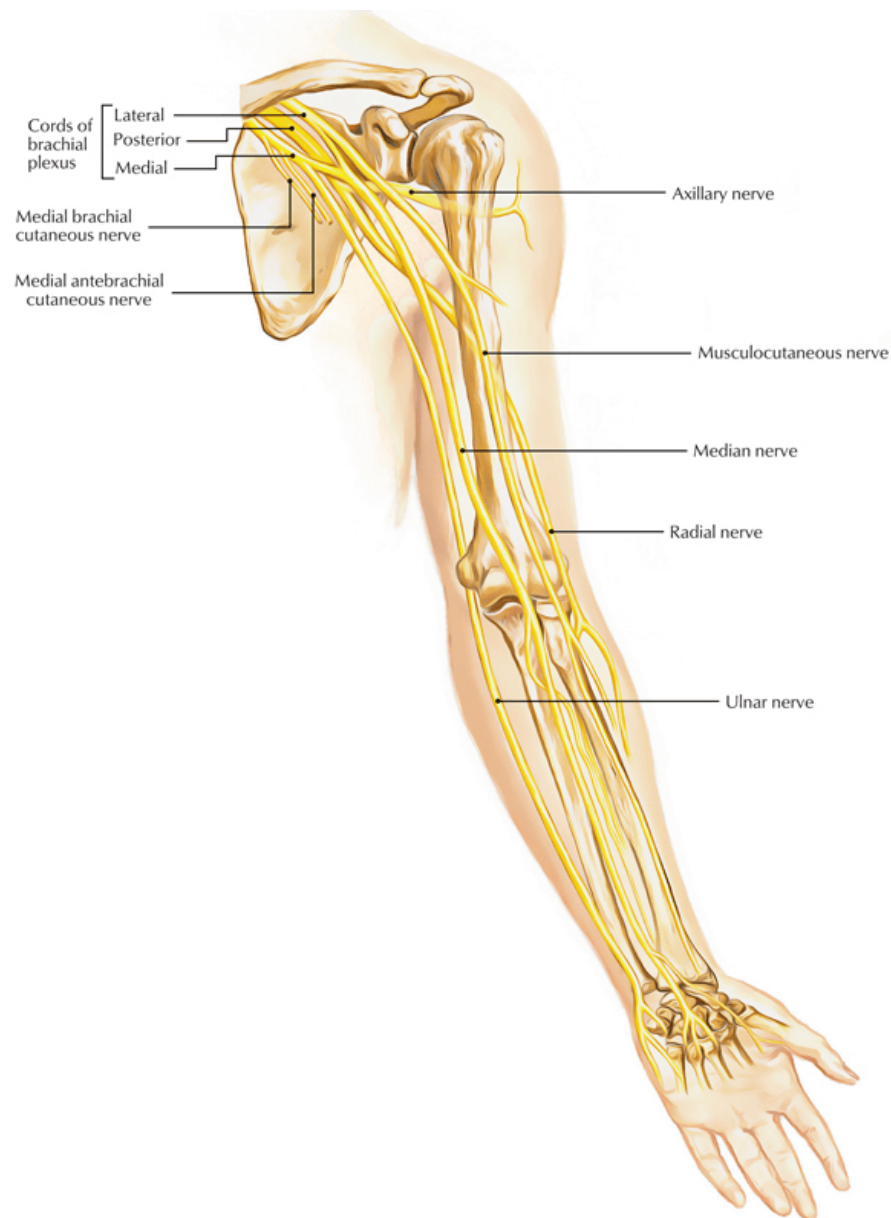


Figure 2.2: **The Nerves that Innervate the Upper Limb** This figure illustrates the five major nerves that innervate the upper limb, each playing a critical role in sensory perception, including tactile stimuli. Of great interest are the median, ulnar, and radial nerves, which innervate the hand. *This figure was adapted from Kandel, Shwartz, and Jessel 2000.*

However, much of the existing literature on tactile perception has concentrated on assessments of the median and ulnar nerves, primarily due to their prominent roles in sensory and motor functions of the hand [14, 23, 28, 40]. The median nerve is of particular interest as

it innervates a large portion of the hand (including the palmar side of the thumb, index, middle, and part of the ring fingers). The median nerve plays a critical role in somatosensation, especially in tasks requiring precision and dexterity such as grasping, manipulating objects, and performing detailed tasks [117]. Additionally, the median nerve is highly relevant in clinical conditions such as carpal tunnel syndrome, a disorder in which compression of the nerve results in symptoms like numbness, tingling, and weakness in the hand [13, 150]. Similarly, the literature also explores tactile perception at the ulnar nerve, as it innervates portions of the palmar side of the hand (including the pinky and half of the ring finger), and has similar roles to the median nerve for functional outcomes [14, 40, 170]. The ulnar nerve is also associated with clinical conditions, such as ulnar neuropathy, which can lead to impairments at the hand [6]. As such, these conditions and characteristics may influence the direction of clinical research, which often aims to capture and examine impairments in the hand. Combined, the median and ulnar nerves are commonly examined for tactile perceptual assessments.

Consequently, findings from these single-nerve studies may not fully capture the complexity of tactile function across the entire hand. Given that the median, ulnar, and radial nerves each innervate distinct regions with unique anatomical and functional characteristics, generalizing tactile perception outcomes from studies of one nerve to the entire hand may be insufficient. The performance of one nerve cannot be directly applied to others, as they vary in dermatomal distribution and anatomical depth. For instance, the radial nerve lies deeper beneath the skin and innervates different dermatomal regions compared to the median or ulnar nerves. As such, tactile perception of electrotactile stimuli on the dorsal portion of the hand may differ substantially from that on the palmar aspect. To gain a comprehensive understanding of tactile perception across the upper limb, it is essential to include all three major nerves to avoid incomplete or misleading interpretations that cannot be generalized

to the entire hand.

2.2.3 The Role of Location Stimulated on Perception of Tactile Stimuli

The upper limb is anatomically divided into three distinct regions: the arm (upper arm), forearm, and hand [117]. However, existing research examining tactile perception at the upper limb is predominantly focused on distal regions, particularly the hand and fingertips [14, 23, 28, 57, 62]. This emphasis on distal regions likely stems from both the functional importance of these areas and the underlying neuroanatomy within the somatosensory cortex [123]. The somatosensory cortex allocates a disproportionate amount of cortical area to the hand, as represented by the sensory homunculus in Figure 2.3. Consequently, distal regions exhibit better tactile perception and discrimination capabilities, which have made them a natural focus for tactile perceptual research.

More proximal regions of the arm, such as the forearm, have received comparatively little attention in current literature, despite their involvement in broader motor control, proprioception, and postural stability [110]. By primarily targeting distal locations, prior studies may overlook potential variations in tactile perception along the upper arm, and as such, examinations may not generalize to the entire arm. To gain a more comprehensive understanding of tactile perception across the upper limb, it is essential to include multiple locations along the upper limb.

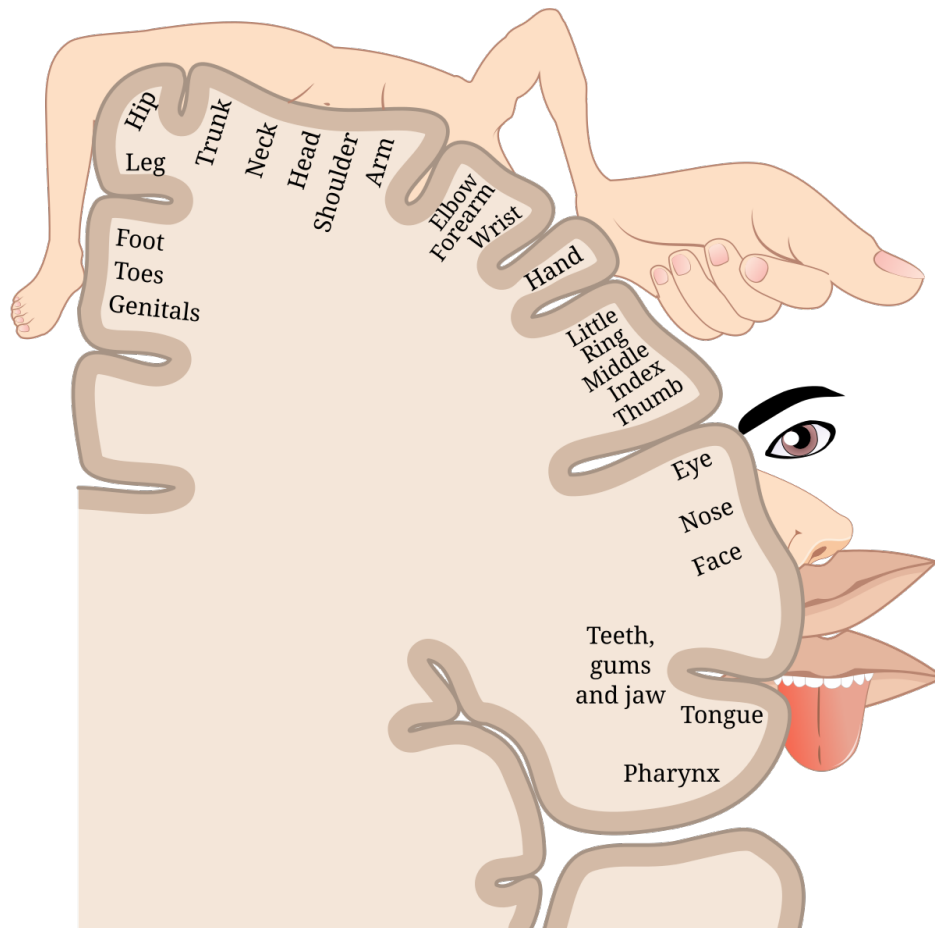


Figure 2.3: **The Sensory Homunculus** This figure illustrates the cortical organization of the sensorimotor cortex, where body regions are represented in proportion to their sensory processing, with a greater resolution indicating greater cortical representation. Notably, the hand occupies a disproportionately large area, reflecting its importance for functional outcomes and use for fine motor control and tactile perception.

2.2.4 The Role of Biological Sex on Perception of Tactile Stimuli

Here, we define sex as male or female based on the binary sex categorization assigned at birth (i.e., male and female). Existing literature demonstrates that sex influences tactile perception in younger adults, with females typically exhibiting greater tactile sensitivity than males. However, this effect appears to diminish with age. In older adults, sex has not been found to significantly impact tactile perception [2, 12, 92, 121, 153, 173].

One explanation for this age-dependent difference is that hormonal changes may attenuate the sex effects observed in younger adults. Estrogen, which has been implicated in neuroprotection [141, 160], declines significantly post-menopause [92]. This hormonal decline may contribute to changes in peripheral nerve sensory function and tactile perception, particularly in older females. Supporting this idea, studies comparing young adult males to older adult males show no significant differences in tactile perception. In contrast, when young adult females are compared to older adult females, significant reductions in tactile sensitivity have been observed [2], suggesting that the enhanced tactile perception seen in younger females may be driven by factors, such as higher estrogen levels, that are no longer present post-menopause.

In younger adults, several factors have been investigated to explore sex-based differences in tactile perception, including fingertip size, skin compliance, hormonal influences, BMI, behavioral socialization, and body temperature. For instance, body temperature negatively correlates with tactile detection, as lower temperatures impair the ability to detect stimuli at higher amplitudes [47, 93, 157]. Females, who tend to have higher baseline body temperatures than males, may thus perceive stimuli at lower amplitudes [93]. Additionally, estrogen has been implicated in neuroprotection, which could further enhance tactile perception in females [141, 160]. Since females have higher circulating estrogen levels than males, this hormonal difference may contribute to their greater tactile perception [92]. Combined, this literature suggests a sex-based difference in tactile perception in young adults.

2.2.5 The Role of Aging on Perception of Tactile Stimuli

Tactile perception declines with age due to changes in both the central nervous system (CNS) and peripheral nervous systems (PNS). These age-related declines impair older adults'

ability to detect and interpret tactile stimuli, contributing to reduced dexterity, increased fall risk, and diminished quality of life [5, 38]. Understanding the mechanisms underlying these changes is critical for developing interventions to mitigate sensory deficits and enhance somatosensory function in aging populations. This literature review explores the central and peripheral mechanisms responsible for the decline in tactile perception with aging.

The CNS, including the brain and spinal cord, plays a critical role in processing tactile information. With aging, structural and functional changes in the CNS impair sensory processing, leading to reduced tactile acuity and slower neural processing [18, 144]. For example, the somatosensory cortex, which processes tactile stimuli, undergoes age-related declines in cortical thickness, gray matter volume, synaptic density, and myelin integrity [75, 119, 176]. These changes impair spatial discrimination, temporal resolution, and ability to distinguish fine textures and vibrations. Neuroimaging studies have also shown decreased somatosensory cortical activation during tactile tasks in older adults, contributing to deficits in grip control, dexterity, and light-touch sensitivity [18, 55, 63]. Additionally, aging reduces neural plasticity, limiting the brain's capacity to compensate for sensory deficits, while diminished efficiency in multisensory integration further impairs tactile perception, especially in noisy or visually distracting environments [63, 64]. Cognitive declines in attention and working memory exacerbate these deficits, leading to slower reaction times and decreased accuracy in tactile detection [52, 72].

In addition to central changes, the PNS, which includes cutaneous mechanoreceptors and afferent nerve fibers, also undergoes degeneration with aging, contributing directly to tactile decline. Age-related changes in the skin, such as thinning of the epidermis, reduced dermal elasticity, and dryness, impair mechanoreceptor function [43, 46, 173]. Additionally, peripheral nerve fibers exhibit decreased conduction velocity, reduced density, and impaired signal transmission, slowing sensory input to the CNS and exacerbating tactile

deficits [26, 120, 166]. Reduced cutaneous blood flow, due to diminished microvascular circulation, further compromises tactile perception as well [32, 53]. Combined, these structural and functional changes in the PNS contribute to the progressive decline in tactile perception observed in older adults.

2.2.6 The Role of Cognitive-Perceptual Load on Perception of Tactile Stimuli

The extent of a cognitive-perceptual load depends on the demands of the task being performed, with corresponding sensory and cognitive resources utilized to first process and interpret sensory information and then respond effectively and appropriately [20]. A well-known illustration of this is the cocktail party effect, which demonstrates the brain's capacity to selectively focus on specific auditory inputs while filtering out irrelevant noise [17]. A higher-cognitive perceptual load occurs when a task demands greater executive functioning (i.e., working memory, attention), potentially limiting an individual's ability to process sensory information or perform a task concurrently [7]. Current literature explores how the extent of a cognitive-perceptual load can influence tactile perceptual outcomes, namely exploring tactile spatial awareness, tactile roughness, and haptic device development, utilizing various additional cognitive and sensory loads [17, 58, 67, 68, 71, 73, 161].

However, there has been limited prior work exploring the role of cognitive-perceptual load on the detection of tactile stimuli [151]. Additionally, factors such as arm dominance, nerve stimulated, location stimulated, and sex have not been explored in relation to the modulation of cognitive-perceptual load. In turn, further examinations of the modulation of cognitive-perceptual load is needed to further explore the different factors that influence intact tactile perception.

2.3 The Utilization of Psychophysics Methodology in Tactile Perceptual Assessments

Psychophysics is a methodological framework used to study the relationship between physical stimuli and sensory perception, allowing for the precise quantification of stimuli detection and interpretation. Common techniques employed in tactile perception research include the method of limits, method of adjustment, and method of constant stimuli. In the method of limits, stimuli are presented in a series that gradually increase or decrease in intensity while the individual indicates when the stimuli are detected. In contrast, the method of adjustment allows participants to continuously adjust the intensity of a stimulus until it is just detectable. The method of constant stimuli, on the other hand, involves presenting a fixed set of stimuli with varied intensities in a random order and measuring the participant's detection response for each intensity level. These methods help generate psychometric functions, which plot the likelihood of detection against stimulus intensity. Psychometric functions typically follow a sigmoidal shape, with a clear threshold where the probability of detecting a stimulus rises sharply. The curve can be used to derive critical values like the just noticeable difference, providing a measure of sensory sensitivity [56].

Psychophysical measures are widely used in research aimed at exploring tactile detection because they offer precise, quantifiable insights into perceptual outcomes. By varying stimulus parameters (e.g., pressure, vibration, spatial location) and using psychometric curves, researchers can identify how different factors can influence tactile perception using these behavior-based outcomes. Here, we utilize the method of limits and method of adjustment, primarily for their accuracy and reduced time demands, to examine tactile perceptual outcomes. These techniques allow for the systematic investigation of detection thresholds under varying conditions, providing a clear framework for understanding the different factors that

can impact intact tactile perception [56].

Chapter 3

Considerations for Tactile Perceptual Assessments: Impact of Arm Dominance, Nerve, Location, and Sex in Young and Older Adults

3.1 Abstract

Intact tactile perception is essential to successfully interact with objects. While tactile examinations exist for capturing tactile impairments, recent investigations underscore that these examinations remain insufficient, particularly for adults following a neurological injury. To inform the design of improved tactile assessments, this study comprehensively captures factors that can influence tactile perception in young and older adults who are neurologically intact. We examined the impact of arm dominance (dominant/non-dominant), nerve (median/ulnar/radial), location (hand/elbow), and sex (male/female) on thresholds at which electrotactile stimuli could be consciously detected when applied to the skin in 20 young and 14 older right-arm dominant participants. Significant differences depending on arm dominance were not found in young ($p=0.6781$) or older ($p=0.2786$) adults. Yet, the nerve tested did yield differing thresholds in young ($p<0.0001$) and older ($p<0.0001$) adults. In young

adults, thresholds were less at the hand than elbow ($p=0.0031$). In older adults, the average threshold was greater at the hand than elbow. Importantly, in older adults the threshold at the hand increased with age to a greater extent than at the elbow ($p<0.0001$). Thresholds were greater in males than females in young adults ($p=0.0004$), whereas no significant sex differences were observed in older adults ($p=0.2560$). This work highlights the importance of addressing numerous factors and their interactions when assessing tactile perception (e.g., arm dominance, nerve, location, sex, age). Findings can inform the design of improved tactile assessments that more accurately capture why impairments arise, including following a neurological injury.

3.2 Introduction

Intact tactile, or touch-related, perception is critical for accurately perceiving and interacting with physical stimuli. Whether hugging a loved one, typing on a keyboard, or holding a cup of coffee, the ability to perceive tactile stimuli greatly influences the successful performance of daily tasks [15, 36]. Various patient populations, including those living with a neurological injury, experience tactile impairments, with the severity of the tactile impairments corresponding to their movement recovery and physical function post injury [65, 147]. Despite this understanding of the importance of intact tactile perception, numerous reviews underscore that existing tactile assessments remain insufficient for reasons including poor reliability, inadequate validity, unsatisfactory sensitivity to change, and limited ability to identify underlying mechanisms eliciting impairments [118, 165]. We are motivated to address these limitations in existing tactile examination methods by first comprehensively examining factors that could influence tactile perceptual outcomes in a population who is neurotypical (young adults), as well as aged (older adults). By testing for interaction effects between

each of these factors that were previously not explored (e.g., arm, nerve, location), findings could potentially inform the future design of more effective tactile assessments.

Tactile perception is known to worsen with aging, leading to tactile impairments in older adults [38]. These tactile impairments correspond to poorer quality of life and decreased functional independence [95, 176]. Identified reasons for why tactile impairments arise with aging include altered neurological, integumentary, cardiovascular, and/or endocrine function [32, 103, 104, 154]. Due to its significance on daily life, and overall indication of well-being, the factors influencing perception of tactile stimuli remain an area of ongoing exploration [2, 5, 18, 23, 38, 115, 146].

Prior work suggests that tactile perception can differ depending on the dominance of the arm examined, given the preferential use of one limb over the other depending on the task being performed [23]. The impact of arm dominance on tactile perception is of particular interest due to the number of daily activities requiring intact tactile perception and the coordinated use of both arms. This effect of arm dominance has been extensively studied in sensorimotor control literature [45, 131, 133]. Based on this prior work, we propose that the threshold at which tactile stimuli are detected may also differ depending on whether the dominant versus non-dominant arm is stimulated. However, existing literature exploring the role of arm dominance on tactile perception remains limited, with testing mainly conducted at single nerves and locations, and findings being inconsistent [14, 23, 57, 62, 181]. Here, we aim to explore how the dominance of one’s arm can influence conscious perception of electrotactile stimuli that are applied to the surface of one’s skin by examining multiple nerves and locations at each arm of individuals who are right-arm dominant.

When considering which nerves in the hand to examine, the median, ulnar, and radial nerves are of particular interest given that they each innervate unique and distinct regions that span across the arm, including complete coverage of the hand. Each of these nerves relays

tactile information from the innervated cutaneous tissue to the brain's higher centers for processing [117]. This innervation forms dermatomes, or specific skin areas, each uniquely supplied by sensory fibers from a particular nerve. The median and ulnar nerves, which innervate the majority of the palmar and dorsal surfaces of the hand, have the greatest dermatomal distribution when compared to the radial nerve [49, 98]. Additionally, the median and ulnar nerves are situated closer to the surface of the hand whereas the radial nerve is located deeper below the skin surface. For these reasons, we can expect differences in tactile assessment outcomes depending on the nerve examined. Notably, impairments in tactile perception can originate at individual nerves due to a variety of factors unrelated to the condition being tested, including undiagnosed conditions. However, much of the existing literature on tactile perception relies on findings from assessments focused on a single nerve, typically the median nerve [23, 57, 62, 181]. We propose that examining multiple nerves is a safeguard to avoid misinterpretation based on single nerve(s), as well as of interest for presenting a complete picture of tactile function at the hand.

Another consideration for tactile assessments is how tactile stimuli are perceived depending on the location of the arm stimulated. Intact tactile perception at each joint, extending along the entire length of the arm, is critical for functional arm use [117]. Accordingly, prior studies and clinical practice have investigated tactile perception by examining outcomes at differing arm locations. Their findings suggest that differences can arise in tactile perception depending on the arm location stimulated (e.g., hand versus elbow) [23, 101, 118, 122]. However, this approach of testing multiple arm locations when examining tactile perception is not always performed, including when investigating which factors impact tactile perception in individuals who have experienced disruption to the nervous system [14, 57, 59, 118, 181]. We propose that incorporating assessments at various locations on the arm ensures a more accurate understanding of tactile perceptual function.

Another important consideration when investigating tactile perception at the upper extremity is sex. Prior work identifies an effect of sex on tactile perceptual outcomes, with the effect depending on one's age [2, 12, 92, 121, 153, 173]. In young adults, females were found to have lower tactile detection thresholds in comparison with males [12, 121, 153, 173]. However, when older adults were examined, findings of whether sex has an effect became conflicted [2, 92].

In this study, we aim to better understand the impact of arm dominance, nerve, location, and sex on tactile perception in young adults and older adults. To address this aim, we examined the role of each of these factors, including and a subset of their previously unexplored interactions, on the conscious perception of electrotactile stimuli that are applied to one's skin. We determined detection thresholds, defined here as the minimum intensity at which electrotactile stimuli applied to one's skin become consciously perceptible. These thresholds were measured at the median, ulnar, and radial nerves, testing both the hand and elbow of each arm in right-arm dominant males and females who are young and older. By systematically measuring these detection thresholds, we could assess how detection of electrotactile stimuli applied to one's skin varies according to arm, nerve, location, and sex. Based on this testing, we provide normative results surrounding how each of the factors, and a subset of their interactions, influence perception of electrotactile stimuli applied to the skin of each arm. These findings can inform the future design and implementation of potentially more reliable electrotactile assessments that capture variability due to each of these factors prior to interpretation. More broadly, insights from this study could also inform the design and optimization of electrotactile stimulation methods for additional applications including haptic feedback devices, sensory substitution systems, and assistive technologies [83, 126, 127].

3.3 Methodology

3.3.1 Human Subjects Study

This study received approval from the Virginia Tech Institutional Review Board (23-1246). For this study, sex was defined as male or female based on the binary sex categorization assigned at birth. Additionally, gender identity, which may differ from sex assigned at birth, was recognized, and categories such as male, female, transgender, and non-conforming/non-binary were included. Demographic data were collected in accordance with the 2024 National Institutes of Health guidelines.

Eligibility Criteria

All participants were required to be right-arm dominant and have no neurological injuries and no musculoskeletal injuries at the upper extremities. In the young adult population, eligibility requirements included being between 18 and 23 years old. This age range was selected given the goal of characterizing typical behavior when processes governing development have largely peaked (in children) and processes inducing decline have largely not begun (in older adults) [16]. Eligibility requirements in the older adult population included being 55 years or older given prior work indicating that tactile perception can start to deteriorate at this age [88, 154].

Study Participants

The study included 20 young adults [7 males, 13 females; aged (median, lower quartile, upper quartile, range): 22, 20, 22, 18 - 23 years] and 14 older adults [7 males, 7 females; aged (median, lower quartile, upper quartile, range): 66, 59, 72, 56 - 79 years]. These sample

sizes for the young adults and older adults were each selected based on power analyses that we conducted. We point out that 15 older adults consented to participate, with one participant withdrawing from the study due to previously suggested externally-related concerns; no data were collected from this participant beyond the initial consenting process. All participants were right-arm dominant, and their sex and gender identity matched.

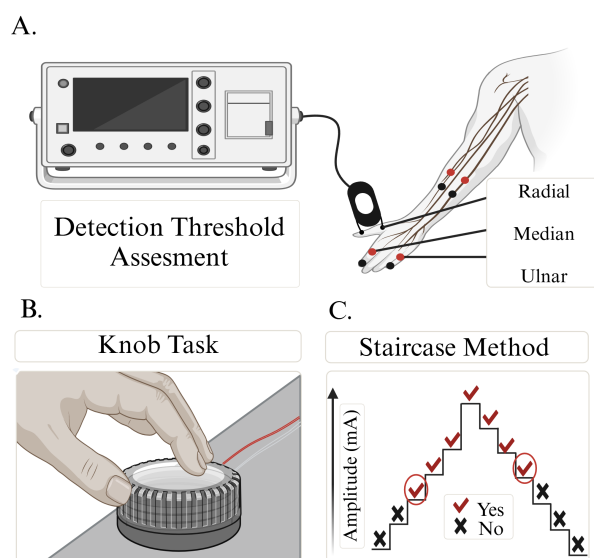


Figure 3.1: **Experimental Design.** **A.** Surface electrodes were positioned at digit 2 (skin innervated by the median nerve), digit 5 (skin innervated by the ulnar nerve), and the snuff box (skin innervated by the radial nerve) for hand stimulation. Stimulating electrodes were positioned at the skin innervated by the median and ulnar nerves of the elbow (1 cm distal from the elbow crease and 4 cm proximal from the ulnar side of the arm, respectively) for elbow stimulation. The cathode electrode was placed 3 cm distal to the anode surface electrode for all testing conditions.¹ **B.** This schematic illustrates the knob task, as participants were asked to turn a physical knob, which, in turn, controlled the stimulus amplitude. **C.** The schematic illustrates the staircase procedure. The symbols ‘✓’ and ‘✗’ represent when the participants were able or not able to detect the electrotactile stimulus, respectively. Encircled responses highlight the first time the participants indicated they could perceive the stimulus on the upward staircase and the final time the participants indicated they could perceive the stimulus on the downward staircase. These encircled responses were used to determine the detection threshold.

¹This image was created with BioRender.com.

3.3.2 Experimental Setup

A commercial device (DIGITIMER, Model: DS8R; Welwyn Garden City, England) delivered electrotactile stimuli to the surface of the skin that was innervated by each targeted nerve of each hand and elbow. An electrotactile stimulus consisted of a 100 μ s monophasic pulse, with its amplitude in the range of 0 - 100 mA given the goal of targeting the tactile $A\beta$ fibers [4, 25]. As shown in Figure 3.1, surface electrodes were positioned on the skin innervated by the median, ulnar, and radial nerves for hand stimulation, and on the skin innervated by the median and ulnar nerves for elbow stimulation. The radial nerve was not assessed at the elbow as subcutaneous needling is required due to the anatomy of the arm.

3.3.3 Tactile Assessments

All experimental data were captured at a sampling rate of 1 kHz. Data captured included electrotactile stimulus magnitude (mA) and time.

Knob Adjustment Assessment

To keep the duration of testing comparable among participants, the threshold at which the electrotactile stimulus could be just consciously detected was initially estimated using the method of adjustments (knob adjustment assessment). As depicted in Figure 3.1B, the participants were instructed to rotate a knob clockwise and counter-clockwise, which respectively increased and decreased the electrotactile stimulus amplitude, until they just detected the electrotactile stimulus. The electrotactile stimulus was automatically delivered every 1 second such that participants were required to indicate every 1 second if they could detect the 100 μ s electrotactile stimulus pulse that was delivered. From this initial estimated threshold of when the electrotactile stimulus was just detected, the longer duration staircase

procedure began to more precisely quantify the detection threshold [56, 94].

Staircase Assessment

During the staircase procedure, each electrotactile stimulus (100 μ s pulse) was administered at randomized time intervals sampled between a 3 to 5 second distribution to prevent participants' anticipation of the stimulus. Starting at 1 mA below the estimated detection threshold (based on the knob adjustment assessment), the magnitude of the electrotactile stimulus increased in an upward staircase. Similar to *Cai et al. (2023)*, stimuli were delivered in increasing intervals of 0.2 mA until participants verbally indicated three times in a row that the electrotactile stimulus was detected [23]. This marked the completion of one upward staircase. Then, the stimulus increased by 0.4 mA and continued in the opposite direction, beginning a downward staircase. Stimuli were delivered in decreasing intervals of 0.2 mA until the participants failed to detect the electrotactile stimulus three times in a row. This marked the completion of a downward staircase. Subsequently, the stimulus decreased by 0.4 mA before the upwards staircase repeated again. Every time the participants verbally confirmed perceiving the electrotactile stimulus, the experimenter pressed a button to record the amplitude of the electrotactile stimulus delivered and detected.

As indicated in Figure 3.1C, data of interest included the first confirmation of the three consecutive verbal indications that the participants could perceive the electrotactile stimulus on the upward staircase and the final confirmation that the participants could perceive the electrotactile stimulus prior to the three consecutive failures on the downward staircase. Each upward and downward staircase was completed three times, producing six total values for when participants confirmed detecting the electrotactile stimuli. The detection threshold was determined as the average of these six values when confirming detection of the electrotactile stimulus.

3.3.4 Experimental Protocol

Participants were instructed to abstain from caffeine and other non-essential medications on the day of each session to avoid potential effects stemming from physiological alterations to nerve signal transmission [22, 169]. Upon obtaining the participants' consent to take part in the study, the experimental protocol began and lasted approximately two hours.

To ensure typical cognitive and sensorimotor function in the older adults, several screening assessments were initially administered with this population. The participants completed the Montreal Cognitive Assessment (MoCA), allowing for screening of cognitive function [76]. Scores of 26 or higher led to inclusion as these scores are indicative of being typical [27]; the maximum score possible is 30. Following, intact tactile perception was determined using Von Frey monofilaments [60]. Aligned with previously described methods, a monofilament was used to apply a force of 2.00 gms to the anatomical snuffbox (thumb – radial nerve), digit 2 (index fingertip – median nerve), and digit 5 (pinky fingertip – ulnar nerve) to ensure participants could detect the tactile stimulus and, accordingly, had intact protective sensation [86]. Additionally, two-point discrimination testing was performed at the same locations to further evaluate tactile function with a perceptual task that involves more cortical processing (discrimination task) than occurs with a detection task. Participants were required to score within the typical range (< 6 mm) on the two-point discrimination task to continue with their participation [102]. Finally, the nine-hole peg test was administered to screen for fine motor coordination and ability to follow simple directions. Participant scores were compared with normative data [51], and performance within these norms was deemed acceptable. Additionally, BMI and body temperature data were collected in the older adults as this interest arose after data collection was completed in the young adults.

Next, our custom tactile examination experimental protocol began. Initially, participants

underwent a training protocol during which they were taught what the electrotactile stimuli felt like and how to perform the experimental tasks (i.e., how to turn a knob for the knob adjustment assessment and how to complete one upward and downward staircase for the staircase assessment, as described in Sections 3.3.3 and 3.3.3, respectively). This training was done to ensure participants understood the testing procedures and completed learning. Once participants indicated feeling comfortable with the procedures, testing began. The participants lay supine in a clinical bed and wore a blindfold and noise-canceling headphones to prevent distraction due to audiovisual stimuli [155, 171]. Data were collected one nerve and one location at a time. After completion of testing at one arm, the procedures were conducted at the opposite arm. The testing conditions were pseudo-randomized using a Latin square design, which determined the sequence of nerve, location, and arm presented.

3.3.5 Statistical Analysis

Initially, the data for the young adults and older adults were analyzed separately to capture effects arising within each group, independently. These data were fit to a linear mixed-effects model, with the fixed effects of testing arm, nerve, location, sex, and age, along with their interactions. In secondary analyses for the older adults, we included BMI and body temperature as fixed effects in the model to explore their potential impacts. Next, we captured differences between the young adults and older adults by analyzing all the data collected all together, with age group (young adult, older adult) as a factor and age removed as a factor. For each of these analyses, participant was included as a random effect and detection threshold as the dependent variable. An analysis of variance (ANOVA) identified significant interactive and fixed effects. The ANOVA was conducted using a hierarchical approach in which non-significant interaction terms were first removed, followed by non-significant main effect terms. Post-hoc pairwise comparisons, adjusted with a Tukey correction, determined

which pairs significantly differed for a significant effect.

3.4 Results

Here, we present the results summarizing participants' ability to detect electrotactile stimuli applied to the skin when at the different nerves (median, ulnar, and radial) and distinct locations (elbow, hand; dominant arm, non-dominant arm) are stimulated.

3.4.1 Power Analysis for Sample Size Determination

To determine the appropriate sample size for this study, an estimate was obtained using a power simulation for a linear mixed-effects model with the objective of achieving 80% statistical power. Power calculations were iteratively conducted for each nerve and location, providing tailored estimates that reflected the distinct variances associated with each. For the young adult population, 16 participants would give 86.80% power to detect a difference of 1.4 mA between arms when comparing the dominant and non-dominant arms. This analysis assumed a within-subject standard deviation of 1.7 mA based on preliminary data collected from three participants. For the older adult population, 14 participants would give 84.50% power to detect a difference of 1.3 mA between arms when comparing the dominant and non-dominant arms. This analysis assumed a within-subject standard deviation of 1.2 mA based on preliminary data collected from four participants. This approach allowed for a comprehensive estimation of participant size needed to observe a difference between arms when assessing tactile perception, with the desired level of statistical power across the study design.

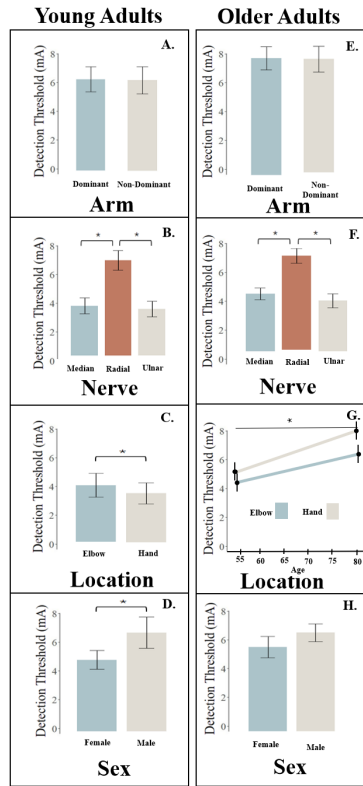


Figure 3.2: **Role of Arm Dominance, Nerve, Location, and Sex on Detecting Electrotactile Stimuli Applied to the Skin in Young Adults and Older Adults.** The bar plots indicate the mean (bar height) and standard deviation (error bars) of the detection thresholds for 20 young adults and 14 older adults who are all right-arm dominant. Statistical significance is indicated by a line with a star above. Plots A-D provide outcomes for the young adults, while plots E-H provide outcomes for the older adults. Plot G illustrates the interactive relationship between age and location, showing how their combined effects significantly influence detection. The different manner by which the data are presented in Panel G is because only these data for the older adults had the interaction effect.

3.4.2 Young Adults

Results for the young adults are summarized in plots A-D of Figure 3.2. The detection threshold did not statistically significantly differ depending on the dominance of the arm examined for the tested right-arm dominant participants ($F(1,176)=0.17$, $p=0.678$). In contrast, nerve had an effect on the detection threshold ($F(2,176)=233.91$, $p<0.001$), with the

radial nerve (7.30 mA) having a higher detection threshold than the median nerve (3.83 mA) and ulnar nerve (3.59 mA). When analyzing the location stimulated, the detection threshold at the elbow (3.92 mA) was higher than at the hand (3.49 mA) ($F(1,176)=9.01$, $p=0.003$). The detection threshold differed depending on sex ($F(1,18)=19.11$, $p<0.001$), with the males (5.38 mA) having a higher detection threshold than the females (3.92 mA). We included age in the statistical model and observed no statistically significant effect on the detection threshold ($F(1,18)=1.86$, $p=0.190$). Combined, these results indicate that thresholds at which electro-tactile stimuli applied to the skin are detected differ depending on the nerve, arm testing location, and sex in young adults. Yet, these findings did not support our initial hypothesis that the detection threshold would significantly differ depending on the dominance of the arm tested in our right-arm dominant participants.

3.4.3 Older Adults

Results for the older adults are summarized in plots E-H of Figure 3.2. Arm dominance was not found to statistically significantly affect the detection threshold in our right-arm dominant participants ($F(1,813)=1.18$, $p=0.279$). Nerve did have an effect on the detection threshold ($F(2,813)=586.56$, $p<0.001$), with the radial nerve (8.67 mA) having a greater detection threshold than the median nerve (5.21 mA) and ulnar nerve (4.59 mA). An interaction effect between age and arm location was observed on the detection threshold ($F(1,812)=68.16$, $p<0.001$); the detection threshold increased with age to a greater extent at the hand than at the elbow. At the age of 55, the estimated detection threshold was 5.05 mA at the hand and 4.77 mA at the elbow. At the age of 80, the estimated detection threshold was 8.00 mA at the hand and 6.43 mA at the elbow. Sex was not found to have a statistically significant effect on the detection threshold ($F(1,12)=2.72$, $p=0.125$). Additionally, body-mass index (BMI) ($F(1,11)=1.35$, $p=0.269$) and temperature ($F(1,812)=2.14$,

$p=0.144$) were not found to have a statistically significant effect on the detection threshold. Combined, these results indicate that the threshold for detecting electrotactile stimuli applied to the skin differed depending on the nerve. Moreover, these results indicate that the negative impact of aging on tactile detection is greater at the hand than at the elbow. However, similar to our finding in young adults, the results did not reveal an impact of the dominance of the arm tested on the detection threshold in our right-arm dominant participants. These findings suggest that tactile perception can vary within each arm, and that this perception is susceptible to decline with aging, which may be more severe distally.

3.4.4 Comparing Young Adults and Older Adults

The between-groups statistical analyses revealed that young adults detected the electrotactile stimuli at thresholds that were, on average, 0.99 mA less than the older adults ($F(1, 1502)=136.70$, $p<0.001$). The amplitude at which the electrotactile stimuli were just detected at the non-dominant arm was, on average, 0.13 mA less than at the dominant arm ($F(1, 1502)=5.30$, $p=0.021$). Nerve did have an effect on the detection threshold ($F(1, 1502)=840.02$, $p<0.001$), with the radial nerve having a greater detection threshold by 3.47 mA than the median nerve and ulnar nerve. We found a significant interaction between age group and location ($F(1, 1501) = 159.69$, $p<0.001$), where the extent to which the detection threshold increased from young adults to older adults was greater at the hand than at the elbow. In the young adults, the estimated detection threshold was 4.2 mA at the hand and 5 mA at the elbow. In the older adults, the estimated detection threshold was 5.4 mA at the hand and 5.6 mA at the elbow. Additionally, we found a significant interaction between sex and age group ($F(1, 1502) = 16.22$, $p<0.001$), where females had a greater increase in the detection threshold with age than males. In the young adults, the estimated detection threshold was 3.8 mA in the female participants and 5.4 mA in the male participants. In

the older adults, the estimated detection threshold was 5 mA in the female participants and 5.6 mA in the male participants. Given that BMI was not obtained for the young adults, BMI was excluded from this between-groups analysis and, hence, is not reported. Combined, these results indicate that electrotactile detection thresholds vary depending on the age group assessed. These findings reinforce that tactile perception declines with age, and that this decline may be more pronounced in distal regions of the arm. Additionally, the findings suggest a greater decline in consciously detecting tactile stimuli with age in females than in males.

3.5 Discussion

Tactile, or touch-related, perception is crucial for successful performance of daily tasks, like buttoning a shirt or holding a cup [15, 36]. While the critical role of intact tactile perception on functional independence is well-established, the underlying mechanisms driving tactile impairments often remain insufficiently understood, including in populations recovering from neurological injuries [118, 165]. Previous studies have highlighted that this gap in understanding is often attributed to limitations in existing tactile assessment methods [118, 165]. Here, we aimed to address this gap by first exploring different factors, and a subset of their interactions, that may influence tactile perception in a population that is neurologically intact. Existing literature indicates that the factors of arm dominance, nerve, location, and sex can influence varying aspects of sensorimotor control independently. Yet, when assessing tactile perception, prior literature does not account for all of these factors combined, including their interactions [23, 57, 62].

In our study, we aimed to address this limitation by investigating if the threshold for detecting electrotactile stimuli applied to the skin generalizes across multiple nerves and locations of the

dominant and non-dominant arms of right-arm dominant male and female young adults and older adults. These results can be used as normative outcomes for subsequent studies that investigate why tactile impairments arise in patient populations. Based on this knowledge, we anticipate that future work can identify how to more accurately examine tactile impairments in patient populations, including those following a neurological injury. Moreover, findings from this work could inform the design of electrotactile stimulators for use in scenarios such as haptic communication, sensory substitution, and assistive technologies [34, 83, 163, 178].

3.5.1 Role of Arm Dominance on Tactile Perception

Prior work indicates hemispheric lateralization, where each hemisphere specializes in differing aspects of a sensorimotor process [131, 133], could contribute to sensorimotor differences depending on the dominance of the arm being used. Aligned with this notion, some prior studies [14, 181] did not find an effect of arm dominance, while others did [23, 57, 62]. In this work, we did not observe a significant impact of whether the dominant versus non-dominant arm was stimulated on the detection threshold when analyzing the data independently for the young adults and older adults who were all right-arm dominant. However, we did observe significantly smaller detection thresholds when the non-dominant arm was stimulated than the dominant arm when all the data were grouped together to compare the young adults to the older adults. The increased number of participants (34 in total) allowed for an effect to be observed, albeit for a relatively small effect size (0.13 mA difference).

A possible reason for not observing a significant effect when analyzing the data for the young adults and older adults in isolation is the simplicity of the task, as literature indicates that more complex tasks are needed to observe an effect of arm dominance on tactile perception [14, 23, 29, 91, 100, 140]. For our protocol, participants were instructed to remain

relaxed (i.e., no muscle activation) and indicate when an externally applied electrotactile stimulus was detected. Future work could use our comprehensive approach of testing multiple nerves and locations to determine whether the impact of the dominance of the arm on tactile perception generalizes across the arm during more complex tasks (e.g., motor activation task, cognitive-perceptual integration task).

Another possible reason for conflicting results regarding an impact of arm dominance on tactile perception is the lack of conformity in how tactile stimuli are provided. Existing literature reports findings based on stimulation using Von Frey monofilaments and electrotactile stimuli [118, 165]. While limitations are known for each of these tactile stimulation approaches, these approaches are identified as the best currently available options for tactile examination [165]. Von Frey monofilaments involve testing with a small, fixed number of physical stimuli magnitudes (e.g., 6, 20), which limits its sensitivity, or ability to detect subtle changes in tactile perception. For example, participants with a very low or very high tactile detection threshold may not show measurable differences, highlighting the limitations in capturing nuanced changes in perception. Additionally, examinations with Von Frey monofilaments have conflicting findings in test-retest reliability, with some protocols demonstrating good reliability while others reporting poor reliability [118, 159]. Differences in reliability may stem from variability in stimulus application, including timing, force, and location [159]. While certain methodologies optimize reliability, the potential for examiner-dependent variability remains a concern, particularly in studies requiring precise threshold measurements. In considering electrotactile stimulation, this approach has great test-retest reliability [178, 180]. One reason for this great test-retest reliability is its sensitivity to capture very small changes due to the ability of delivering precise stimuli repeatably across a very large range of stimuli. Another reason is that variability from the assessor during the examination can be avoided by automating the timing, location, and magnitude when

applying the electrotactile stimuli. Despite these benefits, perceptual outcomes can differ between tested locations when using electrotactile stimuli for reasons including the positioning of the electrodes and the preparation of the skin [178, 180]. Therefore, an impact of the experimental setup, rather than human perception, could lead to differences in perceptual outcomes depending on the tested location. Future work could consider standardized protocols to minimize these inconsistencies and enhance comparability across studies; this study did use a standardized protocol to limit such potential effects. We recommend testing multiple locations on each arm to help reduce this potential undesired experimenter-induced variability, regardless of the tactile assessment approach and standardization protocol used.

3.5.2 Role of Nerve on Tactile Perception

The threshold for detecting electrotactile stimuli applied to the skin was higher at the radial nerve than the ulnar nerve and median nerve in both arms of the young adults and older adults when analyzing the data independently. This trend remained the same when analyzing the data grouped all together for the young adults and older adults. This distinction in the detection threshold between nerves could be attributed to anatomical differences at the upper limb. The palmar aspect of the hand (innervated by the median and ulnar nerves) has greater receptor densities than the dorsal aspect of the hand (innervated by the radial nerve) [74, 110]. It is reasonable to expect that the applied electrotactile stimuli activate more nerve fibers innervating the palmar aspect than the dorsal aspect of the hand, leading to improved perception. Another consideration is that a stronger electrotactile stimulus may be required to activate the radial nerve than the ulnar and median nerves since the radial nerve is situated deeper below the skin [158]. We point out that since the surface electrodes applied electrotactile stimuli to the skin surface, the superficial nerve fibers near the skin were targeted. Intraneural stimulation could access deeper nerve bundles, which could potentially

lead to differing results. All together, we propose that our findings regarding an impact of nerve on thresholds for detecting electrotactile stimuli applied to the skin reflect anatomical differences, including variations in receptor density and nerve depth [74].

3.5.3 Role of Arm Location on Tactile Perception

We observed that the location on the arm where the electrotactile stimuli were applied impacted the threshold at which the electrotactile stimuli could be detected in both the young adults and older adults. When the data were analyzed all together, there was a significant interaction between age group and location, with the extent to which the detection threshold increased from young adults to older adults being greater at the hand than at the elbow. One reason that tactile perception may differ across age groups, particularly in distal regions such as the hands, could be due to age-related physiological changes [18, 38, 42, 108]. These changes are further explored in Section 3.5.3.

Young Adults

In the young adult population, when their data were analyzed independently, we observed that the threshold for detecting the electrotactile stimuli applied to the skin was lower at the hand than at the elbow. This finding corroborates prior work demonstrating that the hand is more sensitive in detecting tactile stimuli than other parts of the arm [28, 31, 122]. An explanation for why the hand is more sensitive than the elbow is the density of innervation is greater at the hand than at the elbow [37, 80, 110]. In turn, we can expect that the applied electrotactile stimuli will have a greater chance at activating more nerve fibers innervating the hand than the elbow. Another important anatomical factor is that the nerves at the elbow are located deeper beneath the skin compared to those at the hand [158]. As a result,

a stronger electrotactile stimulus is needed to activate these deeper-lying nerves, due to the greater physical distance between the nerve and the electrodes. From an evolutionary perspective, humans have relied heavily on their hands for survival when compared to the elbow, further supporting the need for greater innervation at the hand. Consequently, our finding that the hand is more sensitive to tactile stimuli than the elbow aligns with the findings of prior studies.

Older Adults

In contrast to the findings in the young adults, we observed that detection thresholds were, on average, higher at the hand compared to the elbow in older adults when their data were analyzed independently. Additionally, we observed a significant interaction between the location stimulated and the age of the participant, such that thresholds at the hand increased to a greater extent than at the elbow with increasing age. To the best of our understanding, this age-related impact is not currently known. This pattern may reflect age-related physiological changes that occur across systems such as the nervous, circulatory, integumentary, and endocrine systems [32, 103, 104, 154]. Age-related changes within these systems can contribute to poorer tactile perception [38], whereas such age-related changes are not observed in young adults who typically maintain intact physiological function and tactile sensitivity during this stage of their lives [3, 5, 18, 42, 108]. Specifically, the distal regions of the body, such as the hands, are more vulnerable to age-related changes, including peripheral nerve degeneration, reduced capillary density, and compromised skin integrity [108]. These changes may more severely impair signal transmission and tactile sensitivity at distal sites, aligning with literature suggesting that tactile impairments often emerge and are more pronounced distally than proximally, including in an aging population [108, 135].

3.5.4 Role of Sex on Tactile Perception

The threshold at which the electrotactile stimuli applied to the skin could be detected differed depending on one's sex in young adults, but not in older adults, when their data were each analyzed independently. When the data were grouped all together, the analysis revealed an interaction effect between age group and sex, with the detection threshold increasing to a greater extent in females than males with age. Combined, these findings suggest that while sex differences in tactile perception may be evident at a younger age, these differences may diminish with age.

Young Adults

The threshold at which the electrotactile stimuli applied to the skin could be detected differed depending on sex, with females having a lower detection threshold when compared to males. Sex differences in tactile perception are often attributed to factors such as fingertip size, skin compliance, hormones, BMI, behavior socialization, and body temperature, which vary between males and females [14, 87, 93, 121, 173, 177]. In our study, we utilized electrotactile stimuli applied to the skin, which bypasses cutaneous mechanoreceptors to activate free nerve endings directly. This approach ruled out the influence of fingertip size and skin elasticity, putting the focus on other physiological factors including hormonal differences and body temperature.

As relevant to tactile perception, BMI positively correlates with detection thresholds; as BMI increases, it becomes more difficult to perceive tactile stimuli [113]. Based on this information, we would expect males to detect the electrotactile stimuli at higher amplitudes than the females since males typically have a higher BMI [87]. The findings in our study supported this hypothesis, with males have a higher detection threshold than females. That

said, we did not capture BMI in the young adult population, so we do not know if our participants reflected norms of males having a larger BMI, on average, than females.

Body temperature negatively correlates with detection threshold, such that increasing body temperature makes it possible to detect stimuli at lower amplitudes [47, 93, 157]. As relevant to sex, it has been reported that females have a higher body temperature than males [93]. Therefore, it is reasonable to expect that females can detect stimuli at lower amplitudes than males, which aligns with our findings. We did not track or control for body temperature and, hence, cannot indicate whether the differences in the detection threshold were temperature dependent.

Another factor to consider regarding the impact of sex on tactile perception is a potential behavioral socialization effect [177]. Females and males may respond whether they detect tactile stimuli differently based on differing societal expectations, with one group more readily stating ‘yes’ than the other. Future work could determine whether differences in the manner by which females and males socialize correspond to differences in their responses during the tactile examination.

Older Adults

Corroborating previous research [2, 12, 92, 121, 153, 173] in older adults, sex was not found to significantly affect tactile perception in our tested older adults. This finding in the older adults contrasts the significant effect of sex found in the younger adults. As discussed in Section 3.5.4, factors such as BMI and body temperature may impact tactile perception when utilizing electrotactile stimuli. Data were collected from the young adults prior to the older adults so we included BMI and body temperature measures to examine a broader range of influences on tactile perception in the older adult population. When analyzing the

potential roles of BMI and body temperature on sex differences, we found that neither sex nor BMI showed a significant effect on tactile perception in this older population.

Another consideration is a sex-dependent change with aging. Studies comparing young adult males to older adult males show no significant differences in tactile perception [2]. However, when young adult females are compared to older adult females, significant changes in tactile perception are observed [2]. This result suggests that sex differences in tactile perception may be driven by factors present in young adult females, but not in older adult females. One potential explanation is that hormonal changes post-menopause may attenuate observed sex differences. Estrogen, which has been shown to play a neuroprotective role, declines with aging [92, 141, 142, 160]. This decline in estrogen levels with aging might contribute to changes in peripheral nerve sensory function and overall tactile perception, contributing to the sex-dependent results we observed [106, 153]. Future work can explore such variables that could explain differences in detection thresholds depending on sex and age.

3.5.5 Future Considerations

The findings of this study emphasize the need to consider multiple variables and their interactions, including nerve, location, and sex, when designing tactile assessments for patient populations. By establishing normative data and pinpointing variables and a subset of their interactions that influence tactile perception, this work provides a foundation for developing more precise and personalized assessments. To determine whether the observed differences translate to meaningful changes in arm function, future research can determine the minimal clinically important differences for electrotactile stimuli in the context of tactile perception. Moreover, exploring how electrotactile perception compares to other forms of sensory stimulation, such as force or vibrotactile stimuli, could help contextualize these

findings within broader efforts to further our understanding of tactile perception and its underlying mechanisms. Future work can also integrate these insights into clinical protocols to facilitate earlier identification and targeted interventions for tactile impairments, including in individuals with neurological injuries.

To expand beyond our study of electrotactile stimuli, future work can examine perception of tactile stimuli that physically interact with the skin (e.g., vibrotactile stimuli). Examining these physical interactions, along with their respective frequency-dependent effects [61, 69], could provide deeper insight into sensory processing mechanisms that were beyond the scope of this work. Furthermore, future studies can consider the influence of sex-based behavioral biases on tactile perception, perhaps by testing individuals from different cultures who exhibit differing sex-based behavioral tendencies. Finally, future efforts could use our findings to inform the design of electrotactile displays for areas such as haptic feedback and sensory substitution systems.

3.5.6 Limitations

A limitation of this research is the exclusion of individuals who are left-arm dominant, despite research indicating that approximately 10% of the population is left-arm dominant [41]. Accordingly, it remains unclear whether the results obtained from this protocol in individuals who are right-arm dominant would generalize to individuals who are left-arm dominant.

An additional limitation is that we did not examine all nerves at all locations of the arm. Accordingly, our findings cannot be generalized to the entire arm. This limitation is a feasibility constraint since we needed to decide how many nerves and locations to examine to successfully complete this research and draw conclusions. We targeted the three main nerves at the hand, and tracked two of those nerves, which could be tested more proximally,

at the elbow, with the goal of having a robust, while simultaneously practical approach for examining tactile perception. Future studies could be more ambitious in the scope of variables examined to gain an even more comprehensive understanding of the impact of differing factors, and a subset of their interactions, on tactile perception.

Another limitation is that we draw conclusions about tactile perception based on electro-tactile stimuli. Electrotactile stimuli bypass mechanoreceptors whereas physically applied tactile stimuli activate the cutaneous mechanoreceptors. Even so, both electrotactile stimuli and physically applied tactile stimuli largely engage the same neural pathways (e.g., dorsal column medial lemniscal pathway), enabling relevant interpretations of tactile function and perception.

Finally, another limitation is that our conclusions are based on a relatively small sample size from southwest Virginia, which may not be generalizable to broader populations. We acknowledge that our sample of 20 young adults and 14 older adults, while sufficiently powered for this work, may not represent these populations as a whole. Future studies could extend this work by examining diverse populations, thereby enhancing the robustness and applicability of our results. Additionally, our testing scope was limited to young adults (18–23 years old) and older adults (55+ years old), which may influence the interpretation of our findings. Further research is needed to determine whether these effects persist across different age groups and demographics.

3.6 Conclusion

This study explored how a variety of factors (dominance of arm, nerve, location, sex), and their interactions, impact tactile perception by examining ability to consciously detect electrotactile stimuli that are applied to the skin in young and older males and females who are

right-arm dominant. An effect of nerve, location, and sex on detecting tactile stimuli was found in the young adults, and an effect of nerve and an interaction between location and age was found in the older adults. Results obtained here could be used as normative data for comparison with future studies that aim at understanding underlying mechanisms that may elicit impaired tactile perception following a diagnosis, such as a neurological injury. Additionally, given the relevance of electrotactile displays for haptic technologies, our findings may offer valuable insights for the development of electrotactile stimulation methods for these applications.

Chapter 4

Impact of an Auditory Perceptual Task on Consciously Perceiving Electrotactile Stimuli in Young Adults

4.1 Abstract

Tactile perception plays a critical role in sensorimotor integration and functional task performance. Consequently, the various factors, and their interactions, that influence tactile perception are of interest when considering daily function. One such factor, cognitive-perceptual load, is of particular interest, as it reflects the mental demands placed on an individual during complex, multi-sensory tasks. To examine this cognitive-perceptual factor, this study evaluated how adding an auditory discrimination task impacts tactile detection and discrimination accuracy and precision, while also considering additional factors including arm dominance, sex, and age. Participants completed a series of electrotactile detection and discrimination tasks under single-task (tactile only) and dual-task (tactile and auditory) conditions. Auditory stimuli was introduced via a partial auditory stroop task. Secondary factors of interest included arm dominance, sex, stimulation site, and their interactions. Primary outcomes included electrotactile detection and discrimination accuracy and variability. Detecting electrotactile stimuli while discriminating auditory stimuli significantly impacted

how precisely ($p < 0.001$), yet not accurately ($p = 0.359$), the electrotactile stimuli could be detected. In contrast, discriminating electrotactile stimuli while discriminating auditory stimuli significantly impacted how accurately ($p < 0.001$), yet not precisely ($p = 0.987$), the electrotactile stimuli could be discriminated. Arm dominance significantly impacted how accurately the electrotactile stimuli could be detected ($p < 0.001$) and discriminated ($p < 0.001$). Participant sex and stimulation location (elbow, fingertip) had a significant interaction effect when detecting ($p < 0.001$), yet not discriminating ($p = 0.370$) the electrotactile stimuli. This work examined the impact of a cognitive-perceptual load on perceiving tactile stimuli, and highlighted additional important factors including arm dominance, sex, and stimulation location when assessing tactile perception in young adults. Results suggest that the addition of an auditory discrimination task increased variability when detecting electrotactile stimuli. Additionally, the addition of an auditory discrimination task reduced accuracy when discriminating electrotactile stimuli. Future work can expand these investigations to include differing populations including individuals following a neurological injury.

4.2 Introduction

When engaging with the world around us, we often encounter cross-modal sensory stimuli experiences that involve the integration of multiple sensory inputs (e.g., visual, auditory, tactile, olfactory) [44, 84, 124]. These interactions are fundamental to how we perceive and respond to our environment, as different senses work together to create a unified and coherent understanding of the environment around us [66, 103]. This integration of various sensory stimuli plays a critical role in perception and decision-making, enabling individuals to navigate complex and dynamic environments. A common example of this multi-sensory detection and interpretation is the cocktail party effect, where we selectively attend to specific

stimuli, such as a friend’s voice, while filtering out background noise like music or competing conversations [17, 105, 112, 171, 174]. Among the various sensory systems, tactile, or touch-related, perception is especially vital for interacting with the physical world [36, 48]. It provides direct, immediate feedback about objects and surfaces, allowing for the detection of environmental changes, guiding motor actions, and supporting fine motor coordination. The ability to accurately perceive tactile stimuli is essential for both performing routine daily activities and learning more complex motor tasks, making tactile perception a critical aspect of functional independence [36, 95, 176].

The factors that influence tactile perception remain a topic of considerable interest given the many remaining unknowns surrounding the perceptual process. Prior work from our group explored several such factors, including arm dominance, nerve stimulation site, anatomical location, participant sex, and their interactions [156]. While current literature often examines these factors independently [14, 23, 57, 62, 181], our previous findings suggest that a more comprehensive approach is necessary to understand their interactions and combined impact on tactile perception [156]. One factor of particular interest is arm dominance, or the preferential use of one limb over the other. Although some studies report poorer tactile acuity in the dominant arm when compared to the non-dominant arm [14, 23, 57, 181], others suggest no significant difference depending on the arm stimulated [62, 156]. These mixed findings may arise in part from differences in task design, particularly the cognitive and perceptual demands of the task [5, 14, 156]. Previous work in the motor control literature suggests that an arm dominance effect emerges as the complexity of the task increases [14, 131, 133]. As such, a deeper exploration of how arm dominance and task demands interact to influence tactile outcomes is of interest, here in the context an associated cognitive-perceptual load.

Cognitive-perceptual load refers to the mental resources required to process sensory information and complete a task, and it may play a critical role in shaping the efficiency and

accuracy of tactile perception [7, 11, 17, 68, 161]. Theories exploring cognitive-perceptual load distinguish between two differing types of demand: cognitive and perceptual load, which can influence each other in complex and dynamic ways [17]. The associated cognitive load refers to the demands placed on executive functions during the completion of a task, whereas perceptual load refers to the complexity of a sensory-related stimulus. Here, we manipulate the cognitive and perceptual loads associated with a tactile perception task. Namely, we modulate the associated cognitive load by introducing concurrent auditory stimuli, and instructing participants to interpret and verbally indicate specific cues (i.e., partial auditory stroop task) [77, 112]. Additionally, we modulate the perceptual load by introducing both tactile detection and discrimination tasks. According to cognitive-perceptual load theory, when task demands exceed available executive cognitive resources (e.g., working memory and selective attention), performance on tasks can be hindered [8, 10, 17, 58, 97]. This theory is particularly relevant for functional tasks that involve multiple demands, such as a primary task (e.g., tactile perception) and a secondary task (e.g., auditory task), where cognitive resources must be divided between competing demands [7, 114, 136].

The extent of the cognitive-perceptual load required for a task varies based on the nature and complexity of the task [9, 14, 139]. As task complexity increases, greater sensory and executive resources are required to process incoming information and initiate an appropriate response. Higher cognitive-perceptual load conditions demand more working memory and attentional capacity, which can, in turn, reduce available resources for other task components [72]. Working memory plays a particularly important role in managing this load, as it temporarily stores and manipulates sensory information to support real-time decision-making [8, 10]. However, because working memory has a limited capacity, performance can decline when the cognitive-perceptual load exceeds these limitations. In the context of tactile perception, a heightened load may impair an individual's ability to detect or discriminate

stimuli, particularly when the cognitive resources are diverted to a secondary task such as interpreting auditory cues.

This work aims to further examine the role of the cognitive-perceptual load in shaping tactile perception. By manipulating both the cognitive and perceptual demands of a tactile task, we seek to understand how these factors independently and interactively influence tactile accuracy and variability. A deeper understanding of these mechanisms is critical for developing normative data and may offer valuable insights into sensory processing in clinical populations commonly affected by tactile impairments, such as older adults and individuals with neurological injuries [78, 118, 165]. Ultimately, this work underscores the importance of considering cognitive-perceptual load as a factor in studies of tactile perception and highlights its relevance for both basic research and applied clinical settings.

4.3 Methodology

4.3.1 Human Subjects Study

This study received approval from the Virginia Tech Institutional Review Board (23-1246). The study requirements included dominance of the right arm and no self-reported upper extremity musculoskeletal injuries, neurological conditions, or hearing impairments. An age requirement of 18 - 26 years was set based on previous studies defining young adults [156]. Participants noted their sex (male, female) based on their sex assigned at birth and gender identity (male, female, transgender, non-conforming/non-binary), aligning with the 2024 National Institutes of Health guidelines.

4.3.2 Study Participants

The focus of the electrotactile detection study was a sample of 14 young adults [6 males, 8 females; age (median, lower quartile, upper quartile, range): 18, 18, 22, 18 - 25 years]. The focus of the electrotactile discrimination study was a sample of 12 young adults [5 males, 7 females (sex, gender identity); age (median, lower quartile, upper quartile, range): 23, 19, 23, 18 - 25 years]. Based on the initial data for each study, power analyses determined sufficient sample sizes.

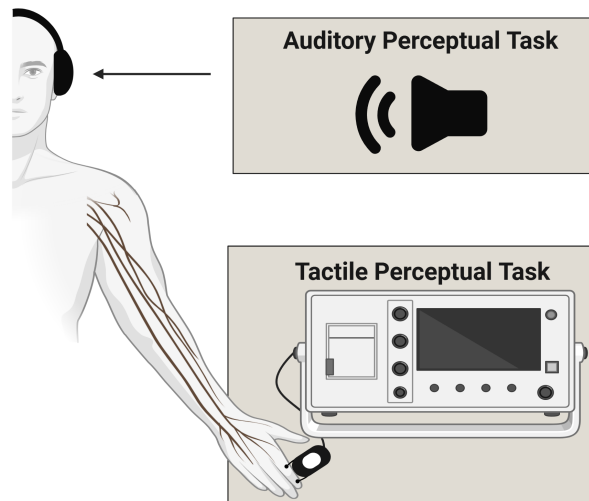


Figure 4.1: **Experimental Design.** Participants were divided into two separate studies: one focused on electrotactile detection and the other on electrotactile discrimination. Each study incorporated an additional auditory task designed to modulate the cognitive-perceptual load, specifically a partial auditory stroop task. Participants were instructed to verbally report the perception of each stimulus.¹

4.3.3 Experimental Setup

A sampling rate of 1 kHz was utilized to capture all experimental data. To apply the electrotactile stimuli, surface electrodes were placed on the skin innervated by the median, ulnar,

¹This image was created with BioRender.com.

and radial nerves, as shown in Figure 2.2. A commercial stimulator (DIGITIMER Model: DS8R; Welwyn Garden City, England) delivered the electrotactile stimuli to a singular nerve, delivering stimuli one location and one nerve at a time. To selectively activate tactile $A\beta$ fibers [4, 25], the stimuli had monophasic pulses of 100 μ s with amplitudes ranging from 0 to 100 mA. During the detection task, one pulse was delivered, while during the electrotactile discrimination task two consecutive pulses were delivered.

4.3.4 Tactile Assessments

Tactile detection and discrimination was investigated during the first and second study, respectively. During the tactile detection study, the electrotactile stimulus magnitude (mA) was captured; during the tactile discrimination study, the primary data captured was the inter-pulse interval (ms) or the duration between two electrotactile stimuli.

The outcomes of interest were electrotactile accuracy and variability. Referred to as the minimal stimulus intensity required for conscious perception, accuracy was defined as the absolute perceptual threshold. This corresponded to the minimum perceivable stimulus magnitude for the detection task. For the discrimination task, this corresponded to the minimum perceivable inter-pulse interval (IPI) or duration between the two electrotactile stimuli to become just detectable as two stimuli. Variability indicated the stability of detection and discrimination responses to stimuli, reflecting the consistency of the perceptual threshold across trials.

Tactile Detection Assessment

Thresholds at which electrotactile stimuli were just detected were identified in the first study using similar procedures to those described in [156]. The method of adjustments was em-

ployed to obtain an initial estimate of the electrotactile detection threshold and to encourage consistent testing durations among participants. During this procedure, participants modified the stimulus magnitude until they could just perceive the electrotactile stimulus by adjusting a knob. Every second, an electrotactile stimulus was delivered, and participants noted when they detected the stimulus. This estimated initial threshold created a starting point for the following staircase procedure, which more accurately determined each participant's detection threshold [56, 94].

To reduce participants' anticipation of the stimuli occurrence, during the staircase procedure the electrotactile stimuli were presented in a uniform distribution between 3 and 5 seconds. The initial magnitude of the stimulus was set at 1 mA below the estimated detection threshold procured during the knob adjustment assessment. The magnitude of the stimulus then increased in increments of 0.2 mA, creating an upward staircase pattern. The ascending staircase would complete upon receiving the participants' verbal confirmation of detection three consecutive times. After this confirmation, the stimulus magnitude increased by 0.4 mA before the descending staircase commenced. During the downwards staircase pattern, the magnitude decreased in increments of 0.2 mA until the participant did not perceive the electrotactile stimulus three consecutive times, after which the downward staircase was complete. The staircase process then repeated, with the staircase pattern switching between ascending and descending. Each stimulus amplitude at which the participant confirmed detection was recorded by the experimenter.

The first of three consecutive detection confirmations during the ascending staircase and the last detected stimulus before three consecutive misses on the descending staircase were data of interest. Two full iterations of both staircase patterns were completed by each participant, which yielded four total detection values. By averaging these four values, the final detection threshold was determined.

Tactile Discrimination Assessment

Participants' ability to discriminate between paired electrotactile stimuli was evaluated in the second study. Using the method of adjustments (see Section 4.3.4), the detection threshold was first estimated to ensure comparable testing magnitudes across participants. Participants underwent another knob adjustment task to ensure comparable testing durations across participants after determining the detection threshold. During this task, an electrotactile stimulus was delivered at a magnitude that was 1.5 mA above the detection threshold. Rather than varying the stimulus magnitude, this task involved adjusting the IPI, which was defined as the time interval (in milliseconds) between two electrotactile pulses. Participants were tasked with rotating a knob to increase or decrease the IPI, identifying the IPI when they perceived two distinct pulses. The two distinct pulses were delivered automatically at one-second intervals. These initial IPI outcomes (magnitude, threshold) provided the basis for the subsequent staircase procedure to refine the discrimination IPI [56].

The paired electrotactile stimuli were transmitted at a uniform distribution between 3 and 5 seconds during the staircase procedure to prevent the participants from anticipating the stimuli. The magnitude of the electrotactile stimuli were fixed at 1.5 mA higher than the threshold of detection. The IPI commenced at a time interval of 20 ms lower than the estimated IPI threshold procured by the knob adjustment task; the IPI was then increased in an ascending staircase pattern by time increments of 5 ms. The upward staircase completed when participants audibly confirmed the detection of two electrotactile stimuli three consecutive times. The IPI was then increased by 10 ms before the descending staircase started, during which the IPI was decreased in increments of 5 ms. The downward staircase was completed after participants did not detect two distinct electrotactile stimuli three times in a row. Following, the IPI was reduced by 10 ms, and the staircase patterns repeated. To ensure the electrotactile stimuli were administered outside the absolute and relative refractory

periods of the $A\beta$ fibers, the IPI were delivered in intervals that changed in increments of 5 ms [4, 25].

The first verbal confirmation during the upward staircase when the two paired electrotactile stimuli were perceived and the final confirmation during the downward staircase when the two paired electrotactile stimuli were perceived made up the primary data points. The upward and downward staircases were repeated two times, contributing to four total measurements of the discrimination IPI. The final discrimination IPI, calculated as the average of these four measurements, was defined as the duration at which participants consistently perceived two distinct electrotactile stimuli.

4.3.5 Auditory Assessment

Here, the methods are discussed for presenting an auditory cognitive-perceptual load. Data collected included auditory cues, auditory cue type (i.e., congruent, incongruent), and duration of the experimental protocol.

Auditory Discrimination Assessment

To facilitate the discrimination of the auditory cues, a partial auditory stroop task was administered [77, 90, 111], which required participants to process and identify contradictory auditory stimuli. Every 2 to 4 seconds (uniform distribution), an auditory cue was presented to prevent participants from anticipating the stimuli occurrences. The word “High” or “Low” was played with a high pitch (448 Hz) or a low pitch (187 Hz), resulting in four unique auditory cues. The auditory cues were presented either as congruent (e.g., the word matches the pitch) or incongruent (e.g., the word does not match the pitch) (i.e., two congruent conditions, two incongruent conditions). A binomial distribution was sampled to determine

the probability of a specific auditory cue playing. The participants were instructed to audibly note when the stimuli were incongruent; to indicate their response, the experimenter pressed a button.

This specific methodology was chosen based on preliminary testing. Initially, we included a complete auditory stroop task (i.e., responding to both congruent and incongruent auditory stimuli) and observed that participants' accuracy in discriminating auditory cues worsened, whereas their perception of the electrotactile stimuli remained comparable. We hypothesized that participants were prioritizing the auditory task over the tactile task [77, 90, 107, 111]. Accordingly, we reduced the emphasis on the auditory task by having the participant respond to one auditory cue (incongruent) rather than both (incongruent, congruent) to place greater emphasis on electrotactile perception. We hypothesized, based on related literature [77, 136, 139], that this partial stroop task would shift participants' focus from the auditory task to the tactile task.

4.3.6 Experimental Protocol

To prevent potential interference with nerve signal transmission, the participants were instructed to refrain from consuming caffeine and non-essential medications on the day of each session due to the physiological changes such substances can produce [22, 169]. The experimental procedures commenced after the participants' consent was secured.

Waist-to-height ratio and body temperature were recorded to capture health-related outcomes related to tactile perception [157, 175]. Waist-to-height-ratio was chosen over our previously used body mass index [156] because it has been found to be a more reliable indicator of metabolic health and visceral fat distribution, which directly impacts nerve function and conduction [175]. In contrast, body mass index does not differentiate between

fat and muscle mass and may not provide as accurate a reflection of overall health-related outcomes [175]. Additionally, temperature was collected as it can have an impact on nerve conduction [157].

The experimental protocol commenced after an initial screening (e.g., right-arm dominance, within young adult age range, no musculoskeletal and neurological injury, no prior/current use of chemotherapy). The training phase familiarized participants with the electrotactile stimuli and the steps required for each experimental task, specifically the knob adjustment task, staircase task, and auditory task. This training determined that the participants thoroughly understood the procedures. Next, an assessment was completed to determine the participants' ability to recognize the different auditory cues. During this assessment, a series of auditory cues were presented in a similar style to the experiment; the cues were presented in a uniform distribution of 2 - 4 seconds. This assessment consisted only of auditory stimuli to ensure participants could reliably discern and properly react to the auditory cues.

Testing commenced after participants demonstrated their understanding of all training procedures. Participants remained in a supine position on a clinical bed throughout testing. To reduce distractions from external visual and auditory stimuli, participants wore a blindfold and noise-canceling headphones [155, 171]. Data were collected sequentially for each nerve. Once testing on the first arm was completed, procedures were conducted on the opposite arm. A Latin square design was utilized to randomize the testing sequence and determine the order in which the arms and nerves were tested.

4.3.7 Statistical Analysis

The data for each study (electrotactile detection, electrotactile discrimination) were analyzed separately. The data were fit to a linear mixed-effects model with dependent outcomes of

accuracy and variability. The primary fixed effect of interest was whether an auditory task was included. Secondary fixed effects included dominance of arm stimulated, nerve, anatomical location, age, sex, body temperature, and height-to-waist ratio. Participant was treated as a random effect. An analysis of variance (ANOVA) identified significant effects. A hierarchical approach was employed for the ANOVA, where non-significant interaction terms were removed first, followed by non-significant main effect terms. Post-hoc pairwise comparisons, adjusted using a Tukey correction, were conducted to determine significant differences between specific pairs for any significant effects.

4.4 Results

We examine how accurately and precisely right-arm dominant participants consciously perceive electrotactile stimuli applied to their skin, both in isolation and while concurrently identifying auditory stimuli. Results for each condition (electrotactile stimuli alone, electrotactile and auditory stimuli simultaneously), are summarized in Figure 4.2.

4.4.1 Concurrent Detection of Electrotactile Stimuli

The primary outcome of interest was whether the auditory cognitive load impacted the ability to detect electrotactile stimuli. Accuracy in detecting the electrotactile stimuli did not significantly differ in the presence and absence of the auditory task ($F(1,1084)=0.84$, $p=0.359$). However, variability in detecting the electrotactile stimuli was significantly affected ($F(1,1084)=495.71$, $p<0.001$), with participants exhibiting greater response variability when the auditory cognitive task was present (0.4 mA spread) compared to when absent (0.1 mA spread).

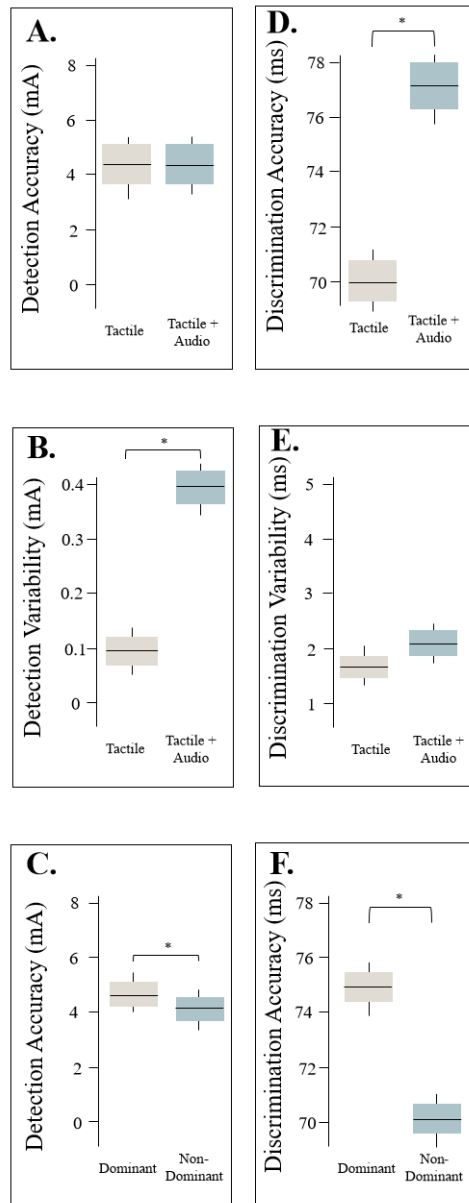


Figure 4.2: **Influence of Auditory Discrimination Task and Arm Dominance on Electrotactile Accuracy and Variability in Young Adults.** The bar graphs display average electrotactile perception outcomes (bar height) along with their standard deviations (error bars). Statistically significant differences are marked by a line and asterisk. Panels A–C present results from the electrotactile detection task, whereas panels D–F correspond to the electrotactile discrimination task.

Secondary analyses investigated whether various factors, including arm dominance, stimulated nerve, sex, age, and their interactions, influenced electrotactile detection in the presence

of the auditory cognitive load. Accuracy in detecting the electrotactile stimuli depended on the dominance of the arm stimulated ($F(1,1084)=24.06$, $p<0.001$), with higher detection thresholds observed in the dominant arm (5.1 mA) compared to the non-dominant arm (4.9 mA). Accuracy in detecting the electrotactile stimuli also depended on the nerve stimulated ($F(1,1084)=45.72$, $p<0.001$), with the radial nerve having a higher threshold (5.7 mA) than both the median (4.7 mA) and ulnar (4.7 mA) nerves. Furthermore, an interaction effect between sex and anatomical location was observed on detecting the electrotactile stimuli ($F(1,1084)=140.09$, $p<0.001$), with male participants having a detection threshold of 4.7 mA at the hand and 6.2 mA at the elbow, and female participants having a detection threshold of 4.2 mA at the hand and 4.7 mA at the elbow. Age did not significantly affect detection accuracy ($F(1,14)=2.02$, $p=0.183$). No significant effect of arm dominance on variability in detecting electrotactile stimuli was found ($F(1,1084)=4.67$, $p=0.310$). Additionally, participant sex ($F(1,14)=3.87$, $p=0.075$) and age ($F(1,14)=1.94$, $p=0.193$) were not found to significantly affect variability in detecting the electrotactile stimuli.

Together, these findings suggest that while the auditory cognitive task did not significantly affect overall accuracy in detecting the electrotactile stimuli, it did lead to increased variability. Therefore, while participants could still detect the electrotactile stimuli under the added auditory cognitive load, their consistency in doing so was reduced. Furthermore, the electrotactile detection thresholds were influenced by both arm dominance and sex, with higher thresholds observed in the dominant arm and with notable sex-based differences depending on the anatomical location. Accuracy in detecting the electrotactile stimuli was not significantly influenced by participant age, and variability was not significantly affected by arm dominance, sex, and age. These findings highlight that while a greater cognitive-perceptual load may not diminish tactile detection accuracy, it does introduce greater inconsistency in tactile perception, and that biological factors such as limb dominance and sex can further

modulate tactile perception.

4.4.2 Concurrent Discrimination of Electrotactile Stimuli

The primary outcome of interest was whether the accuracy and precision in discriminating two electrotactile stimuli pulses applied to the skin would change while concurrently discriminating auditory stimuli. Participant accuracy in discriminating the electrotactile stimuli was poorer in the presence (77 ms) of the auditory stimuli than in the absence (70 ms) ($F(1,553)=43.32$, $p<0.001$). Variability in discriminating the electrotactile stimuli did not statistically significantly differ in the presence and absence of the auditory stimuli ($F(1,553)=0.017$, $p=0.987$).

Secondary analyses focused on whether arm dominance, nerve, sex, and age influenced participants' ability to discriminate the electrotactile stimuli while simultaneously performing the auditory discrimination task. Participants demonstrated poorer accuracy in discriminating the electrotactile stimuli when using their dominant arm (75 ms) compared to their non-dominant arm (70 ms) ($F(1,553)=11.52$, $p<0.001$). However, accuracy in discriminating the electrotactile stimuli was not significantly affected by the nerve examined ($F(2,553)=2.32$, $p=0.099$), sex ($F(1,12)=1.07$, $p=0.327$), or age ($F(1,12)=0.65$, $p=0.442$). Additionally, variability in participants' discrimination of the electrotactile stimuli was not significantly influenced by the arm dominance ($F(1,553)=3.82$, $p=0.051$), nerve ($F(2,553)=1.91$, $p=0.149$), sex ($F(1,12)=1.06$, $p=0.331$), or age ($F(1,12)=0.65$, $p=0.442$).

Combined, these findings indicate that the addition of an auditory discrimination task significantly impaired participants' ability to accurately discriminate between electrotactile stimuli, suggesting that the increased cognitive-perceptual load negatively affected tactile discrimination performance. In contrast, response variability was not significantly influenced by the

added auditory task, indicating that although the electrotactile detection accuracy declined, participants remained consistent in detecting the electrotactile stimuli across trials. Accuracy in discriminating the electrotactile stimuli was significantly poorer at the dominant arm compared to the non-dominant arm, suggesting that the greater cognitive-perceptual load may lead to an arm dominance effect, with tactile perception differing depending on the arm stimulated. No significant effect was observed for nerve location, sex, or age on either electrotactile discrimination accuracy or variability. Together, these results emphasize the role of a cognitive-perceptual load in shaping tactile perception and identify arm dominance as a potentially meaningful contributor to tactile discrimination performance under dual-task conditions.

4.5 Discussion

Many everyday tasks require individuals to attend to multiple external stimuli at once, as represented in the cocktail party effect [174]. These types of multi-sensory environments increase demands on executive functions such as working memory and selective attention [17, 97, 99, 105, 112]. While much of the existing literature has explored how age-related declines in these cognitive systems can affect multi-sensory processing [5, 18, 19, 30, 84, 99, 116, 144], less is known about how these processes function in young adults who are neurotypical, particularly in relation to tactile perception [156]. Even in populations with intact executive functioning, competing cognitive and sensory demands can introduce perceptual challenges that may impact how accurately and consistently tactile information is processed. Although dual-task paradigms have been widely studied in the context of motor control [7, 9, 77, 161], fewer studies have examined their influence on somatosensory performance. Given that tactile perception is essential for motor control and functional independence [36], it

is important to understand how modulating the cognitive-perceptual load influences tactile perception.

The aim of the present study was to investigate how modulating the cognitive-perceptual load through the introduction of an auditory discrimination task influences conscious perception of electrotactile stimuli in young adults. These findings offer insight into the extent to which a cognitive-perceptual load influences tactile perceptual accuracy and variability, and further contribute to our understanding of how sensory and cognitive systems interact under dual-task conditions.

4.5.1 Effect of Auditory Stimuli on Tactile Perception

Our results demonstrate that the introduction of a concurrent auditory load leads to greater variability in detecting electrotactile stimuli, while overall accuracy remains unchanged. This increased variability suggests that the cognitive load from the auditory task may have compromised participants' ability to allocate attention effectively to the tactile stimuli, resulting in shifts in focus and less consistent electrotactile detection performance [85, 99]. This finding aligns with theories that suggest dividing attention between multiple sensory modalities can reduce perceptual efficiency, as limited cognitive resources are shared between tasks [33, 97].

When participants engaged in an electrotactile discrimination task while concurrently processing the auditory load, their accuracy in discriminating the electrotactile stimuli worsened while their variability remained similar. These results suggest that the greater cognitive-perceptual load interfered with the higher-order cognitive processes required for discrimination [79, 139]. Discrimination involves more complex perceptual and decision-making than detection. Hence, the impact on accuracy for an electrotactile discrimination, yet not detection, task may arise due to this greater complexity [139]. Combined, these results suggest

that tasks requiring more cognitive resources, such as discrimination, may be more susceptible to performance deficits when cognitive resources are taxed, aligning with theories of attentional bottlenecks and limited working memory capacity [33, 97].

While our findings highlight the effects of a cognitive-perceptual load on tactile performance in young adults, they also provide valuable insight when compared to existing literature on aged populations. In older individuals, dual-task paradigms often lead to more pronounced deficits in both detection accuracy and variability due to age-related declines in executive function and sensory processing [5, 9, 114, 119, 144]. For instance, older adults may experience greater difficulty in effectively allocating attention between tasks, resulting in more severe declines in both the accuracy and consistency of tactile perception [128]. This comparison suggests that the effects of a cognitive-perceptual load on tactile performance are likely to be exacerbated in aging populations, where age-related changes in sensory and cognitive systems limit the capacity to efficiently process competing sensory information.

4.5.2 Assessing the Role of Arm Dominance on Tactile Perception

The influence of arm dominance on tactile perception has been the subject of debate, with existing literature presenting mixed findings [14, 23, 57, 62, 156, 181]. Some studies report significant differences between the dominant and non-dominant arms, suggesting that the dominant arm may have higher detection thresholds (i.e., poorer sensory processing) due to factors like increased usage and cortical representation [14, 23, 57, 181]. In contrast, other studies fail to find such differences, suggesting that observed effects may stem from individual variability or methodological factors, such as sample size or measurement techniques [62, 156]. These mixed findings highlight the complexity of investigating a role of arm dominance on tactile perception, where both physiological mechanisms and statistical factors must be

carefully considered.

In this study, we observed that detection and discrimination thresholds for electrotactile stimuli were lower in the non-dominant arm compared to the dominant arm. This finding may suggest that sensory processing in the non-dominant arm is more sensitive, or more finely tuned, to detect and discriminate the electrotactile stimuli in our experimental paradigm [14, 23].

When considering the physiological significance of these results, it is important to note that while our findings were statistically significant, the observed effect sizes may not necessarily indicate a large physiological difference between the arms. Our results demonstrate a difference in detection thresholds between arms of 0.2 mA. This difference corresponds to our incremental change in the experimental protocol of 0.2 mA to quantify the detection threshold. Had a larger incremental change been used, and/or a smaller number of participants been included, this study may not have observed a significant impact of the dominance of the arm stimulated on tactile perceptual outcomes [56]. Moreover, the physiological implications of a difference in sensitivity by 0.2 mA remains unclear and, in comparison to our prior work [156], is very small. Therefore, while significance was observed here, the extent to which this difference has functional implications remains unclear. Previous studies with differing sample sizes and experimental designs may have found contrasting results in part due to differences in their statistical power and measurement sensitivity [14, 23, 181]. Accordingly, we propose that examining physiological relevance, in addition to statistical significance, can support translation of these outcomes to understanding implications for functional arm usage.

4.5.3 The Role of Sex on Tactile Perception

Our findings align with previous research in young adults, suggesting that thresholds at which tactile stimuli can just be detected tend to be lower in females than males, indicating better tactile perception in females [14, 54]. In contrast, when discriminating rather than detecting tactile stimuli, no sex-based differences in discrimination thresholds were observed. Therefore, the sex-based differences may arise due to physiological differences in tactile signal transmission for males and females. This sex-based difference may no longer be evident once more cognitive resources are required to interpret these tactile signals, as occurs in a tactile discrimination task. Interestingly, there was also a significant interaction between sex and anatomical location, with males demonstrating poorer perception at the elbow compared to females. This may be partially explained by sex-based differences in anatomy, with males having greater circumferential measurements about the elbow, leading to increased distance between the surface electrodes and innervating nerves [117]. This, in turn, may impact the electrotactile stimuli, as there is higher impedance to the current flow. These results highlight the complexity of the sex-based differences in tactile perception and suggest the continued exploration of the role of sex on tactile perception.

4.5.4 Implications of This Work

In this study, we found notable differences in tactile perception depending on the task in which participants engaged, specifically, electrotactile detection versus discrimination. These findings underscore how the specific demands of a task can influence tactile processing, specifically in young adults. Electrotactile detection, performed alongside an additional cognitive-perceptual load, increased variability in electrotactile detection outcomes. However, this increased variability did not correspond to significant differences in electrotac-

tile accuracy. In contrast, electrotactile discrimination completed with the same auditory cognitive-perceptual demand reduced accuracy, while maintaining comparable variability. Accordingly, future work examining tactile perception would benefit from utilizing a diverse set of tasks, each tailored to assess specific perceptual processes.

Our findings regarding cognitive-perceptual load also have important implications for the design of haptic technologies. The varying effects of an added cognitive-perceptual load on detection and discrimination performance indicate that haptic systems may benefit from being adaptable depending on the type of perceptual task. Since higher cognitive-perceptual demands may increase variability in detecting tactile stimuli, haptic devices that rely on detection cues may benefit from dynamic adjustment features to ensure consistent and reliable feedback. Conversely, because tactile discrimination may be more sensitive to the associated cognitive-perceptual load, devices that depend on fine tactile distinctions could aim to reduce overlapping or concurrent sensory input. By incorporating responsive feedback systems that adjust to executive functioning demands, haptic devices can become more effective, user-friendly, and supportive in contexts like rehabilitation, skill acquisition, and assistive applications.

4.5.5 Limitations

One limitation of this study is the exclusion of individuals who are left-arm dominant. Previous research indicates that left-arm dominant individuals may exhibit distinct neural processing patterns compared to their right-arm dominant counterparts, particularly in how sensory input is integrated and interpreted by the brain [41, 100, 149]. As a result, the current findings may not fully extend to those with left-arm dominance.

Another limitation of this research is the utilization of electrotactile stimulation. Although

effective in activating sensory nerve fibers, the electrotactile stimulation protocol used here does not fully mimic natural tactile experiences. Traditional tactile stimuli engage cutaneous mechanoreceptors, while electrotactile methods primarily stimulate free nerve endings in the skin [24, 178]. To better understand tactile perception, future research could incorporate other stimulus types, such as vibrotactile or force-based stimuli, to assess whether the observed findings hold across different tactile modalities.

Additionally, this study did not investigate all peripheral nerves that innervate the upper limb. Although the research targeted three major nerves, each innervating unique and distinct anatomical regions, these findings may not represent tactile perception across the entire upper arm. Future investigations can consider a broader range of nerves and stimulation sites to provide a more comprehensive understanding of tactile perception across the arm.

4.5.6 Future Considerations

Future investigations could examine how the integration of additional sensory inputs influences tactile performance across different types of tasks. By introducing additional stimuli, such as visual or olfactory, researchers can explore how the presence of competing sensory information affects both detection and discrimination of tactile stimuli. This investigation would also be valuable in different populations, including individuals with sensory or neurological challenges (such as those with vision or hearing impairments, or individuals recovering from a brain injury). Insights into how these groups respond to modulations in the associated cognitive-perceptual load could inform the design of more effective neurorehabilitation approaches and support improved functional outcomes.

4.6 Conclusion

This study examined how young adults detect and discriminate electrotactile stimuli in the presence and absence of an added auditory load. By furthering our understanding of how the added cognitive-perceptual load influences tactile perception in individuals who are neurotypical, we can then explore when and why tactile impairments arise in clinical populations.

Chapter 5

Perceiving Auditory Stimuli Impacts Conscious Perception of Electrotactile Stimuli in Older Adults

5.1 Abstract

As individuals age, the ability to perceive and interpret tactile stimuli declines, impacting daily function and quality of life. One factor contributing to this decline is cognitive-perceptual load, which refers to the demand placed on limited cognitive resources allocated for processing and attending to sensory stimuli. This study investigates the modulation of cognitive-perceptual load on tactile detection and discrimination in older adults, incorporating concurrent auditory stimuli to replicate real-world multi-sensory environments. Detection and discrimination of electrotactile stimuli applied to the skin were assessed in two studies, examining a total of 26 right arm dominant older adults. Participants completed tactile detection and discrimination tasks under two conditions, with and without concurrent auditory stimuli. Detecting auditory stimuli significantly impacted the precision of electrotactile stimuli detection ($p < 0.001$), but not accuracy ($p = 0.145$). In contrast, discriminating auditory stimuli significantly impacted the accuracy of electrotactile stimuli discrimination ($p < 0.001$), but not precision ($p = 0.698$). Arm dominance significantly impacted the accuracy

of electrotactile stimuli discrimination ($p=0.011$), but not detection ($p=0.936$). Participant age significantly impacted the accuracy of electrotactile stimuli detection ($p=0.018$), but not discrimination ($p=0.558$). This work highlights the importance of accounting for cognitive-perceptual load when assessing tactile perception in older adults. Future work can further explore the influence of cognitive-perceptual load in clinical populations (e.g., following a brain injury), and examine additional factors that influence conscious tactile perception.

5.2 Introduction

Understanding the relationship between tactile (touch) perception, and cognition is fundamental to comprehending how we perceive and interact with the world [18, 144, 145, 172, 176]. As individuals age, both tactile perceptual and cognitive ability decline, influencing how sensory information is detected, processed, and interpreted [5, 8, 11, 26, 38, 58, 72, 75, 96, 115, 172]. Here, we examine factors that influence tactile perception in older adults by modulating cognitive-perceptual load using an auditory task to better understand the tactile and cognitive changes faced.

Cognitive-perceptual load theory typically distinguishes between two types of load: cognitive load and perceptual load, which interact dynamically [17]. Cognitive load refers to the demands placed on executive function during a task. In this study, we manipulate cognitive load by introducing concurrent stimuli and requiring participants to interpret and verbally respond to specific auditory cues. In contrast, perceptual load pertains to the complexity of sensory stimuli and, in this body of work, is defined by the detection and discrimination of electrotactile stimuli. The extent of a cognitive-perceptual load depends on the demands of the task performed, with corresponding cognitive and sensory resources utilized to process information and respond effectively. A higher cognitive-perceptual load occurs when

tasks demand greater executive functioning, potentially limiting an individual's ability to effectively process information (e.g., sensory stimuli) or perform tasks concurrently (i.e., task switching) [7]. When cognitive-perceptual load increases, such as through the introduction of a cross-modal stimulus (e.g., an auditory task), individuals must concurrently attend to various stimuli. This division of attention can impair perceptual abilities, depending on which stimuli are prioritized. Working memory plays an important role in managing cognitive-perceptual load by temporarily storing and processing sensory information, enabling effective interpretation, response and adaptation in complex tasks or demanding environments [7, 11, 52, 84, 100, 112, 148, 161]. However, working memory capacity is finite. Thus, when cognitive-perceptual load exceeds capacity, task performance declines [8, 11, 72, 89]. Similarly, excessive cognitive-perceptual load can compromise perceptual functions, such as tactile detection and discrimination, further hindering task performance. [68].

In older adults, executive function ability can be reduced when compared to younger adults [11, 39, 72, 116, 134]. Consequently, older adults may experience greater difficulty detecting and interpreting tactile stimuli when cognitive or perceptual resources are taxed. Dual-task paradigms, where participants perform a primary task (e.g., tactile detection) alongside a secondary cognitive task (e.g., auditory task), offer a unique opportunity to investigate the relationship between cognitive-perceptual load and tactile perception [105]. These paradigms have been used extensively to examine how task switching, particularly the concurrent processing of sensory and cognitive information, impacts an individual's ability to process and respond to external stimuli [11, 19, 67, 77, 99, 112, 125]. In the case of older adults, a decline in sensory processing, coupled with impaired executive functioning, may make these individuals particularly vulnerable to such impairments under conditions of high cognitive-perceptual load [30, 84, 116, 144]. Accordingly, it is critical to explore how perceptual outcomes can change in the presence of an additional cognitive-perceptual load.

Given the significant impact of aging on tactile perception [2, 23, 38, 50, 115, 120, 137, 145], it is important to understand the underlying factors that contribute to age-related tactile impairments to develop more precise diagnostic tools and targeted therapeutic strategies aimed at mitigating these tactile impairments [70, 75]. Age-related declines in tactile perception are multifaceted, involving complex interactions between various physiological systems [32, 103, 104, 154]. Yet, current clinical assessments of tactile function often fail to fully capture the breadth of tactile changes that occur with aging [38, 118]. This is largely due to limitations with existing assessments, including possibly overlooking the dynamic interplay between tactile processing and cognitive function [5, 23]. Conventional methods often focus solely on isolated tactile inputs, disregarding the effects of increased cognitive-perceptual load on the modulation of tactile perception [118, 156]. Such oversight may underestimate the influence of cognitive factors on the detection and discrimination of tactile stimuli in older adults.

Our research investigates how perceiving auditory stimuli affects conscious perception of tactile stimuli in older adults. When an individual has poor accuracy or increased variability in perceiving tactile stimuli, successful interactions with objects or interpretation of the environment can be impaired [36, 109]. Therefore, our study aimed to examine both accuracy and variability in tactile perception. We focus on two aspects of tactile perception. The first, detection, involves identifying the presence of a particular sensory signal, without requiring a deep or complex analysis of its characteristics [139]. The second, discrimination, requires an individual to differentiate between distinct features of sensory stimuli (e.g., differences in intensity, timing, or other distinct characteristics [79, 164]). Additionally we examine the role of the arm stimulated (dominant, non-dominant), sex (male, female), and age on how electrotactile stimuli are perceived. Understanding typical outcomes during intact tactile perception, and evaluating how tactile perception changes with modulations in cognitive-

perceptual load, are informative for future work that can then consider when and why tactile impairments arise.

5.3 Methodology

5.3.1 Human Subjects Study

This study received approval from the Virginia Tech Institutional Review Board (23-1246). All participants were required to be right-arm dominant and have no self-reported neurological conditions, upper extremity musculoskeletal injuries, or hearing impairments. Individuals had to be 55 years or older since previous findings suggest age-related declines in tactile perception begin at this age [154]. Participants were classified by their sex (male, female) according to their designation assigned at birth and gender identity (male, female, transgender, non-conforming/non-binary) according to how they identify, aligned with the 2024 National Institutes of Health guidelines.

5.3.2 Study Participants

The detection study involved a sample of 14 older adults [7 males, 7 females; age (median, lower quartile, upper quartile, range): 66, 59, 72, 56 - 79 years]. The discrimination study involved a sample of 12 older adults [5 males, 7 females; age (median, lower quartile, upper quartile, range): 61, 56, 66, 56 - 69]. Each sample size was determined by power analyses based on the initial data collected. Sex and gender identity were the same for all participants.

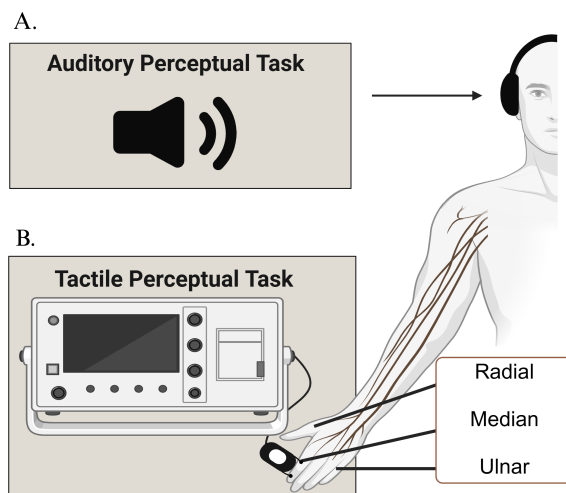


Figure 5.1: **Experimental Design.** **A.** Auditory stimuli were utilized in both detection and discrimination tasks. During the detection task, a beep was played. An auditory stroop task was implemented during the discrimination task. **B.** Electrotactile stimuli were applied to one location at the hand during the detection task (digit 2 skin innervated by the median nerve) and three locations during the discrimination task (digit 2 skin innervated by the median nerve; digit 5 skin innervated by the ulnar nerve; anatomical snuff box skin innervated by the radial nerve).¹

5.3.3 Experimental Setup

Surface electrodes were placed on the skin innervated by the median nerve (detection task) and median, ulnar, and radial nerves (discrimination task), as shown in Figure 5.1, to apply the electrotactile stimuli. The electrotactile stimuli were delivered to a single nerve using a commercial stimulator (DIGITIMER, Model: DS8R; Welwyn Garden City, England). The stimuli consisted of 100 μ s monophasic pulses with amplitudes ranging from 0 to 100 mA, designed to selectively activate tactile $A\beta$ fibers [4, 25]. During the detection and discrimination task, one pulse and two consecutive pulses were delivered, respectively.

¹This image was created with BioRender.com.

5.3.4 Electrotactile Assessments

The first study investigated tactile perception during a detection task and the second study during a discrimination task. All experimental data were captured at a sampling rate of 1 kHz. Data captured included electrotactile stimulus magnitude (mA) and inter-pulse intervals (ms) for the tactile detection and discrimination task, respectively.

Accuracy and variability of electrotactile perception were assessed in this study. Accuracy was defined as the absolute perceptual threshold, referred to as the minimal stimulus intensity required for conscious perception. For the detection task, this corresponded to the minimum perceivable stimulus applied. For the discrimination task, this corresponded to the minimum perceivable inter-pulse interval. Variability reflected the consistency of perceptual thresholds across trials, indicating precision in detecting and discriminating electrotactile stimuli.

Electrotactile Detection Assessment

The first study identified thresholds at which electrotactile stimuli were just detected, using similar procedures to those described in [156]. To ensure consistent testing durations across participants, an initial estimate of the electrotactile detection threshold was obtained using the method of adjustments. In this procedure, participants manually adjusted a knob to modify the stimulus amplitude until they could just perceive the electrotactile stimulus. Stimuli were presented automatically every second, and participants indicated when they detected the 100 μ s pulse stimulus. This preliminary threshold estimate provided a starting point for the subsequent staircase procedure (as described below), which was used to more precisely determine the detection threshold [56, 94].

During the staircase procedure, electrotactile stimuli were delivered at a uniform distribution ranging from 3 to 5 seconds to reduce participants' ability to anticipate their occurrence. The

stimulus intensity initially started at 1 mA below the estimated detection threshold, as determined during the knob adjustment assessment. The intensity then followed an ascending staircase pattern, increasing in 0.2 mA increments. Participants were required to verbally confirm detection three consecutive times before completing an upward staircase. Following this, the stimulus level increased by 0.4 mA before transitioning into a descending staircase, during which the intensity decreased in 0.2 mA increments until the participant failed to detect the stimulus three consecutive times. This marked the completion of a downward staircase. The process then repeated, alternating between ascending and descending staircases. The experimenter recorded each stimulus intensity at which the participant confirmed detection.

Data of interest included the first of three consecutive detection confirmations during the ascending staircase and the last detected stimulus before three consecutive misses in the descending staircase. Each participant completed two full iterations of both staircase phases, yielding four total detection values. The final detection threshold was determined by averaging these four values.

Electrotactile Discrimination Assessment

The second study evaluated participants' ability to discriminate between paired electrotactile stimuli. To ensure comparable testing intensities across participants, the detection threshold was first estimated using the method of adjustments (see Section 5.3.4). After determining the detection threshold, participants underwent another knob adjustment task to ensure comparable testing durations across participants. In this task, an electrotactile stimulus was delivered at a magnitude that was 1.5 mA above the detection threshold. Instead of varying the stimulus amplitude, this task involved adjusting the time interval (in milliseconds) between two electrotactile pulses, referred to as the inter-pulse interval (IPI).

Participants rotated a knob to increase or decrease the IPI, identifying the IPI when they perceived two distinct pulses. The two pulses were automatically delivered at one-second intervals. These initial magnitude and IPI thresholds provided the basis for the subsequent staircase procedure to refine the discrimination IPI [56].

During the staircase procedure, the paired electrotactile stimuli were delivered at a uniform distribution between 3 and 5 seconds to prevent participant anticipation of stimuli. The amplitude remained fixed at 1.5 mA above the detection threshold. The IPI began at a time interval that was 20 ms less than the IPI threshold determined during the knob adjustment task, and then systematically increased in an upward staircase pattern by increasing the time interval by 5 ms. Once participants verbally confirmed detecting two electrotactile stimuli three consecutive times, the upward staircase was completed. Following, the IPI was increased by 10 ms before beginning a downward staircase, where the IPI was reduced in 5 ms increments until participants did not detect two electrotactile stimuli three times in a row. This marked the completion of the downward staircase. Subsequently, the IPI was decreased by 10 ms and the staircase repeated. The IPI were delivered in intervals that changed in 5 ms increments to ensure that the stimuli were administered outside the absolute and relative refractory periods of the $A\beta$ fibers [4, 25].

The primary data points included the first verbal confirmation during the upward staircase when the two paired electrotactile stimuli were perceived and the final confirmation during the downward staircase when the two paired electrotactile stimuli were perceived. Each upward and downward staircase was repeated two times, resulting in four total measurements of discrimination IPIs. The final discrimination IPI was calculated as the average of these four values, representing the point at which participants consistently perceived two distinct electrotactile stimuli.

5.3.5 Auditory Assessments

Here, we discuss the methods for introducing an auditory cognitive-perceptual load. All experimental data were captured at a sampling rate of 1 kHz. Data captured included auditory cues, auditory cue type (i.e., congruent, incongruent), and duration of the experimental protocol.

Auditory Detection Assessment

Each auditory beep was administered at randomized time intervals sampled between a 2 to 4 second uniform distribution to prevent participants' anticipation of the stimulus. Participants were instructed to indicate when they heard the beep. Every time the participants verbally confirmed hearing the beep, the experimenter pressed a foot pedal to record the response.

Auditory Discrimination Assessment

A partial auditory stroop task was administered to enable discrimination of auditory cues [77, 90, 111], requiring individuals to process and identify conflicting auditory stimuli. During the assessment, each auditory cue was delivered every 2 to 4 seconds to prevent participants from anticipating the stimuli. The auditory cue played the word “High” or “Low” with a high pitch (448 Hz) or a low pitch (187 Hz), resulting in four distinct auditory cues. These auditory cues were presented in conditions that were congruent (e.g., word matches pitch) or incongruent (e.g., word does not match pitch) (i.e., two congruent conditions, two incongruent conditions). The probability of a specific auditory cue playing was sampled from a binominal distribution. Participants were instructed to indicate when the stimulus was incongruent, and the experimenter pressed a button indicating their response.

This specific methodology was chosen as, during preliminary testing, we observed that a complete auditory stroop task (i.e., responding to both congruent and incongruent auditory stimuli) reduced participants' accuracy in discriminating auditory cues, whereas electrotactile perception was comparable. We hypothesized that participants were prioritizing the auditory task over the tactile task [77, 90, 107, 111]. To place greater emphasis on electrotactile perception, we reduced the emphasis on the auditory task by having the participant respond to one auditory cue (incongruent) rather than both (incongruent, congruent). We hypothesized, based on related literature [77, 136, 139], that this partial stroop task would shift participants' focus from the auditory task to the tactile task.

5.3.6 Experimental Protocol

Participants were asked to refrain from consuming caffeine and non-essential medications on the day of each session to prevent potential interference with nerve signal transmission due to physiological changes [22, 169]. After securing the participants' consent, the experimental procedures commenced.

We confirmed typical cognitive and sensorimotor abilities through an initial screening. Cognitive function was evaluated using the Montreal Cognitive Assessment (MoCA) [76], with participants scoring 26 or higher being eligible for inclusion as these scores are considered within the normal range [27]. Tactile sensitivity was assessed using Von Frey monofilaments [60]. In line with established methods, monofilament 4.31 (2.00 gms) was applied to specific areas: the anatomical snuffbox (thumb—radial nerve), second digit (index fingertip—median nerve), and fifth digit (pinky fingertip—ulnar nerve) to verify that participants could detect tactile stimuli, ensuring preservation of protective sensation [86]. These locations were examined as prior work indicated differences in tactile perception depending on the nerve

stimulated [156]. To further screen tactile perception, two-point discrimination testing was also conducted at these locations to engage more cortical processing than what occurs during the monofilament detection task. Participants were required to score within the typical range (<6 mm) on the two-point discrimination test to participate [102]. The nine-hole peg test was then used to evaluate fine motor skills and ability to follow simple instructions. Performance was compared to normative data [51], and scores within the normal range were considered acceptable. Additionally, waist-to-height ratio and body temperature were recorded to capture health-related outcomes related to tactile perception [157, 175]. Waist-to-height-ratio was chosen over our previously used body-mass index [156] because it has been found to be a more reliable indicator of metabolic health and visceral fat distribution, which directly impacts nerve function and conduction [175]. In contrast, body-mass index does not differentiate between fat and muscle mass and may not provide as accurate a reflection of overall health-related outcomes [175]. Additionally, temperature was collected as it can have an impact on nerve conduction [157].

Following the screening, the experimental protocol began. Participants first underwent a training phase where they were familiarized with the electrotactile stimuli and instructed on how to perform the experimental tasks, such as adjusting the knob, completing the staircase task, and perceiving the auditory cues. This training ensured participants were comfortable with the procedures and completed learning. Next, participants underwent an assessment to determine their ability to successfully recognize the auditory cues prior to testing. This assessment consisted of a series of auditory cues presented in a manner similar to the experiment itself, with the cues drawn from a uniform distribution of 2 to 4 seconds. Only auditory stimuli were played during this assessment, ensuring that participants could reliably recognize and respond to the auditory cues.

Testing began once participants confirmed their understanding of all training procedures.

Participants were positioned supine on a clinical bed, wearing a blindfold and noise-canceling headphones to reduce distractions from external visual and auditory stimuli [155, 171]. Data collection occurred sequentially for each nerve, with procedures conducted on the opposite arm after completing testing at the first arm. The testing sequence was randomized using a Latin square design, which determined the order in which the nerves and arms were tested.

5.3.7 Statistical Analysis

The data for each study (detection, discrimination) were analyzed separately. The data were fit to a linear mixed-effects model with the dependent outcome of accuracy and variability. The primary fixed effect of interest was whether an auditory task was included. Secondary fixed effects included dominance of arm stimulated, nerve, sex, age, waist-to-height ratio, and body temperature. Participant was treated as a random effect. An analysis of variance (ANOVA) identified significant effects. A hierarchical approach was employed for the ANOVA, where non-significant interaction terms were removed first, followed by non-significant main effect terms. Post-hoc pairwise comparisons, adjusted using a Tukey correction, were conducted to determine significant differences between specific pairs for any significant effects.

5.4 Results

We report how accurately participants who are right-arm dominant consciously perceive electrotactile stimuli applied to the skin while concurrently identifying auditory stimuli. Additionally, we report the variability in participant responses. Each outcome is analyzed when participants perceive electrotactile stimuli only, as well as electrotactile and auditory

stimuli combined. Results are summarized in Figure 5.2.

5.4.1 Concurrent Detection of Electrotactile and Auditory Stimuli

Our primary outcome of interest was whether detecting electrotactile stimuli is poorer in the presence or absence of an auditory cognitive-load. Participant accuracy in detecting the electrotactile stimuli did not significantly depend on the presence or absence of the auditory stimuli ($F(1,654) = 2.13$, $p = 0.145$). In contrast, variability in detecting the electrotactile stimuli significantly differed ($F(1,654) = 43.62$, $p < 0.001$), with greater variability observed in the presence of auditory stimuli (0.8 mA spread) compared to the absence of the auditory stimuli (0.4 mA spread).

Our secondary outcomes of interest were whether arm dominance, sex, or age impacted detection of the electrotactile stimuli in the presence of the auditory stimuli. Accuracy in detecting the electrotactile stimuli did not statistically significantly depend on the dominance of the arm stimulated ($F(1, 654) = 0.006$, $p = 0.936$) or sex ($F(1,14) = 0.74$, $p = 0.409$); however, participant age did impact detection accuracy ($F(1,14) = 7.58$, $p = 0.018$). At the age of 55 and 80, the estimated detection of the electrotactile stimuli was 5.80 mA and 6.79 mA, respectively, in the presence of the auditory stimuli (0.96 mA difference) and 5.69 mA and 6.27 mA, respectively, in the absence of the auditory stimuli (0.58 mA difference). Participant variability in detecting the electrotactile stimuli did not statistically significantly depend on the dominance of the arm examined ($F(1,654) = 0.004$, $p = 0.950$), sex ($F(1,14) = 0.004$, $p = 0.952$), or age ($F(1,14) = 0.003$, $p = 0.954$).

These findings indicate that adding an auditory detection task increased variability in perceiving the electrotactile stimuli without impacting accuracy. Accuracy in perceiving the electrotactile stimuli concurrently with the auditory stimuli worsened with increasing age,

regardless of the dominance of the arm stimulated and individual's sex.

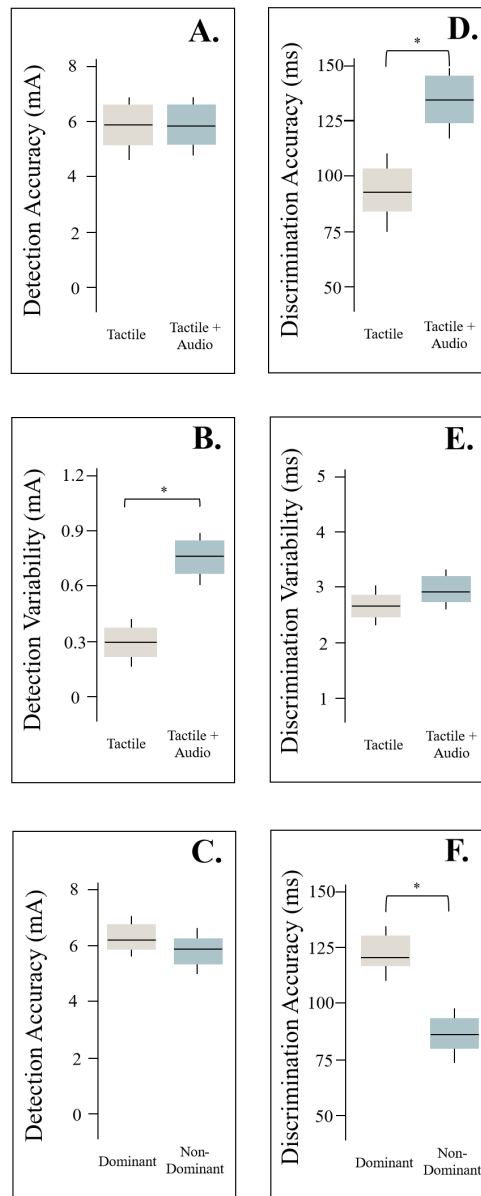


Figure 5.2: **Role of Auditory Task and Arm Dominance on Tactile Perceptual Accuracy and Variability in Older Adults.** The bar plots indicate the mean (bar heights) and standard deviation (error bars) of the tactile perceptual outcomes. Statistical significance is indicated by a line with a star above. A-C provide outcomes for the detection task, while D-F provide outcomes for the discrimination task.

5.4.2 Concurrent Discrimination of Electrotactile and Auditory Stimuli

The primary outcome of interest was whether the accuracy and precision in discriminating two electrotactile stimuli pulses applied to the skin would change while concurrently discriminating auditory stimuli. Participant accuracy in discriminating electrotactile stimuli was poorer in the presence (134 ms) of the auditory stimuli than in the absence (102 ms) ($F(1,540)=614.80$, $p<0.001$). Variability in discriminating the electrotactile stimuli was not found to statistically significantly differ in the presence and absence of the auditory stimuli ($F(1,540)=0.15$, $p=0.698$).

Our secondary outcomes of interest were whether arm dominance, sex, and age impacted participants' ability to discriminate the electrotactile stimuli while concurrently discriminating auditory stimuli. Participant accuracy in discriminating the electrotactile stimuli was poorer at the dominant arm (138 ms) than the non-dominant arm (104 ms) ($F(1,540)=6.50$, $p=0.011$). Participant accuracy in discriminating the electrotactile stimuli depended on the nerve examined ($F(2,540)=19.61$, $p<0.001$), with the radial nerve (141 ms) being worse than the median nerve (134 ms) and ulnar nerve (131 ms), respectively. Participant accuracy in discriminating the electrotactile stimuli did not statistically significantly differ depending on the participant's sex ($F(1,12)=2.27$, $p=0.166$) or age ($F(1,12)=0.37$, $p=0.558$). Participant variability in discriminating the electrotactile stimuli did not depend on the dominance of the arm examined ($F(1,540)=0.17$, $p=0.679$), nerve examined ($F(2,540)=0.13$, $p=0.874$), sex ($F(1,12)=0.02$, $p=0.0880$), or age ($F(1,12)=0.03$, $p=0.0874$).

Combined, these findings indicate that the addition of an auditory discrimination task negatively affects the accuracy, but not the precision of how electrotactile stimuli are discriminated. The accuracy of discriminating electrotactile stimuli may depend on the dominance

of the arm stimulated and nerve examined, regardless of sex and age.

5.5 Discussion

Many daily activities require individuals to perform multiple sensory tasks concurrently, such as preparing a complex meal while following verbal instructions. These dual-task (i.e., task switching) situations place a significant load on executive function, including working memory and selective attention. During the aging process, tactile perception and executive function decline, making it more challenging to interpret and respond appropriately to the world around us [38, 72, 84, 85, 88]. The impaired ability to perform task switching can affect independence in activities of daily living, such as bathing, dressing, toileting, and feeding, especially where sensory perception is required to inform movement [9, 19, 38]. Previous research has extensively examined the effects of dual-tasking on motor control [7, 19, 78, 96], with less attention on how dual-tasking influences tactile perception [114].

The aim of this study was to explore how modulating cognitive-perceptual load, specifically with an auditory perceptual task, affects conscious perception of electrotactile stimuli in older adults. Our results highlight the complex interplay between tactile perception and cognitive processing in older adults, underscoring the importance of comprehensive investigations that account for both sensory and cognitive factors to develop more effective diagnostic tools and therapeutic strategies focused on evaluating age-related impairments in tactile perception.

5.5.1 Effect of Auditory Stimuli on Tactile Perception

Our results suggest when a concurrent auditory stimulus was introduced, participants showed greater variability in detecting an electrotactile stimulus, although overall accuracy remained

intact. The cognitive demand from the auditory task may have overwhelmed participants' ability to allocate attention efficiently to the tactile stimuli, leading to shifts in focus and less reliable performance (i.e., the inability to switch between tasks). Literature suggests that as attention is divided, the limited capacity to process information from both modalities concurrently may hinder detection, possibly worsening in more complex scenarios [33, 97, 167]. This is further observed during the discrimination task. Our results suggest that when a concurrent auditory stimulus was introduced, participants showed poorer accuracy when discriminating electrotactile stimuli. Discrimination tasks inherently require more cognitive resources than detection, as they involve higher-order perceptual processing [139]. When cognitive resources are additionally taxed by an auditory load, the demand of distinguishing between similar tactile stimuli may exacerbate performance deficits. This aligns with theories suggesting that as task complexity increases, cognitive resources are allocated more selectively, potentially prioritizing one modality at the expense of another [14, 33, 97].

These findings highlight the crucial role of executive functioning cognitive resources, possibly working memory and attentional control, in processing sensory information [84, 100]. While detection tasks may only engage basic perceptual mechanisms (automatic responses, minimal cognitive load), tasks that require higher-order processes, such as discrimination, place additional demands on cognitive resources [79]. Consequently, discrimination tasks may exacerbate changes in perception due to attentional demands more than detection tasks. These findings may also illustrate the potential challenges individuals, especially older adults, may face in environments where multiple sensory stimuli compete for limited resources. Switching between tasks or the presence of competing stimuli in the environment could reduce their ability to differentiate sensory inputs with the accuracy required for tactile tasks.

5.5.2 Assessing the Role of Arm Dominance on Tactile Perception

While the presence of an auditory stimulus may increase the cognitive-perceptual load of a task [77, 111], we did not observe significant differences in detection accuracy depending on the dominance of the arm stimulated in our right-arm dominant participants. Prior work indicates that differences between arms are observed during complex tasks, such as tactile roughness-grating and spatial two point discrimination tasks [14, 181]. Therefore, our finding suggests that the detection task may not demand enough cognitive resources to elicit an effect of arm dominance. We observed that the dominance of the arm stimulated significantly affected the more complex task of discriminating stimuli in our right-arm dominant participants. These findings suggest that tactile perception differs depending on the arm examined for conditions requiring a greater cognitive-perceptual load (i.e., discrimination tasks). The significant result indicated that discrimination accuracy is better at the non-dominant arm than the dominant arm. This finding aligns with the outcomes of prior studies that indicate the non-dominant arm is more accurate than the dominant arm in proprioception and mechanosensory perception [14, 181]. This result is also supported in sensorimotor control literature, namely the dynamic dominance hypothesis, that suggests inter-limb specific differences in functional outcomes (i.e., volitional movement, force regulation, fine object manipulation) [131]. When considered alongside our findings and broader literature on somatosensory processing, this body of work reinforces the notion of perceptual asymmetries between the dominant and non-dominant arms, potentially only observable during complex tasks (e.g., cross-modal sensory perception).

5.5.3 The Role of Sex on Tactile Perception

Consistent with previous literature on older adults [1, 12, 92, 121, 153, 173], tactile perception was not found to statistically significantly differ between male and female participants. Aligning with our prior work examining tactile detection in older adults [156], the results presented here suggest that a lack of sex-based differences persists in tactile discrimination tasks with older adults.

5.5.4 The Role of Aging on Tactile Perception

Our findings demonstrate that age significantly affects how accurately electrotactile stimuli are detected, regardless of the auditory load. These findings align with current literature that explored detection of stimuli in older adults [156], suggesting that detection is significantly poorer as we age. While an impact of aging was expected during the discrimination task, we did not observe a statistically significant effect of age on the examined discrimination-related outcomes. Interestingly, while literature suggests that discrimination outcomes typically decline with aging, one study indicated otherwise [143]. This study found an impact of aging on detection, yet not discrimination, in a subset of their examined populations (43%). Their explanation for why discrimination was not impacted within this subgroup was that they possibly had retention associated from use in daily life (i.e., had roles in which tactile discrimination was utilized) [143]. Given that we did not examine career or other lived experiences, this speculation is outside the scope of this work.

An additional explanation for this difference may lie in the timing of cortical processing, as discrimination and interpretation of stimuli engage higher-order cognitive functions that require more time to process. Detection of tactile stimuli is typically completed in approximately 160 ms [129]. In contrast, discrimination of tactile stimuli is typically completed in

approximately 500 ms [71]. As such, one possible reason for our observation could be that the discrimination task involves more complex cognitive processes, which could be less susceptible to age-related declines when compared to the simpler detection task [79]. However, our findings could also be attributed to the fact that our discrimination task sample was limited to individuals up to 69 years of age, whereas the detection group included participants up to 79 years of age. This age range difference may be critical, as it is possible that the higher-order cognitive functions necessary for tactile discrimination may not begin to show noticeable decline until after 69 years of age [38], or that the participants in our discrimination group experienced less cognitive decline than those in the detection group.

5.5.5 Considerations for Tactile Perceptual Assessments and Haptic Device Development

In this study, we observed significant differences in tactile perceptual outcomes based on the nature of the task participants performed (i.e., detection vs. discrimination). This distinction emphasizes the role of task-specific demands in shaping tactile perception, particularly in older adults. Our findings suggest that tactile detection tasks, both with and without an additional cognitive load, may exhibit variability in detection outcomes, but without significantly affecting overall accuracy or revealing differences between arms. In contrast, tactile discrimination tasks, under similar cognitive load conditions, are likely to show differences in overall discrimination accuracy and performance between arms, while not demonstrating significant variability. These differing findings may suggest that different tasks assess different aspects of tactile perception, providing complementary and task-dependent insights into the underlying sensory processes. Thus, future research in tactile perceptual assessments would benefit from a multifaceted approach tailored to the specific outcomes of interest.

Additionally, our findings relating to the modulation of cognitive-perceptual load can be informative for the development of haptic devices. The differential effects of cognitive-perceptual load on detection versus discrimination tasks suggest that haptic systems should be designed with task-specific adaptability in mind. As our findings suggest that modulating cognitive-perceptual load increases variability in detecting electrotactile stimuli, haptic systems that rely on simple touch cues may need adaptive features to keep feedback consistent. In turn, discrimination accuracy is impacted by the modulation of cognitive-perceptual load, suggesting that haptic devices utilizing discrimination stimuli should attempt to minimize competing sensory demands. By integrating adaptive feedback mechanisms that account for cognitive-perceptual load, haptic devices can enhance user experience, improve accessibility, and better support applications in rehabilitation, skill training, and assistive technologies.

5.5.6 Limitations

One limitation of the current study is that individuals who are left-arm dominant were excluded. Research suggests individuals who are left-arm dominant may have different neural processing pathways than individuals who are right-arm dominant, particularly in the way sensory information is integrated and processed in the brain [41, 100, 149]. Therefore, results of this study may not generalize to individuals who are left-arm dominant.

Another limitation of this work is the use of electrotactile stimuli, which, while effective in eliciting tactile sensory axonal responses, do not replicate real-world tactile experiences. Tactile stimuli activate cutaneous mechanoreceptors, while electrotactile stimuli activate free nerve endings in the skin [24, 178]. Future studies could explore other forms of tactile stimuli, such as vibrotactile or force, to further investigate how tactile perception may be impacted in the presence of a cross-modal stimulus. In turn, the future work could determine whether our

results observed with electrotactile stimuli can generalize to other forms of tactile stimulation.

Another limitation of this work is that we did not examine all the nerves that innervate the upper limb. While the upper limb is innervated by three main nerves, which in turn, innervate distinct and unique locations, findings at these three nerves may not generalize to the entire upper limb. Accordingly, future work can explore various other nerves and locations at the upper limb.

5.5.7 Future Work

Future research could explore how additional sensory modalities interact to increase cognitive-perceptual load and affect tactile perception across various tasks. By incorporating concurrent stimuli, like visual and olfactory inputs, studies could examine how competing sensory information influences tactile perception and cognitive processing. Additionally, exploring these effects across diverse populations, including those with sensory or neurological impairments (e.g., blindness, hearing loss, stroke), could reveal how sensory processing and multitasking abilities differ. Understanding how cognitive load is managed in these groups would also provide valuable insights for neurorehabilitation and improving recovery outcomes for individuals with a brain injury.

5.6 Conclusion

This study examined how older adults detect and discriminate electrotactile stimuli in the presence and absence of auditory stimuli. The findings highlight that increased cognitive demands can impair accurate perception of tactile stimuli. By further understanding how cognitive-perceptual load influences tactile perception, we can better understand the different

factors that influence intact tactile perception, and in turn, explore when and why tactile impairments arise in patient populations.

Chapter 6

Summary

The overarching goal of this body of work was to further explore the differing factors that influence intact tactile perception in a population that is neurotypical (i.e., young and older adults). Tactile perception is essential for functional independence, playing a critical role in everyday activities such as grasping objects, manipulating tools, and engaging in social interactions. However, approximately 30% of individuals in the United States experience tactile perceptual impairments, which can significantly impact their ability to detect and interpret sensory stimuli. Given this, a greater exploration of the factors that influence intact tactile perception is necessary to improve assessment methods and clinical interventions.

Existing literature highlights several factors that may shape tactile perception, including arm dominance, nerve distribution, stimulus location, biological sex, age, and cognitive-perceptual load. However, traditional tactile perceptual assessments often examine these factors in isolation, overlooking their complex interactions. This limitation may reduce the accuracy of diagnostic measures and constrain the development of effective rehabilitation strategies, particularly for individuals who experience tactile deficits following a neurological injury. To address this gap, this body of work provides a comprehensive analysis of how these factors, both independently and in combination, modulate tactile perceptual outcomes.

This research first examined tactile perception in young and older adults at rest, utilizing electrotactile stimulation to determine detection thresholds. The findings suggest that in young adults, factors such as the nerve stimulated, location of stimulation, biological sex,

and a subset of their interactions significantly influence tactile perception. In older adults, age, nerve distribution, stimulus location, and a subset of their interactions emerged as primary determinants of tactile perceptual outcomes. Contrary to both preliminary findings and existing literature, arm dominance did not have a significant effect on tactile detection at rest. Collectively, these results suggest that when assessing intact tactile perception, factors such as nerve distribution, stimulus location, sex, and age should be carefully considered.

Additionally, beyond these factors, cognitive-perceptual load may also modulate tactile perception. Cognitive-perceptual load refers to the attentional and executive resources allocated to processing sensory information and performing concurrent tasks. A higher cognitive-perceptual load, such as when an individual engages in multiple tasks simultaneously, may reduce the availability of cognitive resources for tactile processing, leading to altered sensory perception. Previous literature suggests that a role of arm dominance may only become apparent when the associated cognitive-perceptual load is high, implying that differences between dominant and non-dominant arms may be more pronounced under cognitively demanding conditions. To further explore this notion, this research also examined tactile perceptual outcomes while modulating the associated cognitive-perceptual load. Participants completed concurrent tactile and auditory tasks, allowing for an assessment of how cross-modal demands influence tactile perceptual outcomes. The findings indicate that the presence of an auditory stimulus affected both detection accuracy and discrimination variability to electrotactile stimuli in both younger and older adults. Interestingly, an effect of arm dominance was observed only under conditions of high cognitive-perceptual load, supporting the hypothesis that cognitive resource allocation plays a crucial role in modulating tactile perception. These results underscore the importance of accounting for cognitive-perceptual load when assessing tactile perception, as failing to do so may impact observations that emerge under more real-world conditions.

Combined, this body of work highlights the necessity of considering multiple interacting factors when evaluating tactile perception.

Chapter 7

Future Work

While this body of work provides a comprehensive analysis of the factors influencing intact tactile perception in neurotypical young and older adults, important avenues for future research remain. Expanding upon these findings will allow for a greater understanding of tactile perception across diverse populations and under varying conditions.

One avenue of future work can be in the assessment of tactile perception in individuals who have disruptions to the CNS, such as those who have experienced a stroke or traumatic brain injury. CNS disruptions can significantly alter somatosensory processing, leading to impairments in tactile detection, discrimination, and interpretation. Investigating how factors such as arm dominance, nerve, location stimulated, sex, associated cognitive-perceptual load, and their interactions influence tactile perception in these populations may provide key insights into when and why tactile impairments arise. Furthermore, these findings could inform the development of more targeted neurorehabilitation strategies aimed at restoring tactile perception and improving overall sensorimotor outcomes in individuals with CNS impairments.

Additionally, future research should explore tactile perception using physical stimulation (i.e., vibrotactile, force). While electrotactile stimulation provides precise control over axonal stimulus parameters, tactile stimuli more closely resemble the types of physical stimuli experienced in everyday life. Assessing tactile perception using physical interactions, such as vibration or pressure applied to the skin, would enhance the ecological validity of find-

ings and help determine whether the observed effects generalize to more common stimuli conditions. Furthermore, comparing electrotactile and tactile stimulation could reveal important differences in how various methodologies contribute to tactile perceptual outcomes and translate to functional outcomes.

Another promising direction for future work involves investigating tactile perception during voluntary muscle activation. The present study focused on tactile perception while participants were at rest. Yet in real-world scenarios, tactile perception frequently occurs alongside volitional movement. Literature suggests that volitional movement can impact tactile perception [23]. By assessing tactile perception during muscle activation or voluntary movement, future research can further explore how muscle activation influences tactile perception. Understanding these interactions is particularly important for applications in motor rehabilitation, where individuals must integrate both sensory and motor feedback to regain functional abilities.

Lastly, exploring tactile perception in children represents another valuable extension of this work. Investigating how factors such as arm dominance, nerve, location, sex, associated cognitive load, and their interactions influence tactile perception in younger populations could provide insights into the developmental trajectory of somatosensory function. Furthermore, such research could contribute to early identification of sensory processing disorders and inform the design of age-appropriate assessments and interventions to support sensory and motor development in children who experience impairments.

Combined, future work should expand the scope of tactile perception research by examining individuals with CNS disruptions, incorporating various tactile stimulation methodologies, assessing perception during volitional muscle activation, and exploring developmental changes in children. By addressing these areas, researchers can build upon the normative data established in this work, ultimately leading to more comprehensive tactile assessments

and improved interventions for individuals with sensory impairments.

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Appendices

Appendix A

Approved Institutional Review Board Research Protocol

INSTRUCTIONS:

- Use this “*TEMPLATE PROTOCOL (HRP-503)*” to prepare a study protocol outlining your research plan.
- Depending on the nature of your study, some major sections might not be applicable to your research. If so, simply mark as “N/A.” For example, a simple survey might have many sections with “N/A.” For subsections (e.g., 1.x or 8.x) you can mark as “N/A” if you are certain that the subsection is not applicable.
- Once the IRB/HRPP approves your submission, your latest approved version of the protocol will be stored in the IRB Protocol Management online system.
- If your research plan changes and you need to modify the protocol, please submit an amendment to Protocol Management with the requested modifications. Download your current protocol from Protocol Management and indicate the changes/revisions using the track changes feature in order to make review of the modifications easier to follow. If you are unable to use track changes, please create a new paragraph wherever you need to make a change, and indicate “Amendment: Date” before making a change to any section. Protocol management will store the older versions of your protocol if the IRB or HRPP staff need to compare them during the review.

PROTOCOL TITLE:

Include the full protocol title.

Tactile Perception and Peripheral Tactile Signal Propagation in Young Adults, Older Adults, and Individuals with Stroke

PROTOCOL NUMBER:

Include the number assigned in Protocol Management (verify this has been added before submitting protocol to HRPP).

23-1246

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Use this table to keep track of changes. Add more rows as needed.

Revision #	Version Date	Brief Summary of Changes (i.e., the different sections)	Consent Change?

Tactile Perception and Peripheral Tactile Signal Propagation in Young Adults, Older Adults, and Individuals with Stroke

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1.0 Study Summary

Study Title	Tactile Perception and Peripheral Tactile Signal Propagation in Young Adults, Older Adults, and Individuals with Stroke
Study Design	Measure tactile perception and track tactile signals at both arms of (Aim 1) young adults, (Aim 2) older adults, and (Aim 3) individuals with stroke using behavioral measures and physiological measures
Primary Objective	Expose differences in tactile perception occurring in individuals due to (Aim 1) arm dominance, (Aim 2) aging, and (Aim 3) stroke
Secondary Objective(s)	Identify potential neural mechanism(s) governing differences in tactile perception due to (Aim 1) arm dominance, (Aim 2) aging, and (Aim 3) stroke
Study Population	(Aim 1) young adults aged 18-26, (Aim 2) older adults aged 55+, and (Aim 3) individuals with stroke and comparable age individuals who are neurotypical
Sample Size	(Aim 1) 20 young adults, (Aim 2) 20 older adults, and (Aim 3) 13 individuals with stroke and 13 comparable age individuals who are neurotypical
Research Intervention(s)/ Investigational Agent(s)	Psychophysics testing, physiological measures (e.g., electromyography), clinical assessments
Study Duration for Individual Participants	Participation will last 1-2 sessions, with a duration of 2-6 hours per session
Acronyms and Definitions	PNS: peripheral nervous system CNS: central nervous system sEMG: surface electromyography

2.0 Objectives

2.1 Describe the purpose, specific aims, or objectives of this study:

Intact tactile perception is critical for an individual to learn and execute physical activities. Prior work and our pilot testing provide compelling evidence that tactile perception can depend on the arm tested, aging, and brain disruption (due to a stroke). Yet, the understanding of why differences in tactile perception occur remains poor in part given limitations of existing assessments. For example, existing assessments rely on behavioral measurements that address one's conscious tactile perception, yet do not delve into the neural mechanisms. In contrast, existing assessments that identify neural mechanisms are localized to specific regions along the nervous system (e.g., central nervous system only, peripheral nervous system only) and do not necessarily address conscious tactile perception. Furthermore, testing often involves one nerve even though numerous nerves innervate a limb.

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To better understand the factors that influence the propagation of tactile stimuli to conscious tactile perception, we need to study the afferent sensory signaling pathway and factors that modulate signal responsiveness. While the role of the central nervous system (CNS) on conscious perception of tactile stimuli is being examined, this work largely does not consider the role of the peripheral nervous system (PNS) on successful sensory signal transduction. We will examine the role of peripheral sensory signal transduction on conscious tactile perception. We will measure conscious perception of tactile stimuli at the arm and identify the contributing role of the PNS to differences depending on arm dominance, aging, and stroke. We will identify whether sensory nerve conduction at the peripheral nerve correlates with the threshold for detecting the tactile stimuli at various nerves and locations of both arms. Results will provide evidence whether sensory signal transmission is altered at the PNS when processing tactile stimuli at each arm. A potential translational outcome of this research is a more comprehensive assessment including the PNS for populations with CNS-initiated injuries, as well as insight regarding which patients will benefit from therapies targeting the PNS versus CNS (e.g., electrical stimulation).

Aim 1: Determine the role of arm dominance on how conscious detection of a tactile stimulus correlates with the flow of a tactile sensory signal along the peripheral nerve. Our prior work demonstrates that the conscious perceptual threshold for detecting a tactile stimulus when the median nerve is stimulated is less at the non-dominant arm than the dominant arm, indicating improved conscious perception. Prior studies suggest that peripheral nerve signaling is comparable at the non-dominant and dominant arm. We propose that a tactile stimulus applied to the non-dominant and dominant arm will i) differ in thresholds for conscious perception and ii) be comparable in PNS responsiveness. We hypothesize that this difference in conscious perception, depending on arm dominance, will not correspond to the peripheral nerve signaling, regardless of the nerve tested. Therefore, differences in conscious perception can be assumed to be associated with changes in how the sensory signals are processed in each hemisphere of the brain.

Aim 2. Determine the role of aging on how conscious detection of a tactile stimulus correlates with the flow of a tactile sensory signal along the peripheral nerve. Prior work indicates that aging is associated with poorer conscious perception (i.e., larger detection thresholds) and a reduction in peripheral nerve function in response to a tactile stimulus. We propose that a tactile stimulus applied to each arm of older adults will differ from the young adults in i) thresholds for conscious perception (larger) and ii) peripheral nerve signaling responsiveness (smaller). We hypothesize that conscious perception in older adults will not correspond to the peripheral nerve signaling, regardless of the nerve tested. Results will provide evidence whether aging impacts the relationship between sensory signal transmission along the peripheral nerve and conscious tactile perception at both arms.

Aim 3. Determine the role of stroke on how conscious detection of a tactile stimulus correlates with the flow of a tactile sensory signal along the peripheral nerve. We propose that a tactile stimulus applied to the arm will differ at the paretic arm of participants with

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stroke when compared to their non-paretic arm and both arms of comparable-aged adults who are neurotypical in i) thresholds for conscious perception (larger) and ii) peripheral nerve responsiveness (smaller). Prior work indicates that tactile perceptual deficits arise post stroke due to issues in signal transmission at the central nervous system. Our preliminary data suggest that tactile perceptual deficits arise post stroke due to issues in transmitting sensory signals along the periphery, in addition to processing sensory signals centrally. Therefore, we hypothesize that conscious perception will correspond to the peripheral nerve signaling for some, if not all nerves tested. Results will provide evidence whether stroke impacts the relationship between sensory signal transmission along the peripheral nerve and conscious tactile perception at both arms.

2.2 State the hypotheses to be tested:

Our hypotheses are:

Aim 1: We hypothesize that a difference in conscious perception, depending on arm dominance, will not correspond to the peripheral nerve signaling, regardless of the nerve tested.

Aim 2: We hypothesize that conscious perception in older adults will not correspond to the peripheral nerve signaling, regardless of the nerve tested.

Aim 3: We hypothesize that conscious perception will correspond to the peripheral nerve signaling for some, if not all nerves tested in individuals with stroke.

3.0 Background

3.1 Summarize the relevant prior research on this topic and gaps in current knowledge within the field of study:

While traversing through even the simplest daily activities, the nervous system relies on a complex cycle of sensory input and motor output. Just as it is difficult to button a shirt while wearing gloves, interacting with the world in the absence of tactile perception is exceedingly challenging. For most, it is simple to remove these winter gloves and perform necessary tasks. For older adults and those with neurological disorders, such as stroke and sensory neuropathies in which tactile signaling from the periphery to the brain is limited or absent, performing the simplest of such daily physical tasks can become difficult, if not impossible. Understanding the neural processes governing conscious tactile perception is instrumental to identify how conscious perception can be altered for reasons including arm dominance, aging, and stroke.

Our current understanding of the mechanisms underlying tactile perceptual deficits in humans is largely based on numerous patient populations. Individuals with a large-fiber sensory neuropathy have disrupted sensory signal transmission along the nervous system such that tactile perception is largely absent. Only by relying on secondary cues, such as vision, can these individuals consciously perceive their physical interactions with the world. Likewise, upper-limb prosthesis users lack peripheral sensory signals. Therefore, these individuals must rely on secondary cues to consciously perceive physical interactions at their artificial limb. For individuals who are neurotypical, research

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demonstrates an impact of arm dominance and aging on conscious tactile perception. That said, the governing neural mechanisms underlying these changes in the largely intact nervous systems remains unknown. Brain lateralization, where each brain hemisphere specializes for differing processes, is a plausible explanation for an effect of arm dominance on conscious tactile perception. Both changes at the PNS and CNS are plausible reasons for the impact of aging on conscious tactile perception. For individuals with stroke, our understanding of the governing mechanisms inducing changes in conscious tactile perception remains limited to the CNS; yet, our preliminary data suggests a potential role of the PNS. Changes at the CNS, as well as lifestyle changes, could impact PNS function post stroke, resulting in tactile deficits.

3.2 Describe any relevant preliminary data:

Conscious Tactile Perception:

Preliminary data were collected from eight right-arm dominant older adults (Figure 1). Participants received a single- 100- μ s pulse at their testing arm's fingertip or elbow. We identified at both arms the threshold at which the electrotactile stimulus was detected when participants were at rest (Baseline-Pre) and isometrically flexing about the elbow to 25% and 50% of their maximum voluntary torque. The perceptual detection threshold significantly differed between arms at the fingertip ($p<0.001$), yet not the elbow ($p=0.264$).

Peripheral Nervous System:

Preliminary data were collected from six participants with stroke and three comparable age controls (Figure 2). These preliminary results provide evidence that the sensory peripheral nerve signaling may be poorer in the median and ulnar nerves at both the paretic and non-paretic arm of the participants with stroke when compared to both arms of the controls. Differences in the sensory peripheral nerve signaling were not observed between the non-paretic and paretic arm of these participants with stroke. These preliminary findings suggest that we should consider the PNS, in addition to the CNS, when addressing somatosensory perception post-stroke.

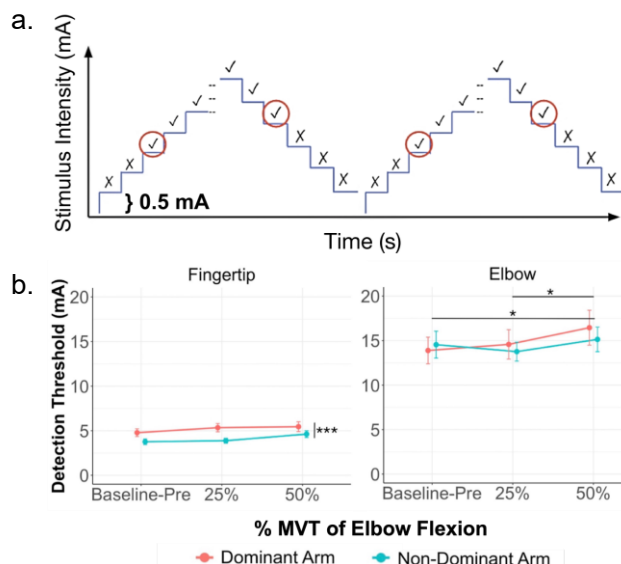


Figure 1. Conscious Detection of Electrotactile Stimuli.
a. The perceptual detection threshold at which the electrotactile stimulus can be detected will be determined using a staircase method. The stimulus intensity at which the stimulus is first detected and last detected will be averaged across two upward and two downward staircases to identify the perceptual detection threshold.
b. Mean and standard error of the perceptual detection threshold at the fingertip and elbow for the dominant and non-dominant arm of controls (Baseline-Pre condition).

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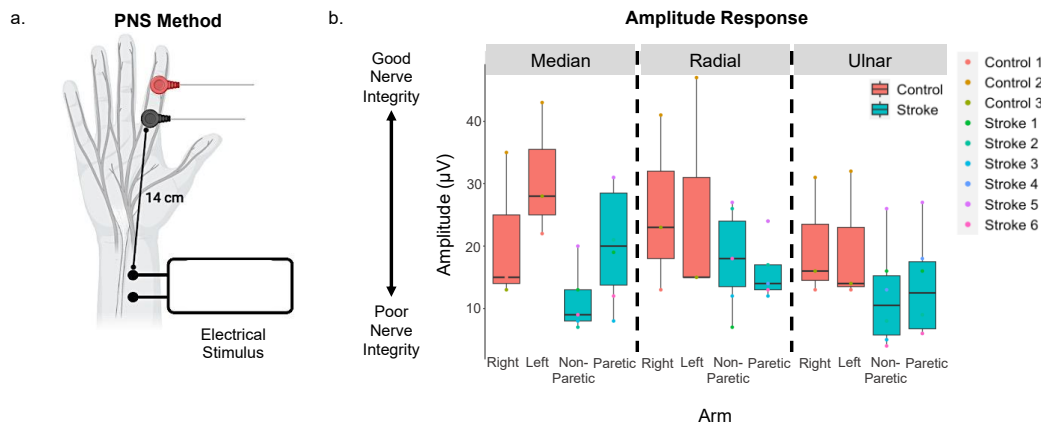


Figure 2. Peripheral Nerve Assessment. **a.** Participants sat with their arm relaxed, and a delivered electrical stimulus elicited a maximal sensory response at the median, radial, and ulnar nerves. Subsequent neuronal activity was measured using electromyography sensors, and outcome measures extracted included peak amplitude and latency response. **b.** Shown is the peak amplitude response at each tested arm based on data from six individuals with stroke and three individuals without stroke.

3.3 Based on the existing literature, provide the scientific or scholarly rationale for and significance of your research and how will it add to existing knowledge:

Accurate tactile perception is critical for effectively controlling one's movements and learning new physical skills. Tactile impairments are associated with poorer outcomes, including quality of life, for individuals with stroke. As stroke is a form of traumatic injury to the central nervous system (CNS), most stroke research has focused on understanding deficits in sensory function of the CNS in isolation. These previous studies have shown that stroke leads to damage in various regions of the CNS, including the cortex, basal ganglia, thalamus, and brainstem. A handful of papers demonstrate changes in sensory nerve conduction at both arms along the peripheral nerve in individuals with stroke, yet these changes are not associated with tactile perception. It is reasonable to expect that changes in sensory signal transduction along the peripheral nerve will impact tactile perception. Therefore, this research will be the first known effort to address the potential role of peripheral nerve signaling on tactile deficits in individuals with stroke.

Simultaneously, much remains to be understood regarding the role of the PNS and CNS on the tactile perceptual process when considering an impact of arm dominance and aging. Poorer tactile perception with aging can impact the ability to dress oneself, complete household tasks, and perform leisure activities. An impact of arm dominance on tactile perception is important for considering rehabilitation approaches and haptic device design. Prior research demonstrates poorer tactile detection and slower signal transmission along the peripheral sensory nerve due to arm dominance and aging. The methods employed in this protocol will enable an understanding of how changes at the peripheral nerve relate to tactile perception when considering the factors of arm dominance and aging, in addition to stroke. Hence, this research is significant for

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investigating the neural mechanisms associated with tactile perception in the intact, aged, and stroke-affected nervous system.

4.0 Study Endpoints

- 4.1 *Describe the primary and secondary **study** endpoints. See links below for discussion of study endpoints and how they may differ from study objectives. These are most common in clinical trials but are sometimes applicable to other types of biomedical research, as well as social, behavioral, or educational research. See link below for a discussion.*

https://docs.google.com/document/d/1Wocz7K7a0hCQJPP0_khh5l1SQQjhGDDGHzcOPRHR5Tw/edit?usp=sharing

Detection thresholds (e.g., mA, N) for behavioral assessments.

Peak latency (ms) and amplitude response (μ V) values for PNS assessments.

- 4.2 *Describe any primary or secondary **safety** endpoints. These should be included for all studies that are greater than minimal risk. (Minimal risk: The probability and magnitude of harm or discomfort anticipated in the research that are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.):*

N/A

5.0 Study Design and Statistical Analysis Plan

- 5.1 *Describe the basic study design/approach (e.g., qualitative study using five focus groups of first year students to describe assimilation into the university community; randomized controlled trial of a behavioral change intervention to increase dietary intake of whole grains; pre- post-test evaluation of new pedagogical techniques to improve adult literacy):*

We will compare outcomes on the behavioral and peripheral nerve assessments between arms of (Aim 1) Young Adults, (Aim 2) Older Adults, and (Aim 3) Individuals with Stroke. The conditions delivered (e.g., arm tested, nerve tested) will be balanced and randomized during the respective approaches of psychophysics testing and peripheral nerve conduction quantification.

- 5.2 *Describe corresponding data analysis plan/approach (e.g., content analysis of focus group transcripts; descriptive analysis followed by linear regression modeling; nonparametric analysis of pre- and post-test measures):*

Linear mixed-effects models will be used with arm as a fixed factor, participant a random factor, and tactile perceptual detection threshold as the dependent variable. An analysis of variance (ANOVA) will identify significant effects for each nerve separately. We will include the peripheral nerve signaling outcome measures as fixed effects, in addition to

variables such as participant age and body-mass index, in the linear mixed-effects models to identify associations of these measures with the tactile perceptual outcomes.

6.0 Setting

6.1 *Describe the sites or locations where your research team will conduct the research. Consider each of the items listed below:*

- *Identify where your research team will identify and recruit potential subjects.*
- *Identify where the team will perform the research procedures.*
- *Describe the composition and involvement of any community advisory board(s).*
- *For research conducted in other locations, describe:*
 - *Site-specific regulations or customs affecting the research at those locations.*
 - *Local scientific and ethical review structure at those locations. Examples include work in other cultures or ethnic groups (within or outside of the U.S.) and work with churches. The HRPP will provide additional guidance for international research.*

We will recruit the older adult controls largely through the Virginia Tech Older Adult Research Registry, a local database containing ~250 individuals.

We will recruit the individuals with and without a stroke largely through the Southwest Virginia Stroke Registry, a registry that is currently being developed by Drs. Parcetich and Gurari. The Southwest Virginia Stroke Registry will include the contact information of individuals with and without a stroke who are interested to participate in stroke-related research. We can also recruit individuals with stroke through the Brain Injury Services of Southwest Virginia, which provides access to ~120 individuals with stroke living in the community. Within the larger Brain Injury Services network of services, there are a total of 12 different support groups based on geographical location. If needed, additional stroke-related networks are available from which we can recruit (e.g., Veterans Affairs).

Individuals without neurological impairments will be chosen from among volunteers in the surrounding area and ResearchMatch.org. Flyers will be posted around the New River Valley community to recruit the controls. The study may be included in VT's newsletter to reach most of VT's community. We may also recruit through local presentations, social media groups, local tv and print media, word of mouth, natural gathering places, faith-based groups, recreational centers, rehabilitation centers, chambers of commerce, festivals, leisure events, stroke support groups, and local health clinics to ensure that awareness of our studies exists in the local community. Information will be distributed from our own institutions and social media accounts, our clinical partners, and support group networks across southwest Virginia.

The experiment will be completed at Radford University's Department of Physical Therapy, which is located at 101 Elm Avenue, Suite 8A, Roanoke, VA 24013.

7.0 Study Intervention(s)/Investigational Agent(s)

7.1 Describe the study interventions (including behavioral interventions) and/or investigational agents (e.g., drugs or devices) to be used in this study. Consider each of the items listed below:

- *Drug/Device Handling: If the research involves drugs or devices, describe your plans to store, handle, and administer the drugs or devices so that they will be used only on subjects, and only by authorized investigators.*
- *Describe whether any of the following will be used: microwaves, X-rays, DEXA scans, general anesthesia, or sedation*
- *If control of the drugs or devices used in this protocol will be accomplished by following an established, approved organizational SOP (e.g., Research Pharmacy SOP for the Control of Investigational Drugs, etc.), please reference the SOP in this section.*

Study interventions are peripheral nerve conduction assessments and conscious detection threshold assessments.

Peripheral Nerve Conduction Assessments:

Electrotactile stimuli will be applied by IRB approved study team members using the commercially-available Natus MOD UltraPro S100. The system will assess peripheral nerve signal transmission by quantifying sensory nerve action potentials using surface electrodes. The electrotactile stimulus will be applied to the median, ulnar, and radial nerves and amplitude and latency responses will be measured using surface electrodes.

Conscious Detection Threshold Assessments:

Conscious detection threshold assessments will be conducted using the commercially-available Digitimer DS8R Biphasic Constant Current Stimulator. We will assess the minimum amplitude of an electrotactile stimulus that is needed for the participant to consciously detect the signal. An electrotactile stimulus will be applied to the median, ulnar, and radial nerves at the fingertips and to the median and ulnar nerves at the elbow. Electrotactile stimuli will be applied using the staircase approach, increasing and decreasing by 0.2 mA every 3-5 seconds until the participant indicates conscious detection or lack of conscious detection of the stimulus three consecutive times, respectively.

List the name of all drugs (including any vitamins, supplements, herbs, or nicotine) to be used in the study. Indicate whether they have FDA approval, and list any limitations for their use:

N/A

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7.2 *List all devices, how they will be used, their purpose in the study, and if they will be used in a manner consistent with their approved uses. If they will be used in ways that are not yet FDA approved, indicate whether they need an IDE or a determination that they are exempt from the IDE Determination. If a determination of significant risk or non-significant risk is needed for any of the devices, include the researcher's recommendation for each of those devices:*

N/A

7.3 *If the drug is investigational (has an IND) or the device has an IDE or a claim of abbreviated IDE (non-significant risk device), include the following information:*

- *Identify the holder of the IND/IDE/abbreviated IDE.*
- *Explain procedures followed to comply with sponsor requirements for FDA regulated research for the following:*

FDA Regulation	Applicable to:		
	IND Studies	IDE studies	Abbreviated IDE studies
21 CFR 11	X	X	
21 CFR 54	X	X	
21 CFR 210	X		
21 CFR 211	X		
21 CFR 312	X		
21 CFR 812		X	X
21 CFR 820		X	

N/A

8.0 Procedures Involved

8.1 *Describe and explain the study design:*

We are interested in whether the peripheral nerve signaling contributes to differences in tactile perception depending on arm dominance in the (Aim 1) younger and (Aim 2) older adult population, as well as after a stroke (Aim 3). We will compare outcomes on the behavioral and peripheral nerve assessments between arms of (Aim 1) Young Adults, (Aim 2) Older Adults, and (Aim 3) Individuals with Stroke by fitting the data to a linear mixed-effects model with the peripheral nerve outcomes as fixed factors and the detection threshold as the dependent variable. We will include measures such as participant age and body-mass index (BMI) as fixed factors to account for corresponding variations that may arise. The conditions delivered (e.g., arm tested, nerve tested) will be balanced and randomized during the psychophysics testing and peripheral nerve conduction quantification.

8.2 *Provide a description of:*

- *All research procedures being performed*

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- *If the study has more than one procedure, session, and/or subject population, describe each procedure, session, and/or study population separately. For complex studies, you are encouraged to include a figure or chart.*

Recruitment:

At the start of each aim, we will initiate community-based recruitment to enroll individuals into our study. This includes recruitment through the Southwest Virginia Stroke Registry, a local registry containing contact information for adult humans interested in joining stroke-related research studies, and the Virginia Tech Older Adult Research Registry, a local database containing contact information for ~250 older adults. Participants will be chosen from volunteers in the surrounding area and ResearchMatch.org. Flyers will be posted around the New River Valley community to recruit. The study may be included in VT's newsletter to reach most of VT's community. Our recruitment efforts may involve postings and presentations through local avenues including social media, local tv, print media, natural gathering places, faith-based groups, recreational centers, rehabilitation centers, chambers of commerce, festivals, leisure events, stroke support groups, and/or local health clinics to ensure that awareness of our study exists in the local community. Information may be distributed from our own institutions and social media accounts, our clinical partners, and support group networks across all regions of southwest Virginia. Recruitment will also occur through word of mouth. A recruitment flyer is included, and a script for how the conversation will be structured is included.

An individual will indicate their interest to participate in a study via phone or email. Once an individual indicates an interest, the study team member will speak with the individual via phone or in person (if preferred).

Initial Screening:

Prior to recruiting an individual into the study, the experiment will be explained, and questions answered. If the participant indicates an interest to participate in the study, then the person will be screened. Screening will be achieved by asking the relevant inclusion criteria questions, including those on the attached questionnaire document, to determine eligibility. Cognitive ability will be initially screened based on an individual's ability to coherently respond to questions. If the individual is eligible, able to engage in coherent conversation, and expresses an interest to participate, then the consent form will be shared via email and a tentative date to participate will be selected.

Screening/Clinical Assessments:

The participant will be screened for their eligibility based on factors that may include their vitals, clinical assessment scores, and self-reported responses. We may assess arm dominance (Edinburgh handedness inventory), somatosensation (e.g., revised Nottingham Sensory Assessment; Semmes-Weinstein monofilaments; two-point discrimination; sensory extinction), motor impairments (e.g., Upper-Extremity Fugl-

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Meyer Motor Assessment), motor strength (e.g., manual muscle testing/dynamometry at shoulder and elbow), arm physical limitations (e.g., Action Research Arm Test, Wolf Motor Function Test), cognition (e.g., Montreal Cognitive Assessment), and hemineglect (e.g., Fluff Test). These assessments are valid, reliable, and commonly used by clinicians in stroke rehabilitation (see the Rehabilitation Measures Database for more details: <https://www.sralab.org/rehabilitation-measures>). Relevant papers summarizing these assessments include:

- Ransil, B. J. & Schachter, S. C. Test-retest reliability of the Edinburgh Handedness Inventory and Global Handedness Preference Measurements, and their correlation. *Perceptual and Motor Skills* 79, 1355–1372 (1994).
- Wu, C., Chuang, I. -ching, Ma, H., Lin, K. & Chen, C. Validity and responsiveness of the revised Nottingham Sensation Assessment for outcome evaluation in stroke rehabilitation. *American Journal of Occupational Therapy* 70, 7002290040p1-8 (2016).
- Sanford, J., Moreland, J., Swanson, L. R., Stratford, P. W. & Gowland, C. Reliability of the Fugl-Meyer assessment for testing motor performance in patients following stroke. *Physical Therapy* 73, 447–454 (1993).
- Suda, M. et al. Validity and reliability of the Semmes-Weinstein Monofilament Test and the Thumb Localizing Test in patients with stroke. *Frontiers in Neurology* 11, 625917 (2020).
- Dellon, A. L., Mackinnon, S. E. & Crosby, P. M. Reliability of two-point discrimination measurements. *Journal of Hand Surgery American* 12, 693–696 (1987).
- Hsieh, C. L., Hsueh, I. P., Chiang, F. M. & Lin, P. H. Inter-rater reliability and validity of the Action Research Arm Test in stroke patients. *Age Ageing* 27, 107–113 (1998).
- Morris, D. M., Uswatte, G., Crago, J. E., Cook, E. W. & Taub, E. The reliability of the Wolf Motor Function Test for assessing upper extremity function after stroke. *Archives of Physical Medicine and Rehabilitation* 82, 750–755 (2001).
- Hoops, S. et al. Validity of the MoCA and MMSE in the detection of MCI and dementia in Parkinson disease. *Neurology* 73, 1738–1745 (2009).
- Cocchini, G., Beschin, N. & Jehkonen, M. The Fluff Test: A simple task to assess body representation neglect. *Neuropsychological Rehabilitation* 11, 17–31 (2001).
- Cuthbert, S. C. & Goodheart, G. J. On the reliability and validity of manual muscle testing: A literature review. *Chiropractic Osteopathy* 15, 4 (2007).

We will document potential sources of peripheral sensory nerve signal disruption. This could include using an ultrasound to measure nerve cross-sectional area to address whether the nerve is compressed. Additionally, we will obtain stroke-related medical records for individuals with stroke to identify brain location(s) affected by the stroke. Based on these items, a licensed clinician would determine participant eligibility for individuals with stroke.

Experimental Testing Overview:

Data collection will consist of 1-2 sessions spanning 2-6 hours, accounting for breaks to rest, have snacks, and go to the restroom. Activities in these session(s) may include screening, clinical assessments, tactile assessments, and peripheral nerve conduction

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assessments. The participant will be asked to not exercise the day prior to and of each session and to avoid caffeine and other non-essential medications the day of each session to reduce potential effects arising from muscle fatigue and physiological modifications.

Conscious Tactile Perception Assessment:

We will use a custom similar device (DS8R Constant Current Stimulator) to apply an electrotactile stimulus to targeted nerves of each hand and elbow (one nerve and one location at a time). The electrotactile stimulus will range from 0mA - 100mA, with a duration of 100us pulses. The electrotactile stimulus will be delivered at randomized time intervals, sampled from a distribution between approximately 2s and 5s to prevent the participant from predicting when the stimulus occurs. Prior to placement of the stimulator electrodes, the skin at the fingertips and elbow will be prepared by cleaning each targeted area with alcohol wipes and scrubbing the surface of dead skin cells. Surface electrodes will be placed at digit 2 (Median), digit 5 (Ulnar), and the snuff box (Ulnar) for fingertip stimulation. Surface electrodes will be placed at the median and ulnar nerves of the elbow (at 1 cm distal from the elbow crease and 4 cm proximal from the ulnar side of the arm, respectively) for elbow stimulation. Presentation order of the arm, nerve, and location tested will be pseudo-randomized using a Latin square design.

To begin testing, the participant will lie supine in a clinical bed. The testing arm will be heated to at least 34 degrees Celsius using heating pads. We will roughly estimate conscious detection thresholds using the method of adjustments. The participant will turn a knob, which will control the stimulus amplitude, to indicate when the electrotactile stimulus is first consciously detected. Once the conscious detection threshold is estimated, we will use a method of limits (staircase method) to identify the conscious detection threshold more accurately (see Figure 1a). We will reduce the stimulus amplitude by 2mA, and then deliver electrotactile stimuli with a stimulus amplitude that increases in intervals of 0.2mA. Once the participant indicates that the stimulus is detected three times consecutively, we will increase the stimulus amplitude by 2mA. Then, the stimulus amplitude will decrease by 0.2mA until the participant does not detect the stimulus three times consecutively. By using this approach of first the method of adjustments, followed by the method of limits, we can encourage that the data collection duration is comparable amongst participants. The staircase method will be repeated three times for every nerve and location. Subsequently, the same procedures will be conducted with the opposite arm.

Arm muscle activation patterns may be measured (e.g., biceps brachii, triceps brachii, anterior/medial/posterior deltoid, pectoralis major, lower/middle trapezius) using surface electromyography (sEMG) sensors. If included, we will obtain the maximum voluntary isometric contraction for each of these muscles to enable sEMG normalization and, in turn, comparison.

The automated software for each automated experimental protocol will run at ~1 kHz, and collected data (e.g., time, tactile stimulus, sEMG) will be saved for offline processing.

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Peripheral Nerve Conduction Assessment:

We will use similar procedures as in the 'Conscious Tactile Perception Assessment' to prepare participants and their arm for testing (e.g., supine position, electrodes attachment). A commercial device (Natus MOD UltraPro S100) will quantify how sensory signals flow along each targeted nerve of each hand and elbow. An electrotactile stimulus will be applied and subsequent sensory afferent neuronal activity will be measured using the surface electrodes. We will extract the maximal sensory signal response and signal velocity.

8.3 Describe:

- *Procedures or safeguards intended to reduce the probability and magnitude of risks. (For example: Reducing the risk of injury in a virtual reality study either by having the subjects sit during the study or by providing an obstacle-free space for walking.)*
- *Be sure to describe all drugs and devices used in the research, when they will be administered or used, and their purpose.*
- *Methods used to collect data about subjects. Please upload all data collection forms to Protocol Management. Some common examples are:*
 - *Screening questionnaires*
 - *Survey(s), including online surveys*
 - *Demographic questionnaire(s)*
 - *Interview guide(s), e.g., questions or pool of questions for semi-structured interviews*
 - *Focus group guide(s)*
 - *Other documents used to collect data*

Physical Risks from Participation.

Stimulator device: The device interacting with the participant's skin to provide touch-related cues may produce minor irritation of the skin. The possibility of irritation will be minimized by reducing the magnitude of the stimulation and/or ending the stimulation task.

Ultrasound and Surface electrodes: The ultrasound and self-adhesive surface electrodes may produce minor irritation of the skin; there is also the possibility of an allergic reaction to the electrode paste. The possibility of irritation will be minimized by cleaning the skin with alcohol before and after the application of the electrodes. The electrodes and testing surfaces will be cleaned using alcohol wipes and/or disinfecting wipes.

Reaching movements: Repeated activation of the muscles may cause minimal temporary discomfort in the arm by the end of the study session. This potential discomfort may be addressed by stretching or massaging the participant's arm prior to and following the experiment.

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Community Risk from Participation.

Participating in this investigation may exclude the participant from partaking in other investigations for which the participant is recruited, or those in which the participant is currently participating.

Privacy Risks from Participation.

This study involves the use of identifiable, personal information and there is a chance that a loss of confidentiality could occur. The researchers have procedures in place to lessen the possibility of this happening.

8.4 What data will you collect during the study and how you will obtain them? Please include descriptions of electronic data collection, database matching, and app-based data collection:

Data will be manually inserted and/or automatically generated and saved using electronic documents, REDCap, and/or custom software. Demographic data will be obtained from the participant based on self-report, such as their arm dominance and year and month of birth. Weight and height may also be collected to estimate the participant's BMI. Clinical information will be obtained for relevant participants, which will include data from their medical records and outcomes obtained on their clinical assessments. Information relevant to the stroke will be included, such as date and type of stroke. Data regarding participant's interactions during the behavioral and PNS assessments will be stored digitally. All raw/unprocessed data will be coded with a unique participant identifier and stored on encrypted and password-protected university hard drives and SharePoint, and possibly REDCap. The identifiable data will be accessible only to study investigators.

8.5 Who will transcribe or code audio and/or video recordings?:

N/A

8.6 Include a description of any deception to be used in the study. Include justification for the use of deception (why the deception is necessary), describe the debriefing process, and describe how the study meets all the following criteria for alteration of consent (deception is considered an alteration of informed consent):

- *The research involves no more than minimal risk to the subjects*
- *The alteration will not adversely affect the rights and welfare of the subjects*
- *The research could not practicably be carried out without the alteration/deception*
- *(Optional but encouraged in most cases) Subjects will be provided with additional pertinent information after participation (i.e., debriefing for studies involving deception)*

N/A

- 8.7 *If the study involves long-term follow-up (once all research related procedures are complete), describe what data will be collected during the follow up period and when it will occur:*

N/A

9.0 Data and Specimen Long Term Storage and Use

- 9.1 *If you will store data or specimens for future use, describe where you will store the data or specimens, how long they will be stored, and how and by whom the data or specimens will be accessed:*

All identifiable participant data will be stored and accessed on encrypted and password-protected university hard drives, as well as a folder in SharePoint that is only accessible to members of the study team. REDCap may also capture and store this data. Access to the identifiable data will be granted by the PI to relevant members of the study team. All identifiable and de-identified data will be stored and maintained if the study is active, and for at least 5 years following study closure.

- 9.2 *For specimens, list the data to be stored or associated with each specimen:*

N/A

- 9.3 *Describe the procedures to release data or specimens outside of the research team, including the process to request a release, approvals required for release, who can obtain data or specimens, and what data will be provided with specimens:*

N/A

- 9.4 *Describe the identifiers to be included with stored data or specimens, as well as any key or code that could be used to make them identifiable. Describe where the code will be stored, who will have access to it, and when it will be destroyed:*

Project records that identify participants will be kept confidential as required by law. Federal Privacy Regulations provide safeguards for privacy, security, and authorized access. Except when required by law, participants will not be identified by name, address, telephone number, or any other direct personal identifier in project records disclosed outside of the study site at which the participant is tested. Each participant will be assigned an alphanumeric code for the study; the participant will not know their code. The linkage between the participant's name and their alphanumeric code will be stored on the consent form. For participants with stroke, identifiable data will be included with their medical records. The identifiable data will be maintained on encrypted and password-protected hard drives and SharePoint, as well as potentially REDCap, and maintained by the PI and the relevant study personnel who are involved in organizing and analyzing the data. Identifiable data will also be stored in ClinCard to enable participant payments. Participant records may be reviewed to meet federal or state regulations. Reviewers may include representatives of the Virginia Tech Institutional Review Board. The project results and pictures will be retained in the participant's research record if the study is active and for at least 3 years following study closure.

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9.5 Please select the identifiers you will obtain (whether directly from participants or from another source), including but not limited to:

☒	Name
☒	Geographical subdivisions smaller than a state, including street address, city, county, precinct, zip code, and equivalent geocodes (note, the initial three digits of a zip code are not considered identifiable)
☒	Elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death, and single year of age over 89 and all elements of dates (including year) indicative of such age (note, such ages and elements may be aggregated into a single category of age 90+)
☒	Phone numbers
☐	Fax numbers
☒	Electronic mail addresses (e-mail)
☐	Social Security numbers
☒	Medical record numbers
☐	Health plan beneficiary numbers
☐	Account numbers
☐	Certificate/license numbers
☐	Vehicle identifiers and serial numbers, including license plate numbers
☐	Device identifiers and serial numbers
☐	Web Universal Resource Locators (URLs)
☐	Internet protocol (IP) address numbers
☐	Biometric identifiers, including finger and voice prints (audio recording)
☐	Full face photographic images and any comparable images (including video recording)
☐	Student record number or identification number
☐	User name for online or computer accounts
☐	Any other unique identifying number, characteristic, or code (note this does not mean the unique code assigned by the investigator to code the data): Click here to explain.

10.0 Sharing of Results with Subjects

10.1 Describe whether you will share results (study results or individual subject results, such as results of investigational diagnostic tests, genetic tests, or incidental findings) with subjects or others (e.g., the subject's primary care physician). If so, describe how you will share the results and include this information as part of the consent document. Upload materials you will use to explain the results to subjects:

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The study results will be published in academic journals. If the participants are interested, we will share these published articles with them that provide aggregate group information; no participant-specific results will be shared.

11.0 Study Timelines

11.1 Describe:

- The duration of an individual subject's participation in the study (for example, 1 hour, 2-4 weeks, 3-5 years).
- The amount of time expected to enroll all study subjects (weeks, months, years, etc.)
- The amount of time expected for the investigators to complete this study including primary data analyses.

Participants will partake in the research study for 1-2 sessions for each study. The participant will be asked to partake in assessment portions. Participation in each session will span 2-6 hours. An overview of the expected timeline for enrolling all participants and completing the studies is provide in Table 1.

		Year 1	Year 2	Year 3	Year 4	Year 5
Aim1	Data Collection and Analyses	■	■			
	Dissemination of Results		■			
Aim 2	Data Collection and Analyses		■	■		
	Dissemination of Results			■	■	
Aim 3	Data Collection and Analyses				■	■
	Dissemination of Results					■

Table 1. Tentative Timeline. Shaded boxes indicate when effort will be focused on data collection, data analyses, and dissemination of results for each aim throughout the five years period.

12.0 Inclusion and Exclusion Criteria

12.1 Describe how you will screen individuals for eligibility. When will screening occur and what procedures will you use? Upload any screening scripts or surveys to Protocol Management:

All participants will first be screened by a study team member via phone or in-person to determine their eligibility according to the inclusion and exclusion criteria. All participants with stroke will be subsequently screened by a licensed clinician to determine their eligibility.

12.2 Describe the eligibility criteria that define who will be included and who will be excluded from enrollment for each procedure of your study. Include

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any geographic criteria (e.g., Virginia Tech undergraduate students, a national sample of adults with engineering degrees, minors aged 8-12 in the New River Valley, university faculty in Virginia and Paris, France):

Requirements for all participants will include: i) ability to understand and complete the experimental tasks, ii) capacity to provide informed consent, iii) at least 18 years of age, iv) no history of chemotherapy, and v) no major injury to either arm for reasons other than stroke.

The inclusion criteria for the young adults includes right-hand or left-hand dominance so that our results are not confounded by a potential arm dominance effect. For Aim 1, the age range is 18-26 (young adults).. The inclusion criteria for the older adults includes right-hand dominance so that our results are not confounded by a potential arm dominance effect. For Aim 1, the age range is 18-26 (young adults). For Aim 2, the age range is 55+ (older adults). For Aim 3, the controls will be a comparable age to the participants with stroke and will have no musculoskeletal and neurological conditions. The controls will serve as an indicator of normal performance, providing tactile results in the absence of the stroke condition.

Additional inclusion criteria for Aim 1 i) be right-hand or left-hand dominant, ii) have no history or current use of chemotherapy, iii) have no musculoskeletal or neurological disorders, iv) no diagnosis of diabetes, v) no major injury or pain in either arm, vi) and no implant electrical devices (i.e. a cardiac pacemaker). Additional inclusion criteria for Aim 2 are that the individuals: i) be right-hand dominant, ii) have no history or current use of chemotherapy, iii) have no musculoskeletal or neurological disorders, iv) no diagnosis of diabetes, v) no major injury or pain in either arm, vi) and no implant electrical devices (i.e. a cardiac pacemaker).

The inclusion criteria for our individuals with stroke are: i) single stroke incident resulting in a unilateral lesion (ischemic and hemorrhagic), ii) chronic phase (>1 year from stroke onset), iii) onset of stroke after the age of 18, iv) no use of antispastic injections in the past six months, v) lesion not in the brainstem and/or cerebellum, and vi) stroke not arising due to brain surgery. We will include individuals with stroke who do not show hemineglect, as identified using the Fluff Test, to have confidence that the outcomes are a result of the tactile sensory signal transmission and processing. We will include individuals with aphasia who meet the criteria of having the capacity to provide informed consent.

12.3 Indicate specifically whether you will include or exclude each of the following special populations: (You may not include members of these populations as subjects in your research unless you indicate them in the description of your subject population.)

- *Minors, as defined by state law where the study is performed (infants, children, teenagers)*
- *Pregnant women (can be included in minimal risk studies by mentioning in section 13.1)*

- *Prisoners (including all incarcerated individuals)*
- *Adults not capable to consent on their own behalf*

We will exclude minors, pregnant women, prisoners, and adults not capable of consenting on their own behalf. We will be screening individuals during our initial questionnaire, asking directly if they are pregnant or have reason to believe that they are. Some literature suggests that pregnant individuals are at a higher risk for developing nerve entrapments and have varied nerve conduction results as well. As this may impact our data analysis and conclusions, pregnant individuals will be excluded.

13.0 Vulnerable Populations

13.1 If the research involves individuals who are vulnerable to coercion or undue influence, please describe additional safeguards you will include to protect their rights and welfare. Consider the applicable items listed below:

- *If the research involves Virginia Tech students, indicate whether these are students of any of the investigators. If so, describe whether the activities will take place during class time as part of the curriculum and the steps you will take to reduce the possibility that students feel obliged to participate in order to improve their course grade. The HRPP can provide further guidance as needed. Describe whether you will request access to student records (e.g., SAT, GPA, GRE scores).*
- *If the research involves employees of Virginia Tech or the research sponsor, describe steps you will take to ensure that the employees are freely participating and describe how their data will be protected from inspection by their supervisors.*
- *If the research involves Virginia Tech NCAA athletes, you must obtain approval from the athletic department.*
- *For research involving Montgomery County Public Schools, you must obtain county approval (after obtaining contingent Virginia Tech approval). Other locales have different requirements; please check on these and describe here. Approval is typically granted by the superintendent, principal, and classroom teacher (in that order). Approval by an individual teacher is insufficient. School approval, in the form of a letter or a memorandum should be uploaded as a supporting document.*
- *If the research involves pregnant women, review “CHECKLIST: Pregnant Women (HRP-412)” to ensure that you have provided sufficient information in this protocol.*
- *If the research involves prisoners, review “CHECKLIST: Prisoners (HRP-415)” to ensure that you have provided sufficient information in this protocol.*
- *If the research involves persons who have not attained the legal age for consent to treatments or procedures involved in the research*

- (minors), review the “CHECKLIST: Minors (HRP-416)” to ensure that you have provided sufficient information in this protocol.*
- *If the research involves cognitively impaired adults, review “CHECKLIST: Cognitively Impaired Adults (HRP-417)” to ensure that you have provided sufficient information in this protocol.*

Virginia Tech students are permitted to join these studies. Their participation is voluntary and will not be part of a class time or a curriculum. We will make clear that participation is voluntary and will not impact one's performance in their coursework. No student records, such as SAT and GPA, will be requested. NCAA athletes must obtain approval from their athletic department to participate in the research.

Virginia Tech employees are permitted to join these studies. Their participation is voluntary and will not impact their employment. Discussion regarding the employee's participation will only be permitted amongst study team members for research-related purposes.

14.0 Number of Subjects

14.1 Indicate the total number of subjects to be enrolled and how this number was determined (e.g., sample size calculation [show], number of available subjects in a finite pool, number of tests funding award would allow):

For each of Aims 1 and 2, we estimated a sample size of 40 participants are needed. This estimate was obtained using a two-sample t-test power calculation. This number of participants would give 80% power to detect a difference between arms on the PNS amplitude outcome with an effect size of at least 10 μ V when comparing the dominant and non-dominant arm of controls. This analysis assumed a within-subject standard deviation of 10.8 μ V based on the preliminary data collected.

For Aim 3, we estimated a sample size of 26 participants are needed, with 13 stroke and 13 controls. This estimate would give more than 80% power to detect a difference between arms on the PNS amplitude outcome with an effect size of at least 10 μ V when comparing the non-paretic and paretic arms to the dominant arm of the controls. To be conservative, we assume large within-subject and between-subject standard deviation of 80 μ V and 30 μ V, respectively. With this sample size and assumed variances, we also have 55% power to detect an individual effect of size 10 μ V when comparing the paretic and non-paretic arms to each other and to both arms of the controls, at the 1.67% significance level, using the Bonferroni method to correct for multiple comparisons. This power estimate was done via a simulation.

14.2 If this is a multi-site study, indicate the number of subjects to be enrolled at this site and the total to be enrolled from all sites:

N/A

14.3 If applicable, indicate the number of potential subjects you expect to screen for enrollment, and the number of subjects you will need to complete the research procedures:

N/A

14.4 If the study has more than one procedure, indicate the total number of subjects to undergo each procedure separately:

For Aim 1 we will complete testing with an estimated 20 controls, Aim 2 with an estimated 20 controls, and Aim 3 with an estimated 13 controls and 13 participants with stroke.

15.0 Recruitment Methods

15.1 Describe when, where, and how you will recruit potential subjects:

At the start of each aim (see Table 1), we will initiate community-based recruitment to enroll individuals into our study. This includes recruitment through the Southwest Virginia Stroke Registry, a local registry containing contact information for adult humans interested in joining stroke-related research studies, and the Virginia Tech Older Adult Research Registry, a local database containing contact information for ~250 older adults. Additionally, we will create a registry of contact information from participants who communicate interest in participating in current and future projects. Participants will be chosen from volunteers in the surrounding area and ResearchMatch.org. Flyers will be posted around the New River Valley community to recruit. The study may be included in VT's newsletter to reach most of VT's community. Our recruitment efforts may involve postings and presentations through local avenues including social media, local tv, print media, natural gathering places, faith-based groups, recreational centers, rehabilitation centers, chambers of commerce, festivals, leisure events, stroke support groups, and/or local health clinics to ensure that awareness of our study exists in the local community. Information may be distributed from our own institutions and social media accounts, our clinical partners, and support group networks across all regions of southwest Virginia. Recruitment will also occur through word of mouth.

15.2 Describe the source of subjects (for example, clinic patients with specific conditions, students in the library, community members at a gathering, or members of a local gym):

Participants will be (Aim 1) young adults, (Aim 2) older adults, and (Aim 3) adults with stroke.

15.3 Describe the methods that you will use to identify potential subjects:

Individuals interested in the study who are not on the registry will notify the study team either via email or verbally. Individuals on a registry will be contacted given that their inclusion on the registry indicates a potential interest in being involved and willingness to be contacted. A study team member will contact the individual via phone to provide details regarding the study. If the individual indicates an interest to participate in the study, the individual will be screened. If the individual meets the inclusion/exclusion criteria, the individual will be invited to participate.

15.4 Describe materials that you will use to recruit subjects. Attach copies of these documents with this protocol in Protocol Management and be sure to include the IRB protocol number on each document.

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- *For flyers, attach the final copy of printed flyers.*
- *For Virginia Tech News, Facebook postings and ads, newspaper ads, websites, MTurk/SONA/online survey systems, etc., attach the final wording and graphics to be used.*
- *For email recruitments, please include the subject line.*
- *For advertisements meant for audio broadcast, please submit the wording of the advertisement prior to taping (to avoid having to re-record with approved language) and submit the final recorded version for IRB review before use.*
- *Describe any compensation to subjects. Separate compensation into appropriate categories, such as: reimbursement for expenses, time and effort, and additional incentives for study participation. For each category, specify the amount (including any pro-rated amount), schedule, and method of payment.*

Please see the included recruitment flyer.

We include a budget of up to \$20/hr for remuneration for up to 6-hour sessions. For transportation times exceeding 1 hr, we will pay participants \$20/hr of travel time. For participants needing transportation services, funding is possibly available via public/private services (e.g., Lyft, Uber). This decision will be based on recruitment needs for the targeted population (e.g., inability to recruit enough participants).

Payments will be made via ClinCard at the completion/termination of each experimental session. Funds will be loaded onto the card immediately after participants have completed research related activities or the research has been terminated. The funds should be available for use within 24 hours.

16.0 Withdrawal of Subjects

16.1 Describe circumstances under which you anticipate subjects could be withdrawn from the research without their consent:

The person in charge of the research study can remove a participant from the research study for reasons including inability to complete experimental tasks, chronic tardiness or absenteeism, or lack of cooperation with research staff.

16.2 If applicable, describe any procedures for orderly termination (e.g., discontinuation of a study drug or debriefing after a behavioral intervention):

N/A

16.3 Describe procedures that you will follow when subjects withdraw from the research, including partial withdrawal from procedures with continued data collection (e.g., participant declines to continue with regular blood draws, but continues with periodic behavioral questionnaires):

Participants are free to withdraw from the study at any time without penalty. Any collected data will be included in the study unless the participant revokes authorization in writing.

17.0 Risks to Subjects

17.1 List the reasonably foreseeable risks, discomforts, hazards, or inconveniences to the subjects related the subjects' participation in the research. Include for the IRB's consideration a description of the probability, magnitude, duration, and reversibility of the risks. Consider physical, psychological, social, legal, privacy, and economic risks. Do not indicate "No risk" or "N/A." Instead, for studies with very low risk (e.g., anonymous online questionnaire on a mundane topic) indicate "The investigators are not aware of any risks from participation in this study." or "No more than risks than are found in everyday life." The example consent form presents a tabular method for risk information, which you can also use here. Common risk types include:

- *Physical (e.g., potential for pain, discomfort, infection)*
- *Psychological (e.g., potential for stress, discomfort, and/or embarrassment)*
- *Social (e.g., potential for discrimination or stigmatization and disruption of personal and family relationships)*
- *Legal (e.g., potential for disclosure of illegal activity, negligence)*
- *Privacy (e.g., potential for personal information being accessed, used, or disclosed without the subjects' knowledge or consent, breach of confidentiality/security)*
- *Economic (e.g., potential for individuals to lose access to economic services, employment, insurability)*

We identify possible physical, psychological, community, and privacy risks. All risk is minimal and is comparable to routine medical or rehabilitation assessments and interventions, such as low-grade physical activity, application of surface electrodes, and sensory level electrical stimulation. Risks are explained in greater detail below:

Physical Risks from Participation.

Stimulator device: The device interacting with the participant's skin to provide touch-related cues may produce minor and temporary skin irritation.

Ultrasound and Surface electrodes: The self-adhesive surface electrodes may produce temporary minor irritation of the skin; there is also the possibility of a minor dermatological allergic reaction to the electrode adhesive.

Reaching movements: Repeated activation of upper extremity muscles may cause minimal temporary discomfort in the arm by the end of the study session. This discomfort is comparable to what might be experienced during a common resistance training exercise.

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Community Risk from Participation.

Participating in this investigation may exclude the participant from participating in other investigations for which the participant is recruited, or those in which the participant is currently participating.

Privacy Risks from Participation.

This study involves the use of identifiable, personal information, and there is a chance that a loss of confidentiality could occur.

We do not anticipate this study to have any increased risk related to legal, economic, or social considerations.

17.2 Indicate the measures you will use to minimize risks and monitor subjects for safety. (e.g., asking a subject at regular intervals to rate how they are feeling from 1 to 10, or to slowly crouch in order to check their balance.)

The methods to minimize the risks mentioned above is explained below:

Physical Risks from Participation.

Stimulator device: Minor and temporary skin irritation will be minimized by frequent questioning from the researchers and by reducing the magnitude of stimulation and/or ending the stimulation task based on the participant's responses.

Surface electrodes: The possibility of irritation will be minimized by cleaning the skin with alcohol before and after the application of the electrodes, pre and post skin assessment, removal of excessive hair, avoiding application over broken skin, and inquiring if a participant has ever had an adverse reaction to surface electrodes.

Reaching movements: All participants will be informed that the expected discomfort is comparable to low intensity exercise and will be instructed to report discomfort that is not expected given this low level of exercise and movement. The potential discomfort may be addressed by providing rest breaks, decreasing the magnitude of upper extremity movements, and stretching or massaging the participant's arm prior to and following the experiment.

Privacy Risks from Participation.

The researchers have procedures in place to lessen the possibility of loss of confidentiality happening.

17.3 If applicable, indicate which procedures might have risks to the subjects that are currently unforeseeable. This will be rare, and usually applicable

when testing a new drug or device or a new use of an existing drug or device:

N/A

17.4 If applicable, indicate which procedures might have risks to an embryo or fetus should the subject be or become pregnant:

N/A

17.5 If applicable, describe risks to others who are not subjects (e.g., collection of sensitive health data that might affect sexual partners if disclosed, mandatory reporting of abuse, DNA testing that might affect family members or relationships):

N/A

18.0 Potential Benefits to Subjects

18.1 Describe the potential benefits that individual subjects might experience from participating in the research. Include the probability, magnitude, and duration of the potential benefits, as this will be useful to the IRB's risk:benefit analysis. Do not include benefits to society or others. Do not list monetary or non-monetary compensation for participation, as this is not a benefit. These should be included in section 2 or 3 of this document:

There will not be any direct benefits to study participants if they decide to participate in this research project.

18.2 If applicable, specify that there are no anticipated direct benefits for participants:

There will not be any direct benefits to study participants if they decide to participate in this research project.

19.0 Data Management and Confidentiality

19.1 Describe procedures that you will use for quality control to ensure validity of collected data:

Study investigators will review the study protocol prior to initiation of enrollment. All study investigators will be trained in the maintenance of security and confidentiality of research data.

Overall trial monitoring will be the responsibility of the PI. The PI will monitor the overall conduct of the study (including issues with safety, ethics, patient recruitment and accrual, retention, adequacy of the study design to achieve the specific aims) and will provide to the study team possible protocol amendments. The study team members will generate data monitoring reports to share with the PI.

Research data will be monitored for completeness at the end of each session. The data will be analyzed after each session to ensure that the data are complete and valid. Data quality issues, if any, will be discussed with the PI, and recommendations will

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be made for an immediate solution. All outcomes will be reported to the PI. Direct remediation such as re-training or re-certification of study personnel will be managed by the PI.

19.2 Describe any existing data or biospecimens you will obtain as part of this study. Include:

- *Variables or samples to be obtained*
- *Source of the data or specimens*
- *Your authorization to access or receive the data or biospecimens*
- *Whether the data or biospecimens are publicly available*
- *Whether the data or specimens you receive will contain identifiers*

N/A

19.3 Describe the steps that you will take to handle and secure study data during data collection, storage, use, and transmission. Include information about training of study staff, authorization of access, password protection, encryption, physical controls, certificates of confidentiality, separation of identifiers and data, etc.:

REDCap or an electronic database will be utilized for obtaining participant-related data including demographic information, clinical assessment scores, and perceptual measurements. The raw, unprocessed, and deidentifiable data collected throughout the experiment will be initially obtained and organized on lab computers. The data will be transferred to encrypted and password-protected university hard drives, as well as SharePoint. The data will be analyzed from the hard drives. Study team members will be trained on these procedures prior to initiating data collection. The PI will provide authorization to access the identifiable data (including information from the registry) only to the study team members involved with analyzing the data in the study, and this data will be stored within SharePoint. The linkage between the alphanumeric code and participant identifiers will only be included with the consent forms and, for participants with stroke, their medical records.

19.4 For multi-site studies, describe how data or specimens will be handled and secured for each site (e.g., central or disseminated data storage, data coordinating center):

N/A

19.5 Describe the plan for data disposition following the conclusion of the study (e.g., long term maintenance of data, data destruction methods).

- *What information will be included in the long term storage of data or specimens?*
- *How long will the data or specimens be stored?*
- *Where and how data or specimens will be stored?*
- *Who will have access to the data or specimens during long term storage?*

- *Who is responsible for receipt or transmission of the data or specimens?*
- *How will data or specimens be shared or transported?*
- *When and how will personal identifiers be destroyed?*

All data will be stored for at least 5 years following the closure of the study. The data will be stored on encrypted and password-protected hard drives and SharePoint, and potentially also REDCap. Only study team members approved by the PI will be able to access the identifiable data. The PI will be responsible for maintaining and destroying the data. All digital files, including linkages between the alphanumeric code and identifiers, will be deleted from the hard drives and SharePoint, and if relevant, REDCap, no sooner than 5 years after closure of the study.

20.0 Provisions to Protect the Privacy Interests of Subjects

20.1 Describe the steps that you will take to protect subjects' privacy interests.

"Privacy interest" refers to a person's desire to place limits on with whom they interact or to whom they provide personal information (e.g., collecting the minimal amount of private information required to complete the study, protecting the data once it is obtained):

Data will be deidentified (represented by alphanumeric code) and stored in encrypted and password-protected hard drives and SharePoint, and possibly REDCap. Only study team members approved by the PI will be permitted to access the identifiable data. Data will only be used for research purposes. The only people present during the testing sessions will be the participant and the study investigators to protect the participant's privacy.

20.2 Describe steps that you will take to make subjects feel at ease with the research situation in terms of the questions being asked and the procedures being performed. "At ease" does not refer to physical discomfort, but the sense of intrusiveness a subject might experience in response to questions, examinations, and procedures (e.g., use of a same gender investigator to place sensors on the torso, a private changing area if clothing must be changed, sensitivity when discussing pregnancy testing with subjects, making it clear on surveys that participants can discontinue at any time, not asking questions about private or sensitive issues unless necessary for the research):

Participants will be informed that they can withdraw from the study at any point if they feel uncomfortable. Participants will be provided with ample time to ask and receive answers to any questions. Furthermore, the testing procedures are non-invasive, and the protocol will be conducted slowly to promote the participant's comfort.

20.3 Describe how you plan to access existing sources of information about the subjects (e.g., medical records, grades) and how you will protect participant privacy through the data security plan:

We will require medical records to determine if participants with stroke meet the inclusion criteria for the study. These medical records will be requested, with permission from the participants with stroke, from the location(s) where the participants were treated for their stroke. The medical records release request form will be submitted by a study team member who is approved to work with the identifiable data.

20.4 Describe any required reporting that might occur as a result of your research questions, study populations, and data collection methods. Examples for Virginia and Virginia Tech include:

- **Any** suspicions (e.g., circumstantial, disclosed) of child abuse (physical, emotional, sexual) and neglect
- Sexual discrimination and/or sexual violence that involves a student
- Disclosure or signs of intention to harm oneself (i.e., suicidal ideation and/or plan)
- Disclosure or signs of desire to harm others (i.e., homicidal ideation and/or plan)
- Suspected abuse, neglect or exploitation of vulnerable adults (e.g., individuals with a disability, elderly persons)

While these are unlikely to become apparent during the short testing visit(s), these incidents will be taken seriously and reported as appropriate to the situation.

21.0 Provisions to Monitor the Data to Ensure the Safety of Subjects

Safety monitoring is required when research involves greater than minimal risk and is sometimes appropriate for other studies.

21.1 Describe:

- The plan to periodically evaluate the data collected regarding both harms and benefits to determine whether subjects remain safe (e.g., periodic reporting to the IRB, establishing a data monitoring committee, reporting data monitoring committee findings to the IRB and the sponsor).
- What data you will review, including safety data, unexpected events, and data that show the ability to produce the intended results.
- How the safety information will be collected (e.g., with case report forms, at study visits, by telephone calls with subjects).
- The frequency of data collection, including when safety data collection starts.
- Who will review the safety data and with what frequency.
- The statistical tests for analyzing the safety data to determine whether harm is occurring.
- Any conditions that will trigger an immediate suspension of the research (e.g., a serious adverse event).

Data safety and monitoring will be overseen by the PI. The PI will monitor the overall conduct of the study (including issues with safety, ethics, patient recruitment and accrual, retention, and adequacy of the study design to achieve the specific aims) and will provide possible protocol amendments to the study team. To ensure proper involvement, all study investigators will review the study protocol and be trained in using the research data securely and confidentially. Any protocol violations will be handled by the PI, including re-training or re-certification of study team members.

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Research data will be monitored and analyzed for completeness and validity at the end of each data collection session by the relevant study team member. The study team member will discuss the data in person with the PI within one week of data collection and share a summarizing report quarterly. The quarterly reports will include summaries of data quality, recruitment metrics, and outstanding queries to be shared with all relevant study team members. Data quality issues, if any, will be shared with the PI at the time of an event, and recommendations will be made for an immediate solution. Direct remediation, such as re-training or re-certification of study team members, will be managed by the PI.

To protect against risks to confidentiality, collected data will be immediately coded using an alphanumeric identifier in lieu of the participant's name for internal data analysis purposes. Any data publicly shared will be sufficiently deidentified to minimize risks to participant confidentiality. The data appearing in publication and other external presentations will be coded. The raw, unprocessed data will be organized using the alphanumeric identifiers.

The risks associated with this research are minimal, and the research team will ensure that this risk is kept minimal throughout. Any adverse events will be immediately reported to the PI and addressed to ensure the safety of future participants. All reportable new information (safety data) will be reported to the IRB by the PI within 5 days of its collection. After review and follow-up with relevant study investigators, the study team member will generate an IRB report and queue for review and submission by the PI within the 5-day period. Reportable new information includes, but is not restricted to, new or increased risk, adverse events, serious adverse events, non-compliance with IRB policy, researcher error/protocol violation, and unresolved participant complaint.

No interim analysis will be conducted on the data. Minimal adverse events are expected and no a priori stopping rules will be assigned.

Incidental findings arising for reasons including the screening, clinical assessments, and neuroimaging will be shared with participants so that these findings can be discussed with their medical providers.

22.0 Compensation for Research Related Injury

22.1 If the research involves more than minimal risk to subjects, describe the available compensation in the event of research-related injury, if any:

This research does not involve more than minimal risk.

22.2 Provide a copy of contract language, if any, relevant to compensation for research-related injury. At Virginia Tech, this is most common for sponsored research:

Any expenses for seeking or receiving medical treatment will be billed to the participant and will not be the responsibility of the research project, research team, or Virginia Tech.

23.0 Economic Burden to Subjects

23.1 Describe any costs that subjects might be responsible for because of participation in the research, including any uncompensated costs for items such as transportation, missed work, and childcare:

There are no direct costs for participating in this study. Any costs associated with travel, missed work, or childcare beyond those offered in this study will be the responsibility of the participant.

24.0 Consent Process

24.1 Indicate the process by which you will obtain consent for study participation. Please upload all consent, parental permission, and assent forms, documents, and scripts referenced in this section to Protocol Management.

Describe the following:

- *Where the consent process will take place (e.g., clinic waiting area, classroom, online)*
- *The time interval between sharing the consent information with the prospective subject and obtaining consent. For lab, interview, and focus group studies, the Virginia Tech IRB prefers that subjects have at least 24 hours to review the consent form and study information before the appointment where consent will be obtained. For simple online survey studies, you can typically present the consent information immediately before subjects begin participation.*
- *If applicable, processes to ensure ongoing consent or assent (e.g., for multiple sessions; for research in which a minor will turn 18 during the study; for longitudinal research with minors who will later be asked to provide or affirm their assent).*
- *Please review “SOP: Informed Consent Process for Research (HRP-090)” for recommended procedure. Describe your process, being sure to include:*
 - *The name and role of all study personnel who will be trained and certified by the PI to conduct the consent process*
 - *The time that will be devoted to the consent discussion*
 - *Steps that you will take to minimize the possibility of coercion or undue influence*
 - *Steps that you will take to gauge or ensure the subjects’ understanding*

Informed consent will be obtained for all individuals enrolled in the study. During the initial phone call, the study procedure will be explained in detail and the potential participant will be given time to ask any questions. If the individual is interested in participating, a consent form will be sent to the participant at least 24 hours before the in-person session for them to review prior to their first scheduled data collection session. At the first session, prior to any data being collected, the study coordinator will obtain consent using the attached consent form. The consent process will take place in the testing area, and at least 15 minutes will be provided for the explanation of the study, answering of questions, and completion of consent documents. These processes will be

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completed by one of the PI-appointed study team members. Both the PI and relevant study team members will be available to answer any questions before, during, and after the consent process. Participants will be given the option of discussing participation with individuals outside of the study (family members, friends).

Individuals who have neurological impairments will be enrolled, but individuals who are unable to consent will not be enrolled. We will employ the help of a licensed clinical specialist to screen participants to determine whether an individual can give consent. Individuals without neurological damage will be screened during the initial screening process.

Participants will be notified that they can leave the study at any point. We will check in on user comfort throughout the experimental testing. If participants indicate discomfort, we will remind participants that they can terminate the study at any point.

Non-English Speaking Subjects

- *Indicate what language(s) other than English are understood by prospective subjects or representatives.*
- *If non-English speakers will be recruited, describe the process you will use to ensure that the oral and/or written consent information provided will be in a language that they understand.*
- *If you translate consent forms and study materials, please provide a certified translation of the form as well as the certification document.*
- *Indicate the spoken language that study personnel obtaining consent will use. Describe how you will assess fluency of personnel obtaining consent to ensure that the translation is accurate.*

Only English speakers will be recruited.

Waiver or Alteration of Consent Process (consent will not be obtained, required information will not be disclosed, or the research involves deception)

- *Review the “CHECKLIST: Waiver or Alteration of Consent Process (HRP-410)” to ensure you have provided sufficient information for the IRB to make these determinations (i.e., that it meets the criteria for a waiver or alteration of the consent process).*

N/A

Subjects who are not yet adults (minors: infants, children, teenagers)

- *Describe the criteria that you will use to determine legal age for consent to treatments or procedures involved in the research under the applicable law of the jurisdiction in which the research will be conducted (e.g., in Virginia, individuals under the age of 18 years).*
 - *For research conducted in Virginia, review “SOP: Legally Authorized Representatives, Minors, and Guardians (HRP-*

- 013)” to determine which individuals in the state meet the definition of “minor.”*
 - *For research conducted outside of the state, please describe the legal requirements for the definition of “minor.”*
- *Describe the process for obtaining parental permission.*
 - *Permission from one parent is acceptable for studies that involve no greater than minimal risk OR involve greater than minimal risk but present the prospect of direct benefit to the minor subject.*
 - *Permission from both parents is required in all other cases (unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the minor).*
- *Describe whether you will obtain permission from individuals other than parents or Legally Authorized Representatives, and if so, who will be allowed to provide permission. Describe the process you will use to determine these individuals’ authority to consent to the minor’s general medical care.*
- *Indicate whether you will obtain assent from all, some, or none of the minors. If you will obtain assent from some minors, indicate which minors will be required to assent. Consider chronological age and intellectual capacity when determining who will be required to provide assent (e.g., infants are unable to assent. However, teenagers are likely able to read and sign an assent form).*
- *When assent of minors is obtained, describe whether and how you will document it. Will minors sign an assent form or give verbal assent?*
- *Attach parental permission and minor assent forms or scripts in Protocol Management.*

N/A

Adults Unable to Consent

- *Describe the process you will use to determine whether an individual adult is capable of consent.*
- *List the individuals from whom you will obtain permission in order of priority (e.g., durable power of attorney for health care, court appointed guardian for health care decisions, spouse, and non-minor child).*
 - *For research conducted in the Virginia, review “SOP: Legally Authorized Representatives, Minors, and Guardians (HRP-013)” to determine which individuals in the state meet the definition of “legally authorized representative.”*
 - *For research conducted outside of Virginia, please describe the legal requirements for obtaining permission from a legally authorized representative in the state where the research will occur.*

- *Describe the process for assent of the subjects.*
 - *Indicate whether you will require assent from all, some, or none of the subjects. If some, indicate which subjects will be required to assent and which will not.*
 - *If you will not obtain assent from some or all subjects, please provide justification for not obtaining assent.*
 - *Describe whether and how you will document assent.*

N/A

25.0 Process to Document Consent in Writing

25.1 Consult “SOP: Written Documentation of Consent (HRP-091)” for recommended procedures, and describe whether and how consent of the subject will be documented in writing:

Consent will be provided by the participant and a copy of the signed consent document will be provided to each participant. All consent will be documented in REDCap.

25.2 If the research presents no more than minimal risk of harm to subjects and involves no procedures for which written documentation of consent is normally required outside of the research context, you can request that the IRB waive the requirement to obtain written documentation of consent (e.g., consent to participate is indicated by pressing a button for an online questionnaire – after the consent information is presented and before the questionnaire begins):

N/A

25.3 If you will document consent in writing, attach a consent document with places for signatures. If you will obtain consent, but not document consent in writing, please attach the consent script or text. Review “CHECKLIST: Waiver of Written Documentation of Consent (HRP-411)” to ensure that you have provided sufficient information. You should use “TEMPLATE CONSENT DOCUMENT (HRP-502)” to create the consent document or script:

The consent document is uploaded.

26.0 Resources Available

26.1 Describe the resources available to conduct the research. For example, as appropriate:

- *Describe the PI’s availability to supervise the research.*
- *Justify the feasibility of recruiting the required number of suitable subjects within the agreed recruitment period. For example, how many potential subjects do you have access to? What percentage of those potential subjects do you need to recruit?*
- *Describe the time that you will devote to conducting and completing the research.*

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- *Describe your facilities.*
- *Describe the availability of medical or psychological resources that subjects might need as a result of an anticipated or unanticipated consequence of participation in the research.*
- *Describe your process to ensure that all persons assisting with the research are adequately informed about the protocol, the research procedures, and their duties and functions (e.g., training plans, detailed study notebooks).*

The PI is available on a regular basis to meet with the study team members to advance this research. One graduate student is dedicated to this research full time and is supported by a research therapist. All relevant study team members will be sufficiently trained by the PI prior to initiating data collection.

We do not anticipate challenges in recruiting the estimated sample size of (Aim 1) 20 young adults, (Aim 2) 20 older adults, and (Aim 3) 13 participants with stroke and 13 controls. The timeline permits up to 1.5 years to collect the data for each aim, which we expect to be more than sufficient for the relatively small sample size of each study.

Dr. Gurari (PI) directs the Robotics and Sensorimotor Control Laboratory, an approximately 700 sq ft laboratory that is located in Norris Hall and is populated with custom and commercial mechatronic systems and physiological measurement systems. The Robotics and Sensorimotor Control Laboratory contains ~200 sq ft of office space for lab members (e.g., graduate students, undergraduate students, clinical research assistant, technical research assistant), in addition to two laboratory spaces.

Human subject testing will be conducted at Radford University in the Department of Physical Therapy under the guidance of the research therapist (Kevin Parcetic, PT/DPT/NCS). Testing will be conducted in a ~200 sq ft laboratory that includes treatment tables. Portable resources will be transported from the Robotics and Sensorimotor Control Laboratory in Blacksburg for use in the research space.

27.0 Multi-Site Research

Contact the HRPP for multi-site research (involving multiple institutions) and the details required for this section will be provided. Otherwise, indicate N/A.

N/A

Appendix B

Informed Consent for Subjects

Consent to Take Part in a Research Study

Title of Research Study

Tactile Perception and Peripheral Tactile Signal Propagation in Young Adults, Older Adults, and Individuals with Stroke (IRB: #23-1246)

Principal Investigator

Netta Gurari, PhD

Email: gurari@vt.edu

Phone Number: [540-231-3073](tel:540-231-3073)

Key Information

The following is a short summary of this study to help you decide whether or not to be a part of this study. More detailed information is listed later on in this form.

Why am I being invited to take part in a research study?

We invite you to take part in a research study because you are older than 18 years of age and either i) do not have any musculoskeletal or neurological impairments or ii) have had a stroke.

What should I know about being in a research study?

- Someone will explain this research study to you
- Whether or not you take part is up to you
- You can choose not to take part
- You can agree to take part and later change your mind
- Your decision will not be held against you
- You can ask all the questions you want before you decide

Why is this research being done?

The overarching purpose of this research study is to study how touch-related perception occurs depending on the arm used, age, and incidence of stroke. While this area of research has been explored in the past, the role of the peripheral nervous system remains largely unexplored. Through our simplified approaches and advanced techniques, we aim to learn more about the reason that touch-related perceptual differences occur so that we can develop appropriate rehabilitation approaches for those in need.

How long will the research last and what will I need to do?

We expect that your participation in this research study will last 1-2 sessions, with each session occurring on a separate day. One session will span 2-6 hours. During each session, you will be involved in a behavioral assessment, peripheral nerve assessment, and/or clinical assessment.

You will be asked to participate in a behavioral assessment protocol in which we will apply a tactile stimulus and you will provide feedback on what is felt. You will also be involved in a protocol that applies a tactile stimulus and measures how the signal transmits along your arm. You may also be

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asked to participate in a clinical assessment protocol, which would include generating movements and indicating what is felt.

Behavioral Assessment Protocol: Participation in the behavioral assessment protocol will last up to 4 hours per session.

Peripheral Nerve Assessment Protocol: Participation in the peripheral nerve assessment protocol will last up to 2 hours per session.

Clinical Assessment Protocol: Participation in the clinical assessment protocol will span approximately 2 hours.

More detailed information about the study procedures can be found under, **“What happens if I say yes, I want to be in this research?”**

Is there any way being in this study could be bad for me?

There are no major risks to those who participate in this study. This study involves potential minor risks, including skin irritation due to the electrodes attached to your skin. There is also a minimal risk to your confidentiality. We will minimize these risks to the best of our ability.

More detailed information about the risks of this study can be found under **“Is there any way being in this study could be bad for me? (Detailed Risks)”**.

Will being in this study help me in any way?

We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits include an enhanced understanding of movement disturbances following stroke, which could lead to improved treatment.

What happens if I do not want to be in this research?

Participation in research is completely up to you. You can decide to participate or not to participate. If you choose to not participate, there will be no penalty to you or loss of benefit to which you are entitled.

If you are a student, the decision whether to participate or not participate will have no effect on your grades or relationship with Virginia Tech.

Detailed Information

The following is more detailed information about this study in addition to the information listed above.

Who can I talk to?

If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team at 540-231-7482 (Study Team Member) or 540-231-3073 (Dr. Netta Gurari, Principal Investigator).

This research has been reviewed and approved by the Virginia Tech Institutional Review Board (IRB). You may communicate with them at 540-231-3732 or irb@vt.edu if:

- You have questions about your rights as a research subject

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- Your questions, concerns, or complaints are not being answered by the research team
- You cannot reach the research team
- You want to talk to someone besides the research team to provide feedback about this research

How many people will be studied?

We plan to include about 66 people in this research study.

What happens if I say, yes, I want to be in this research?

Participation in the study will last 1-2 sessions, with a duration of up to six hours per session. You will be asked to come to the Radford University Department of Physical Therapy at 101 Elm Avenue, Suite 8A, Roanoke, VA 24013.

During the experiment, you will be at rest in an experimental chair or treatment table. Tactile stimulators and surface electrodes will be placed on your arm to create physical experiences and measure nerve and muscle responses. You will receive physical stimulation (e.g., mechanical, electrical) that produces a sensation that can range from not noticeable to a buzzing or pressing feeling. Simultaneously, you may receive visual and/or auditory cues regarding the experimental procedures. You may wear headphones to mask sounds in the room and/or to hear sounds/words being played. Non-touch related information about your hand may be limited (e.g., you may wear a sleep eye mask so that you will not be able to see what is happening). You may be asked to respond with how you perceive the applied physical stimulus. Ultrasound may be used to measure nerve integrity. Testing will be conducted at both your arms to draw conclusions regarding how tactile perception occurs.

During the clinical assessment protocol, we will gain insight regarding relevant tasks such as your movement, perception, cognition, and memory via clinical assessments such as the Upper-Extremity Fugl-Meyer Motor Assessment, revised Nottingham Sensory Assessment, and Montreal Cognitive Assessment. During these clinical assessments, you will interact with an assessor through tasks such as moving your limbs and responding to questions.

What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible to attend all experimental sessions and follow-ups, and/or to promptly notify the investigative team if you are unable to make an appointment.

What happens if I say yes, but I change my mind later?

You can leave the research at any time, for any reason, and it will not be held against you.

If you decide to leave the research, contact the investigator so that the investigator can plan accordingly. If you stop being in the research study, we will use the data we have collected up to that point, unless you state that you do not want your data to remain in the study.

Is there any way being in this study could be bad for me? (Detailed risks)

Physical Risks from Participation

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Stimulator device: The device interacting with your skin to provide touch-related cues may produce minor irritation of the skin. The possibility of irritation will be minimized by reducing the magnitude of stimulation and/or ending the stimulation task.

Ultrasound and Surface electrodes: The ultrasound and self-adhesive surface electrodes may produce minor irritation of the skin; there is also the possibility of an allergic reaction to the electrode paste. The possibility of irritation will be minimized by cleaning the skin with alcohol before and after the application of the electrodes.

Reaching movements: Repeated activation of your muscles may cause minimal temporary discomfort in your arm by the end of the study session. This potential discomfort may be addressed by stretching or massaging your arm prior to and following the experiment.

Community Risk from Participation

Participating in this investigation may exclude you from participating in other investigations for which you are recruited, or those in which you are currently participating.

Privacy Risks from Participation

This study involves the use of your identifiable, personal information and there is a chance that a loss of confidentiality could occur. The researchers have procedures in place to lessen the possibility of this happening. See the section below titled: “What happens to the information collected for the research?”.

What do I need to know about reproductive health and/or sexual activity if I am in this study?

If you are or become pregnant, you are no longer eligible to participate in the study. If already consented, please notify the experimenter of your pregnancy and you will be required to stop participation in this study.

What happens to the information collected for the research?

We will make every effort to limit the use and disclosure of your personal information, including research study and medical records, only to people who have a need to review this information. We cannot promise complete confidentiality. Organizations that may inspect and copy your information include the IRB, Human Research Protection Program, and other authorized representatives of Virginia Tech.

The sponsor, monitors, auditors, Virginia Tech Institutional Review Board Office (IRB), Virginia Tech Office of Research and Innovation, US Office of Research Integrity (ORI), US Office for the Protection of Human Research Protections (OHRP), and US Food and Drug Administration (FDA) may be granted direct access to your medical records to conduct and oversee the research. By signing this document, you are authorizing this access. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

All study investigators are trained in the maintenance of security and confidentiality of research data. The raw/unprocessed data will be coded with a unique participant identifier and stored offline on encrypted and password-protected university hard drives and SharePoint.

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If identifiers are removed from your private information or samples that are collected during this research, that information or those samples could be used for future research studies or distributed to another investigator for future research studies without your additional informed consent.

The results of this research study may be presented in summary form at conferences, in presentation, reports, academic papers, and as part of a thesis/dissertation.

If identifiers are removed from your private information or samples that are collected during this research, that information or those samples could be used for future research studies or distributed to another investigator for future research studies without your additional informed consent.

Can I be removed from the research without my OK?

The person in charge of the research study or the sponsor can remove you from the research study without your approval. Possible reasons for removal include inability to complete testing, equipment failure, and not showing up on time for study visits.

What else do I need to know?

This research is being funded by an ICTAS JFP award and lab start-up funds.

If you agree to take part in this research study, you will receive \$20/hour for up to a 6-hour session, with the amount predetermined based on a conservative estimate of the experiment duration. Costs to cover transportation are available and should be discussed and agreed upon prior to involvement in the research. Payments will be made via ClinCard at the completion or termination of each day of testing. The money should be available for use within 24 hours of completion of the testing session. If any questions or concerns arise, please contact a Study Team Member (540-231-7482) or the Principal Investigator (540-231-3073; Dr. Netta Gurari).

Your information and samples (both identifiable and de-identified) might be used to create products or to deliver services, including some that may be sold and/or make money for others. If this happens, there are no plans to tell you, or to pay you, or to give any compensation to you or your family.

We will not offer to share your individual test results with you.

We are committed to respecting your privacy and to keeping your personal information confidential. When choosing to take part in this study, you are giving us the permission to use your personal health information that includes health information in your medical records and information that can identify you. For example, personal health information may include your name, address, and phone number.

Your health information we may collect and use for this research includes:

- Medical history
- Information from a physical examination including upper extremity range of motion, strength, sensory capabilities, and/or functional movement
- Measurement of muscle activity in your upper extremity with non-invasive surface electromyographic electrodes.

The results of this study may also be used for teaching, publications, or for presentation at scientific meetings.

Unless you revoke your consent, it will expire at the end of the research study.

VIRGINIA POLYTECHNIC INSTITUTE AND STATE UNIVERSITY

Consent to Take Part in a Research Study

Although you may revoke consent to participation in this research at any time and in any format, you must revoke authorization for use of your data in writing. To revoke your authorization, write to:

Principal Investigator: Netta Gurari
Institution: Virginia Tech
Department: Biomedical Engineering and Mechanics
Email: gurari@vt.edu
Address: Norris Hall, Room 224, 495 Old Turner Street, Blacksburg, VA 24061

You do not have to authorize the use or disclosure of your information; however, you will not be allowed to take part in this research study. If you do not authorize the use or disclosure of your information, it will not affect your treatment by health care providers, payment or enrollment in any health plans, or your eligibility for benefits.

Optional Elements

The following research activities are optional, meaning that you do not have to agree to them to participate in the research study. Please indicate your willingness to participate in these optional activities by placing your initials next to each activity.

I agree

☐	The researcher may add me to a registry to contact me in the future to see whether I am interested in participating in other research studies by the Principal Investigator of this study.
☐	The researcher may add me to the Virginia Tech Older Adult Research Registry, and I am at least 55 years of age.
☐	The researcher may add me to the Southwest Virginia Stroke Registry.

Signature Block for Capable Adult

Your signature documents your permission to take part in this research. We will provide you with a signed copy of this form for your records.

Signature of subject

Date

Printed name of subject

Signature of person obtaining consent

Date

Printed name of person obtaining consent