DISTRIBUTED TRANSCUTANEOUS ELECTRICAL STIMULATION - NOVEL METHOD FOR INDUCING PROPRIOCEPTIVE ILLUSIONS

A Thesis

by

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ABSTRACT

Proprioceptive feedback plays a crucial role in motor control, especially in absence of visual feedback and/or tactile feedback. Unfortunately, many people suffer from lack of proprioception by physical injuries or neurodegenerative diseases. Prosthetic limb and telerobotic users also experience proprioceptive mismatch, which limits the control accuracy and intuitiveness. To address the proprioceptive deficit, several invasive and non-invasive approaches have been introduced, via vibration, invasive electrical stimulation, and skin stretch. However, compensating proprioceptive deficit is still challenging as the current solutions have limitations in terms of effectiveness, usability, and consistency.

In this study, we proposed a new way of proprioceptive modulation using transcutaneous electrical stimulation. We hypothesis that transcutaneous electrical stimulation on elbow flexor muscles will augment the spindle afferent and induce illusion of elbow joint extension. Eight human subjects participated in the study to test the hypothesis. We first identified the best location of electrodes to induce the proprioceptive illusions of elbow joint angle, as one electrode on the belly of biceps brachii short head and another on the distal tendon of brachioradialis. Based on the results of two arm matching test and Pinocchio illusion test, we found that 6 of 8 subjects experienced illusion of elbow joint extension by transcutaneous electrical stimulation, which supports our hypothesis. On average, they reported 7.1° angular illusion of elbow joint extension and 1.5x increase of nose height at Pinocchio illusion test. However, 2 of 8 subjects reported illusion of elbow

joint flexion by the same transcutaneous electrical stimulation, which falsifies our hypothesis. We interpret this contradictory result as, transcutaneous electrical stimulation can either augment or interfere (i.e., add noise) muscle spindle afferent signal. Note that, the direction of proprioceptive illusion was consistent per subject, and the effect of proprioceptive illusion was clear for all subjects. This result suggests that, transcutaneous electrical stimulation may shed a light to address limitations of current approaches of providing proprioceptive information, by improving effectiveness, usability, and consistency.

DEDICATION

To my parents.

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CONTRIBUTORS AND FUNDING SOURCES

Contributors

This work was supervised by a thesis committee consisting of Dr. Hangue Park, Dr. Steven M. Wright and Dr. Paul Gratz of the Department of Electrical and Computer Engineering and Dr. John Buchanan of the Department of Health and Kinesiology. I have received continuous feedback from Dr. Hangue Park which has helped me improve and strategize my work throughout this research.

All other work conducted for the thesis was completed by the student independently.

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NOMENCLATURE

TIME	Transverse Intrafascicular Multichannel Electrode
FINE	Flat Interface Nerve Electrode
TENS	Transcutaneous Electrical Nerve Stimulation
FES	Functional Electrical Stimulation
EMG	Electromyography
AMI	Agonist-antagonist myoneural interface
BiM	Biceps short head Muscle belly
BiT	Biceps Tendon
BrM	Brachioradialis Muscle belly
BrT	Brachioradialis Tendon

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1. INTRODUCTION AND LITERATURE REVIEW

1.1. What is proprioception?

Proprioception is a perception or awareness of position or movement of one's own body [1]. It includes both the sense of body position in space and the sense of force applied to each joint, as the somatosensory cortex processes a combination of evoked action potentials from sensory receptors in muscles, tendon, and skin [1-6]. Proprioception also includes dynamic perception of the body, i.e., sense of body movement, along with the stationary perception, and it is called as dynamic proprioception or kinesthesia [1,4]. Proprioception is deemed to be primarily mediated by muscle spindles(shown in Fig. 1.1) augmented by skin receptor [1]. Golgi tendon organs(shown in Fig. 1.2) are argued to mostly sense force and heaviness, while joint receptors play minimum roles at most joints [1].

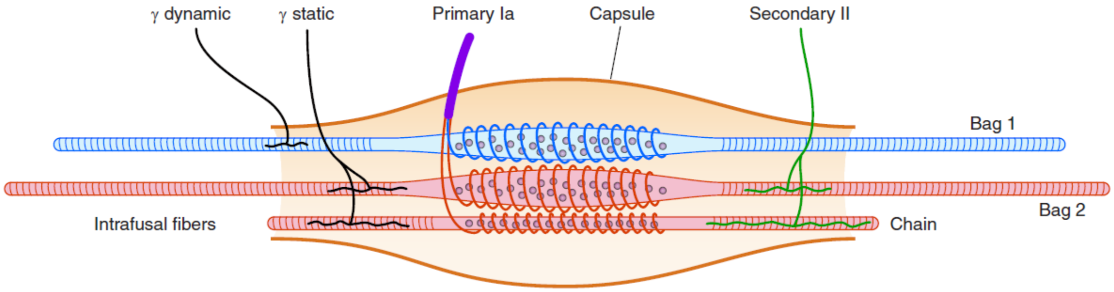
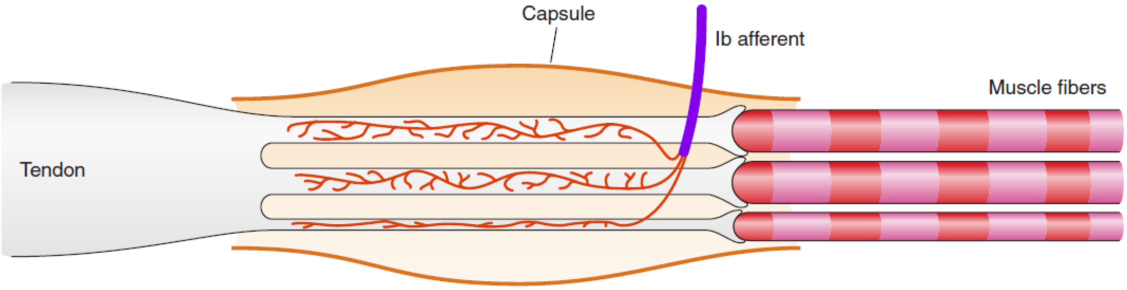


Figure 1.1 Illustrative representation of mammalian muscle spindle [Reprinted with permission from 1]



(b)

Figure 1.2 Illustrative representation of mammalian Golgi tendon organ [Reprinted with permission from 1]

1.2. Importance of Proprioception in daily life

Proprioception provides us sensory information necessary to complete motor tasks with minimal reliance on vision. For example, we can walk on the street or step on car pedals without looking at our legs and foots. Indeed, we rely on proprioception for most of our motor activities throughout the day without even acknowledging it. Assessment of proprioception is critical for clinical intervention and training required for musculoskeletal rehabilitation[7]. Loss of proprioception causes serious deficit in motor control, as can be seen in several human and animal experiments. Loss of proprioception in the arm muscles was shown to disrupt inter-joint coordination and degrade following control accuracy in arm reaching [8]. Another example showed that a local loss of proprioception in one of the leg muscles could induce the cats to select inefficient locomotor strategy [9].

1.3. Proprioception deficit and its effect

While the natural deficit of the proprioception is rare, proprioceptive deficit is often caused by several physical injuries and neurodegenerative diseases. Stroke and traumatic brain injury directly damage the somatosensory area of the cortex [10,11] , and spinal cord injury damages the communication pathway between central and peripheral nervous system. Parkinson's disease degrades proprioceptive-motor integration and multiple sclerosis degrades integrity and excitability of proprioceptive pathways in the brain, respectively [12,13] . As proprioception plays a crucial role in motor learning, the proprioceptive deficit is critical in the progression of rehabilitation, as shown in clinical studies with patients, post stroke [14]. The epidural stimulation studies with subjects after spinal cord injury also showed that proprioceptive deficit, following the epidural stimulation, limits the rehabilitative efficacy of the stimulation [15].

1.4. Proprioceptive deficit in neuroprosthetics and human robotic interfaces

Prosthetic and telerobotic limbs provide man-made situations of proprioceptive deficit. Currently available prosthetic limbs in the market do not provide proprioceptive feedback yet, although the active joints have become available a few years ago [16] . Even in the past research studies, scope of the artificial sensory feedback has been mostly limited to tactile feedback [17,18] , and artificial proprioceptive feedback is shown to be functional in very limited way [19,20]. In telerobotic applications, non-idealities in telerobotic control induce proprioceptive mismatch between master and slave. For example, limited resolution in fine motor control or control delay in controlling heavy telerobotic parts results in corresponding proprioceptive mismatch, which limits telerobotic control accuracy [6,21]. In absence of proprioceptive feedback, the control of prosthetic or telerobotic limb can hardly be accurate, especially for the fine and sophisticated motor tasks [22,23]. Although the prosthetic or telerobotic limb mimics the operator's limb in terms of outlook and operation, proprioception along with other sensory feedback is necessary to close the loop, enable the real-time error correction and make it intuitive.

1.5. Invasive approaches to address proprioceptive deficit

To address the proprioceptive deficit in the above applications, potential of neuromodulation has been actively investigated to modulate proprioception, in both invasive and non-invasive ways. Invasive methods like intraneural stimulation techniques using high-resolution electrodes such as transverse intrafascicular multichannel electrode (TIME), flat interface nerve electrode (FINE), and Utah microneedle electrodes [24-27] have shown high potential of invasive techniques in providing users with proprioceptive feedback from prosthetic limbs. However, the amount of proprioceptive modulation is hardly consistent over time and across subjects [27]. Also, the chronic usage of these invasive approaches needs to be further validated before clinical adaptation [28]. Further, the entry barrier for users, in accepting the surgical procedures and associated risks, makes these invasive approaches less attractive for non-desperate applications like rehabilitation, human-robot interfaces, etc.

1.6. Non-invasive approaches to address proprioceptive deficit

1.6.1. Muscle Vibration

Non-invasive methods using mechanical vibration have been actively investigated to modulate proprioception, and successfully generated proprioceptive illusion [1-4]. Vibration onto the tendon or myotendinous junction elicited illusions as extension of the associated muscle, as shown in Fig. 1.3 [28-30]. However, the vibration-induced illusions are still hard to be elicited in a consistent manner [29]. For example, the vibration-induced

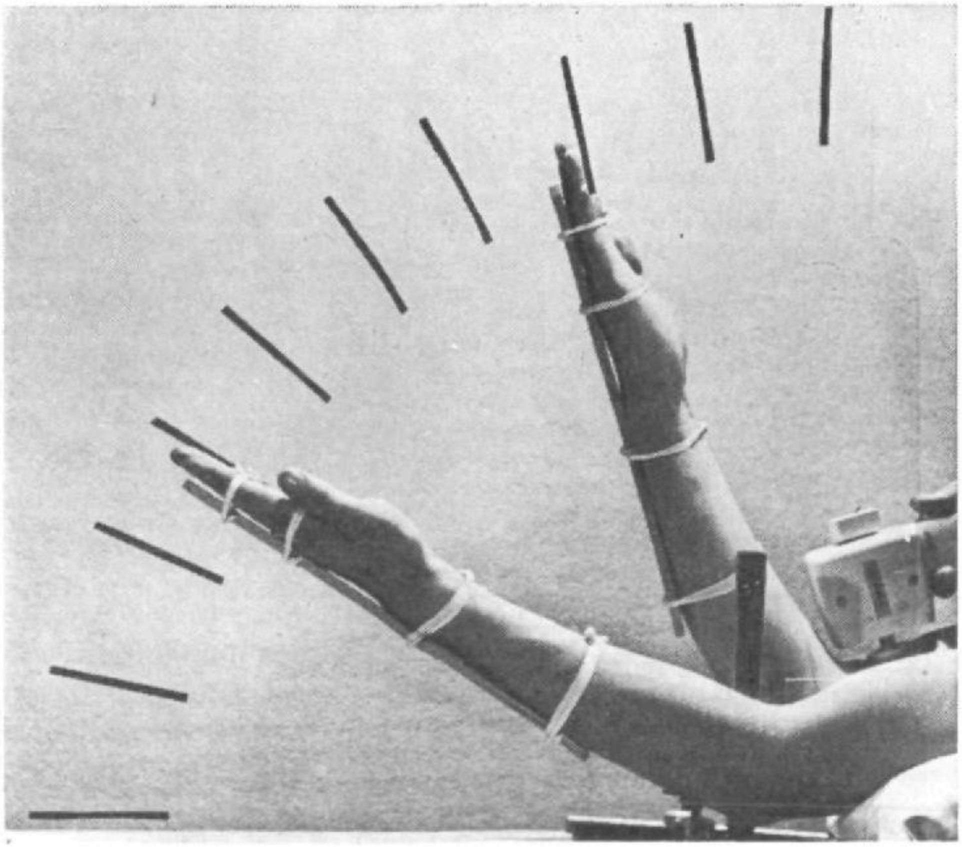


Figure 1.3 Illustration of vibration-induced movement illusion, difference between position of the vibrated arm and tracking arm used for matching by the subject. [Reprinted with permission from 30]

illusions are sensitive to the location of vibrators, quality of contact, and fatigue of target muscle [29], which are hardly consistent over time. The vibration-induced illusions are also sensitive to vibration parameters, and the direction of vibration-induced illusions sometimes can be even opposite [22,29]. It has been also reported that application of subthreshold vibrations with random frequencies augmented joint proprioception for both extension and flexion [31]. The neural adaptation in both skin receptors and nervous system further changes the vibration-induced illusions over time [31,32].

1.6.2. Skin Stretch

Skin stretch is another non-invasive approach of providing proprioceptive information. As the skin stretch is known as important contributing factor to the perception of joint extension/flexion, people have investigated its feasibility [33,34]. Skin stretch is a very straightforward approach and it can be also used together with other proprioceptive modulations as a compensatory approach. However, skin stretch system is hard to design, especially if wearable option is considered as shown in Fig. 1.2, because rotational skin-stretch device needs to be well attached onto the skin with proper friction [33].

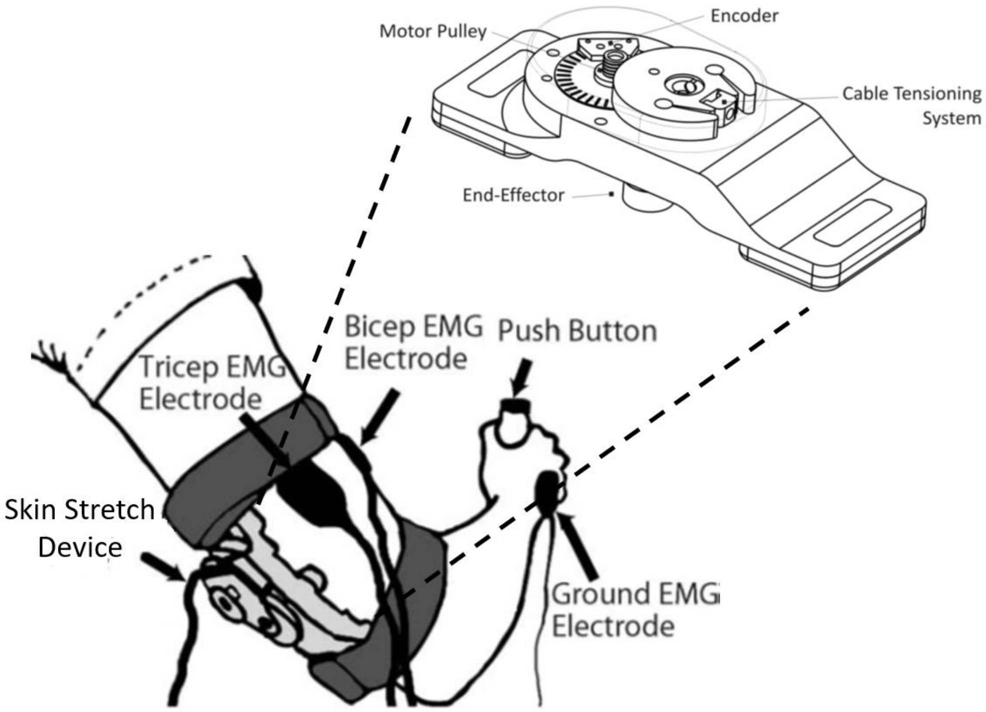


Figure 1.4 Wearable rotational skin stretch device with myoelectric system [Adapted and reprinted with permission from 33]

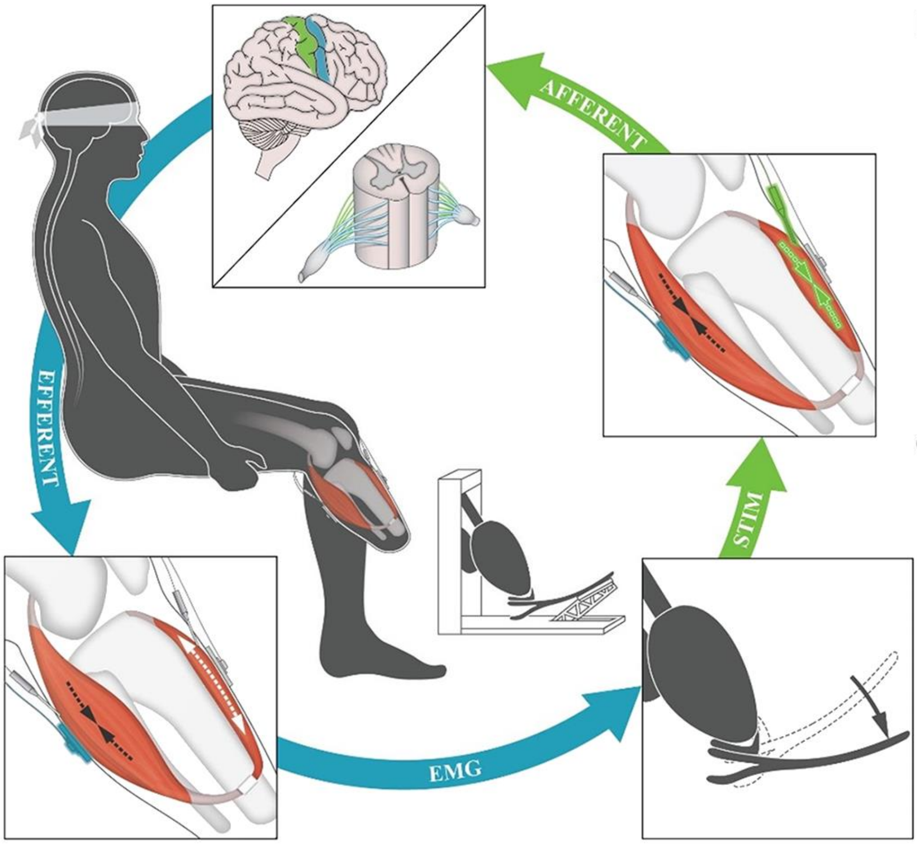


Figure 1.5 Agonist-antagonist myoneural interface(AMI). Patient receives the afferent feedback of prosthetic joint torque via functional electrical stimulation, FES of the antagonist muscle, and perceives it as a natural sensation of ankle torque. [Adapted and reprinted with permission from 36]

1.7. Compensatory approaches to address proprioceptive deficit

As providing proprioceptive information in an appropriate manner is hard, and inconsistent results were observed even with the complex invasive and mechanical preparations, multiple compensatory approaches have been investigated. Modulation of joint impedance is one of the most popular proprioceptive-modulation methods in these days, based on the assumption that the perception of joint impedance can intuitively change the mapping between the proprioception and the intrinsic kinematic variables [35,36]. The joint impedance could be modulated by either exoskeleton [35] or functional electrical stimulation and targeted muscle reinnervation like AMI [36]. Figure 1.3 shows AMI used to provide prosthetic joint torque information.

Tactile augmentation and proximity feedback are other candidates to compensate for the proprioceptive deficit [23,37]. As tactile feedback and proprioception usually work together as an ensemble, to deliver the static and dynamic information of the body parts, tactile augmentation or haptic feedback can help the nervous system to make a better decision under the lack of proprioception [37]. However, the efficacy of this ensemble drops significantly if the motor task does not involve any physical interaction with the object. Proximity feedback has been introduced recently to enjoy the power of tactile augmentation even without any touch [23], but the quality of information and intuitiveness are limited.

1.8. Our approach to address the current limitations

Transcutaneous electrical stimulation has been investigated to modulate and generate artificial sensory feedback. However, it is mostly targeted to provide tactile feedback because of the limited accessibility to the nerves from the skin. Transcutaneous electrical stimulation can easily stimulate the receptors on the skin or cutaneous nerves located near to the skin [38,39]. However, similar to the approach of mechanical vibration, transcutaneous electrical stimulation can be used to target the muscle spindle or Golgi tendon organ [40,41] to induce proprioceptive illusions. The approach of electrical stimulation induced proprioceptive modulation is promising, because of the small form factor of the electrical system and the fairly robust contact interface with the gel-type surface electrode. Also, parameters of electrical stimulation can be well controlled in real time to adjust the proprioceptive-illusion effect with precision.

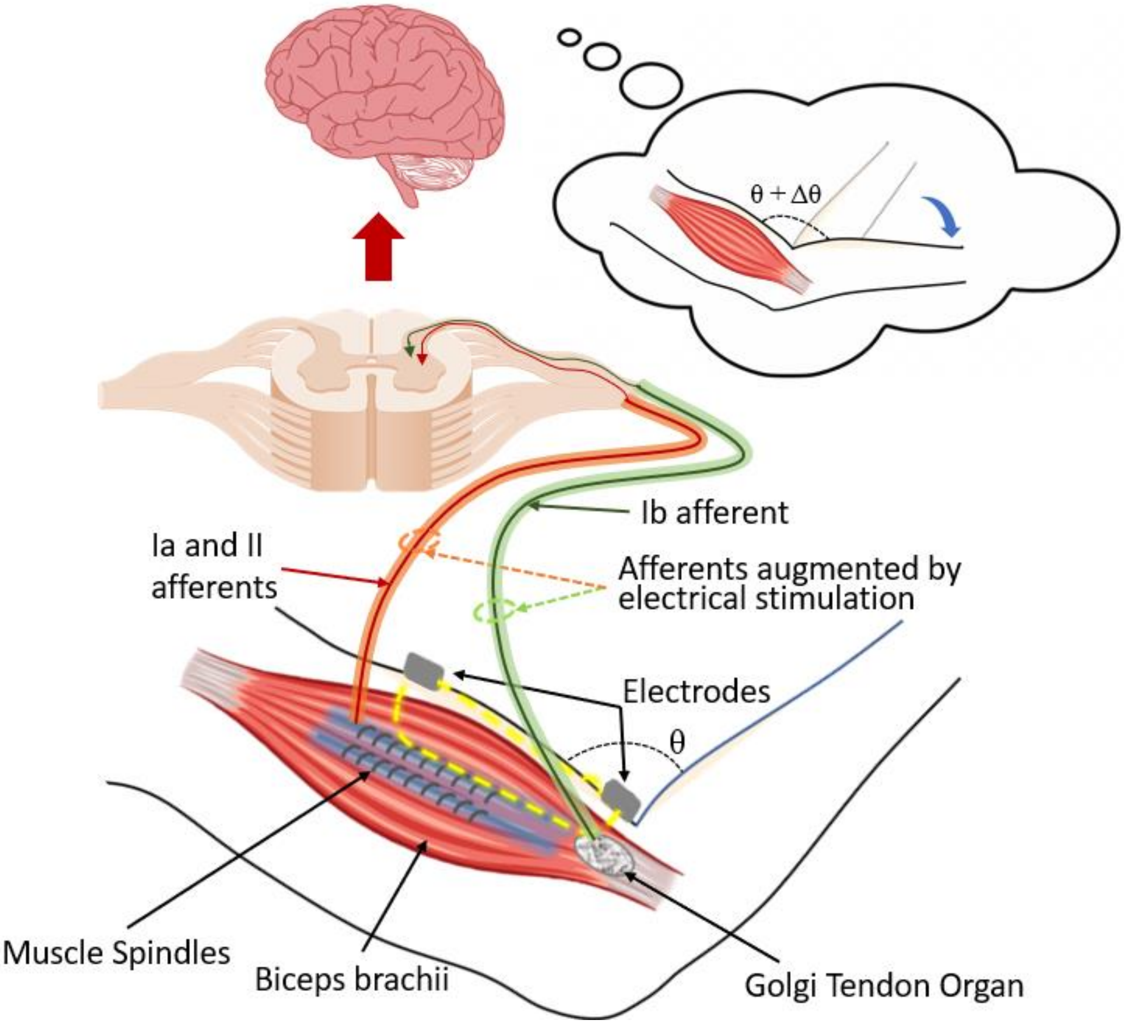


Figure 1.6 Concept Figure. Transcutaneous electrical stimulation using surface electrodes targeting biceps brachii muscle to augment muscle spindle afferents to induce proprioceptive illusion of arm extension.

As a proof of concept, we hypothesis that transcutaneous electrical stimulation on biceps brachii and brachioradialis, with appropriate stimulation parameters at appropriate location, will augment the perception of the elbow extension. Because both biceps brachii short head and brachioradialis are synergistic elbow flexors, the augmented afferent signal from the muscle spindles will augment the elbow extension. In this thesis, we developed and validated the efficacy of transcutaneous electrical stimulation on inducing proprioceptive illusion of the elbow joint. We use the term proprioceptive illusion to include both the displacement and movement illusion of elbow extension for consistency.

The further sections describe in detail the methodology, results obtained, critical discussion of the observations and the conclusions with potential directions for future work.

2. METHODOLOGY

An experimental setup to perform experiments for validation of the hypothesis was developed and human subjects were recruited to test and validate the hypothesis.

2.1. Human subject recruitment

All experiments were performed adhering to relevant guidelines and regulations, in accordance with the procedure described in the protocol approved by Institutional Review Board, Texas A&M University (IRB2018-1583D). Eight healthy human subjects in age group 20-26, one female and 7 males participated in the study. All subjects except one were right-handed. All subjects provided their informed consent for the experimentation according to the IRB approved protocol.

2.2. System Implementation

2.2.1. Biphasic Electrical Stimulator

A biphasic voltage-controlled electrical stimulator was designed for providing transcutaneous electrical stimulation. Voltage controlled stimulator provides an effective and easy way to generate transcutaneous electrical stimulation required. The system consisted of a microcontroller (STM32 ARM Cortex M3 based Particle Photon) to generate input pulse-width-modulated (PWM) waveforms followed by an electronic circuit to increase the voltage level from low to high and convert it into biphasic output. Microcontroller was programmed to generate PWM output with frequency ranging over 0-10k Hz and duty factor over 0-100%, according to the operator input. A small signal NPN transistor (MMBT3904) was used for voltage level shifting to generate the actual voltage stimulus ranging over 3-30V. The biphasic voltage output was generated using an H-bridge circuit, composed of CMOS n-channel and p-channel FET pairs (CD4007UE). The system was powered using a rechargeable Li-Po battery system. A step-up voltage buck converter was used for converting 3-4V from Li-Po battery to high voltage levels up to 30V.

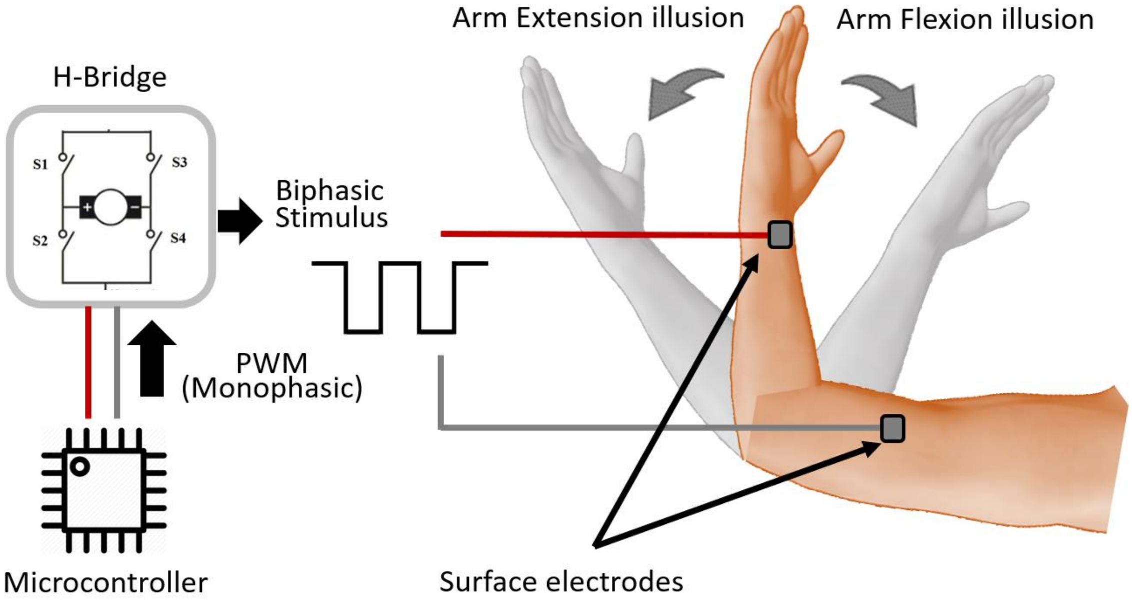


Figure 2.1 System functional diagram. Illustration of proprioceptive illusions of arm extension/flexion elicited using biphasic transcutaneous electrical stimulation generated by microcontroller and h-bridge circuit.

2.2.2. Custom surface electrodes

Custom designed transcutaneous gel electrodes were used to deliver the electrical stimulus to the skin over the target muscle. The custom designed electrodes were made using the typically used 30mm reusable self-adhesive electrode available in market. These reusable electrodes were decreased in size and multithreaded connecting wires were stacked on top using silver conducting epoxy. The small footprint (approx. 1.2x0.8 cm2) of electrodes was targeted to ensure high localization of the electrical stimulation and identify the appropriate electrode locations with maximum effect. The custom electrode used reusable self-adhesive hydrogel to stick to skin surface. Additional latex free adhesive tape was tapped over the electrodes to ensure stable contact of electrodes during active motions.

2.2.3. Gyroscope sensors

Two gyroscope sensors (MPU9250) were strapped to both right and left forearms, one for each arm, to record the angular data for both elbow joints. An elastic strap with Velcro was used to fasten the gyroscope sensors on subjects' arms to allow for minimum perturbations. The sensitivity scale factor of 131 (LSB)/°/s and a full-scale range of ± 250°/s is used for the MEM gyroscope used. The gyroscope data is digitalized using an integrated 16-bit ADC on MPU9250 providing high resolution. The gyroscope data was sampled at 100 Hz by the microcontroller. Gyroscope provides the derivative over time of an angle; the integration over time of the values generated by gyroscope was calculated to get the desired angle values. Sensor calibration was done every time before the experiment, for data integrity. The calibration ensured that the gyroscope data for gyroscopes on both the arms was matched for same elbow angle. The sensor data was delivered to the microcontroller via SPI interface, converted to angular value using programmed microcontroller and saved to the computer via USB interface.

2.3. Experiment procedure

2.3.1. Identification of electrode placement

The first experiment was designed to identify the location of electrodes for transcutaneous electrical stimulation. The first experiment was executed only for the first three subjects, under the assumption that the appropriate locations for the stimulation would be similar for all the subjects, to restrict the duration of the experiment under 2 hours for the other five subjects.

We selected four different locations of bipolar electrodes, on biceps brachii short head and brachioradialis. We selected those two muscles, as they cross the elbow joint and the afferent signal from these muscle spindle contributes to the perception of the elbow joint angle [42]. As it is hard to determine the accessibility of transcutaneous current to reach the muscle spindle between the muscle belly area and the myotendinous junction, we targeted both of those areas for two selected muscles. Accordingly, the selected locations of electrodes are composed of: (1) both electrodes on the belly of biceps brachii short head (will be called as biceps in the following), (2) both electrodes on the distal tendon of biceps, (3) one electrode on the belly of biceps and another on the distal tendon of biceps, (4) both electrodes on the belly of brachioradialis, (5) both electrodes on the distal tendon of brachioradialis, (6) one electrode on the belly of brachioradialis and another on the distal tendon of brachioradialis, (7) one electrode on the belly of biceps and another on the belly of brachioradialis, (8) one electrode on the belly of biceps and another on the distal tendon of brachioradialis, (9) one electrode on the distal tendon of biceps and another on the belly of brachioradialis, and, (10) one electrode on the distal tendon of biceps and another on the distal tendon of brachioradialis. Fig. 2.2 shows all four identified electrode locations and combination of these resulted in 10 electrode pair locations as mentioned above.

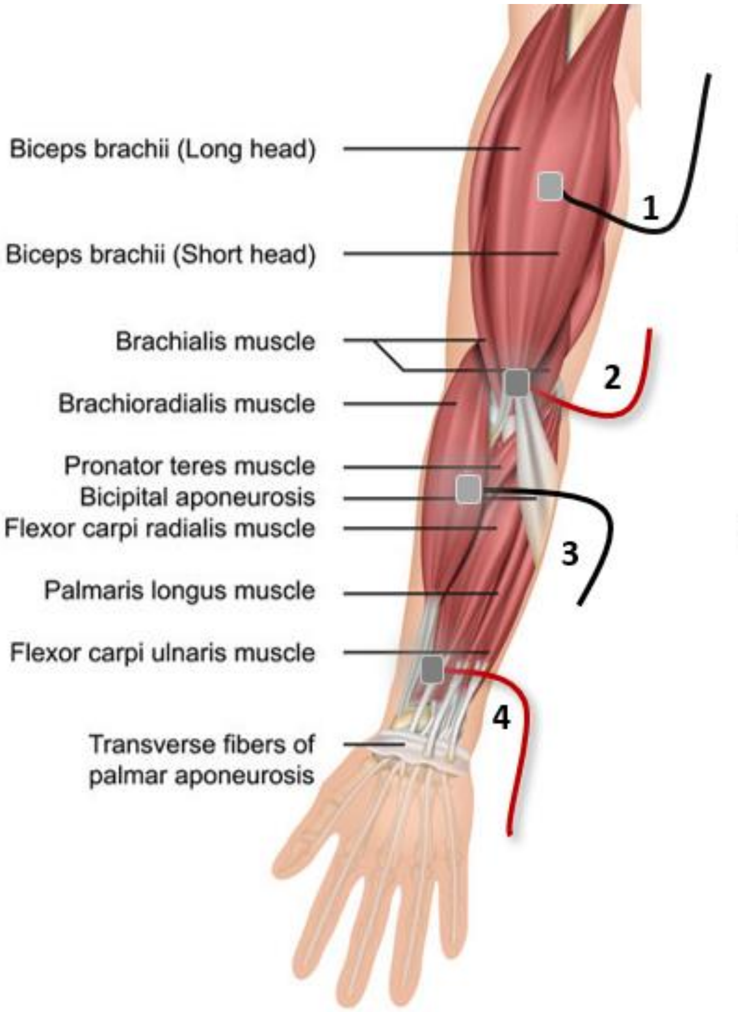


Figure 2.2 Representation of the relevant electrode locations for transcutaneous stimulation for evoking proprioceptive illusions, identified in the first experiment, (1) belly of biceps brachii short head, (2) distal tendon of brachii short head, (3) belly of brachioradialis, and (4) distal tendon of brachioradialis.

With electrode pair placed on selected locations, we applied biphasic electrical stimulus with 5V peak-to-peak amplitude, which is much lower than perception threshold, and increased the voltage gradually until subjects reported any discomfort. We found that subjects first experienced paresthesia/tingling sensation, and the sensation changed to mixed sensation of pressure/push and paresthesia/tingling, which interestingly evoked proprioceptive illusion. If the voltage was further increased, subjects reported the stimulation as uncomfortable, where we stopped applying the stimulation. Once the required voltage for proprioceptive illusion was identified, the electrical stimulation was turned on and off and subjects were asked to report the subjective feeling of arm flexion/extension imagery by 1-5 subjective rating. The 1-5 scale was defined to evaluate induced proprioceptive illusion effect, as 1 represents minimal effect and 5 represents clear perception of arm flexion or extension.

Frequency was fixed at 100 Hz for this experiment and the duty factor of the biphasic input was fixed as 50%, according to the previously successful parameters for electrotactile feedback [43]. Subjects were asked to maintain elbow joint angle in the range of 90˚-135˚, where 180˚ means fully extended elbow joint. The stimulation voltage used for biphasic voltage along with the subjective rating from 1-5 were recorded for flexion or extension illusion. The kinesthetic after-effect (i.e., perception after the stimulation was turned off) was also recorded using a subjective rating from 1-5. Based on the rating, we intended to select the best location for electrode pair, to be used for the following experiments.

2.3.2. Characterization of electrical stimulation parameters

The second experiment was designed to identify the appropriate amplitude and frequency of electrical stimulation for the proprioceptive modulation, with positioning electrodes on the best location found at the first experiment. When determining the amplitude, stimulation frequency was fixed at 100 Hz, based on previous experiments that successfully showed the effect of electrotactile feedback [43]. Subject were asked to place their arm at rest with elbow firmly placed and maintain the elbow joint angle at 90° using help of a 90° armrest for reference (with their arm barely touching it and not resting on it) [21]. Subjects were then blindfolded, and voltage level was slowly and gradually increased. Subjects were asked to report when they started feeling electrotactile feedback, generally described as tingling. The voltage level was increased, until subject reported any illusory flexion or extension of the elbow joint angle. We stopped increasing the stimulation amplitude if subjects reported any discomfort caused by the stimulation.

We also identified the appropriate frequency of electrical stimulation for the proprioceptive modulation, with the same procedure of arm resting and blindfold. In this part we fixed the voltage to the value found with the frequency fixed at 100 Hz. Subjects were asked to report the effect when the stimulation frequency was changing from 100 Hz. Subjects were provided stimulation with a set of frequencies (30, 100, 300, 1000, 3000) and asked to rate the proprioceptive illusion effect from 1-5 for those frequencies.

2.3.3. Two arm Matching Experiment

This experiment was designed to quantify the angular displacement induced by transcutaneous electrical stimulation. Arm matching between left and right was selected for quantification of the illusory flexion/extension of the elbow joint, proved as a reliable way in prior works [1,4,5]. As shown in Fig. 2.3, subjects were asked to place their right elbow joint at armrest having specific reference angle on the desk, to avoid fatigue on the arm muscles during experiments. Subjects were blindfolded during the experiment to avoid any bias from the visual feedback. First, for baseline measure, subjects were asked to do two arm matching task without any stimulation provided. Subjects maintained their right arm at the reference angles and used their left arm to match it, this sequence was repeated four times to ensure that the baseline was consistent. The stimulation on/off sequence and corresponding audio commands were generated from the computer and the gyroscope data was saved to a computer.

The electrical stimulation was then applied to electrodes placed on the right arm, on the best location identified in the first experiment. Subjects were asked to move their left arm to match the elbow joint angle between left and right arms, following changes in perception of their right elbow joint angle. Each stimulation sequence consists of stimulation-on phase for 20s and following stimulation-off phase for another 20s. Audio command was provided to subjects after the stimulation was turned on, for them to move their left arm for matching. Another audio command was provided to subjects to bring their left arm to completely extended position. Similar to stimulation on sequence, subjects were instructed to move their arm for matching at the instant the stimulation was turned off. This sequence was repeated for two times for stimulation on and off conditions. A minimum inter stimuli interval of 30 sec was provided between the trials. The complete experiment was done for two reference angles for each subject: 90° and 135° and two trials

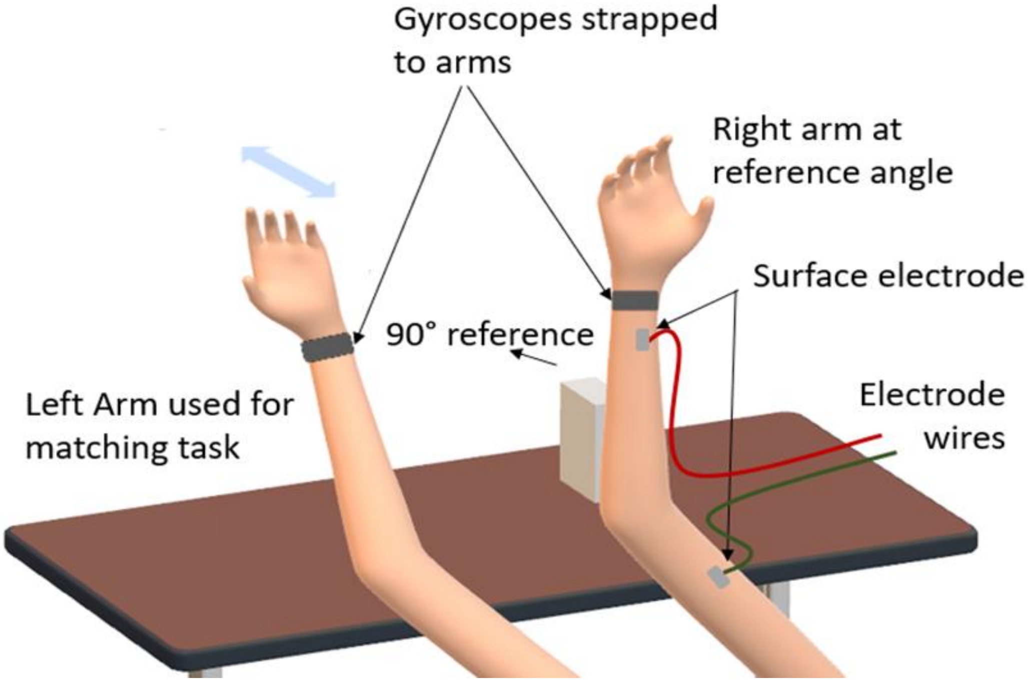
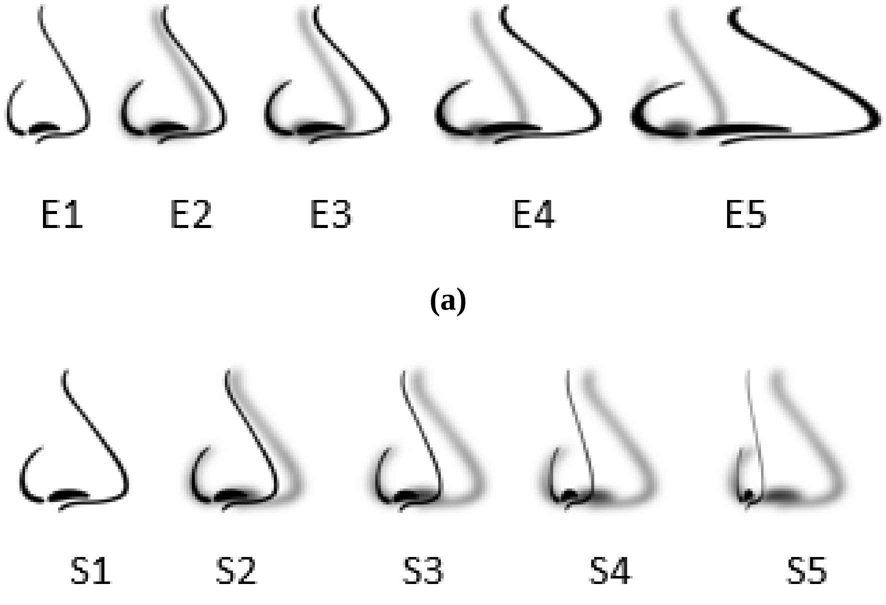


Figure 2.3 Schematic representation for two arm matching experiment. Right arm elbow angle is maintained at a specified reference angle with help of a reference object and subjects use their left arm to match to the perceived right arm angle with or without electrical stimulation applied, to measure the angular proprioceptive illusion with help of the gyroscope strapped to both the arms.

for each reference angle. During the experiment, subjects were asked to maintain their right arm at the reference angle using help of an angular reference object, as they were blindfolded. For ensuring consistent muscle conditioning, before the stimulation sequence was started the subjects were instructed to bring their right arm close to shoulder before maintaining it at reference angle at start of each trial. According to previous conducted vibration-based studies [1,29], such muscle conditioning/thixotropy maximizes the illusory effect of elbow extension.

2.3.4. Pinocchio illusion experiment

The fourth experiment was designed to confirm that the induced illusion is proprioceptive in nature. Pinocchio illusion experiment has been used in past studies [44], to establish and understand the kinesthetic illusions induced using vibration. This classical experiment involves subject touching their nose with a fingertip of the same arm on which the stimulus for inducing kinesthetic illusion is applied. Subjects were blindfolded for this experiment as well and we used the specific voltage, frequency and the best electrode location identified in previous experiments to induce maximum proprioceptive illusion. Based on direction of illusion, subjects perceived their nose tip growing or shrinking.



(a)

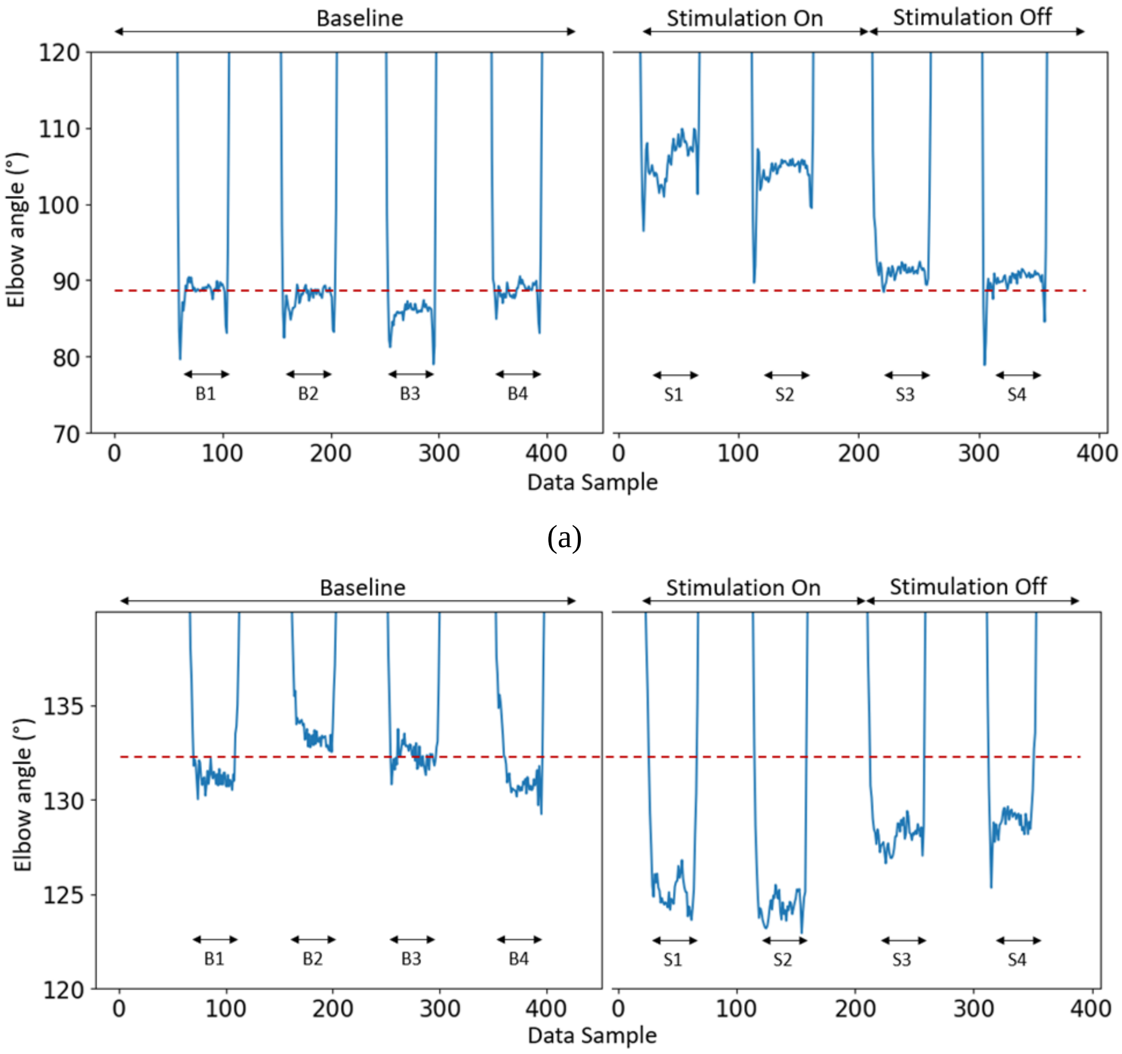
(b)

Figure 2.4 Illustrations of nose for subjects to select from for Pinocchio illusion experiment (a) for nose extension illusion corresponding to arm extension illusion and, (b) for nose shrinking illusion for arm flexion illusion.

Subjects were instructed to touch their nose tip using right index fingertip after being blindfolded. The biphasic electrical stimulation was provided for a duration of 10s on their right arm with electrodes placed on earlier identified locations. Subjects were required to keep their index fingertip on the nose tip for 10s after the stimulation was turned off to report any aftereffects. Subjects were asked to select the pictorial representation of nose on a scale of 1-5 from a series of nose representations which best describes their feeling (as shown in Fig. 5). For extension, E1 represents normal nose size and E5 represents 3 times the normal size. For nose shrink, S1 represents normal nose and S5 represents nose shrunk to 0.1 times of normal nose size. The experiment was repeated twice for data integrity.

2.4. Data Analysis

For the subject who felt elbow extension during stimulation (i.e., extension group), maximum of the average of elbow angle during S1 and S2, respectively, as shown in Fig. 2.5a, was selected as value for stimulation effect and minimum od the average during S3 and S4 was selected as representative value for aftereffect. For Fig. 2.5a, the value used for analysis would be average over S1 for stimulation effect and average of left arm elbow angle over duration S4 for aftereffect. For the subject who felt elbow flexion during stimulation (i.e., flexion group), minimum among the average of left arm elbow angle during S1, and S2, respectively, as shown in Fig. 2.5b, was used as representative value for stimulation effect and maximum of average during S3, and S4 was used as value for after-effect. For Fig. 2.5b, the value used for analysis would be average over S1 for stimulation effect and average over S4 for aftereffect.



(a)

(b)

Figure 2.5 Representative subject data, blue line represents the left arm angle for two arm matching task with right arm at reference angle and red dashed line represents the average of the baseline elbow angles(B1-B4): (a) subject 1, extension effect observed with right arm at reference angle of 90°, and (b) subject 3, flexion effect observed for right arm at reference angle 135°.

3. RESULTS

The results for the experiments conducted showed that transcutaneous electrical stimulation is effective in generating the illusion of arm extension (and flexion) when stimulation is provided at identified electrode locations with appropriate stimulation parameters.

3.1. Proprioceptive illusion was observed for all subjects

All subjects reported proprioceptive illusion over their elbow joint, in either extension or flexion direction, when stimulation with appropriate parameters was applied with their right arm stationary at specific elbow angle, either 90° or 135°. Subjects described the effects as "gradual angular change in elbow angle when stimulation is applied", "a rope between two electrodes being pulled or relaxed", "weights pushing the arm down and then being removed", etc.

3.2. Stimulation across the two synergistic elbow flexor muscles was most effective for evoking proprioceptive illusion

In the experiment identifying the appropriate location of electrodes, the first three subjects were asked to report strength of proprioceptive illusion when electrical stimulation was applied in multiple different locations. Fig. 3.1 shows the proprioceptive illusion for ten selected electrode locations, reported by the first three subjects on a scale of 1-5. The result suggests that, the electrode pair, with one on the belly of biceps brachii short head and another on the distal tendon of brachioradialis (in proximity of tendon of flexor carpi radialis), could evoke maximum proprioceptive illusion.

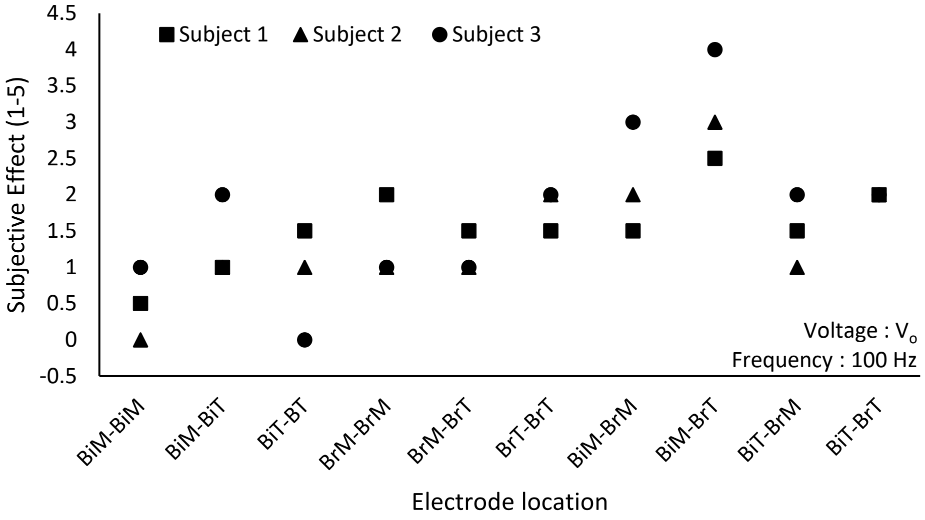
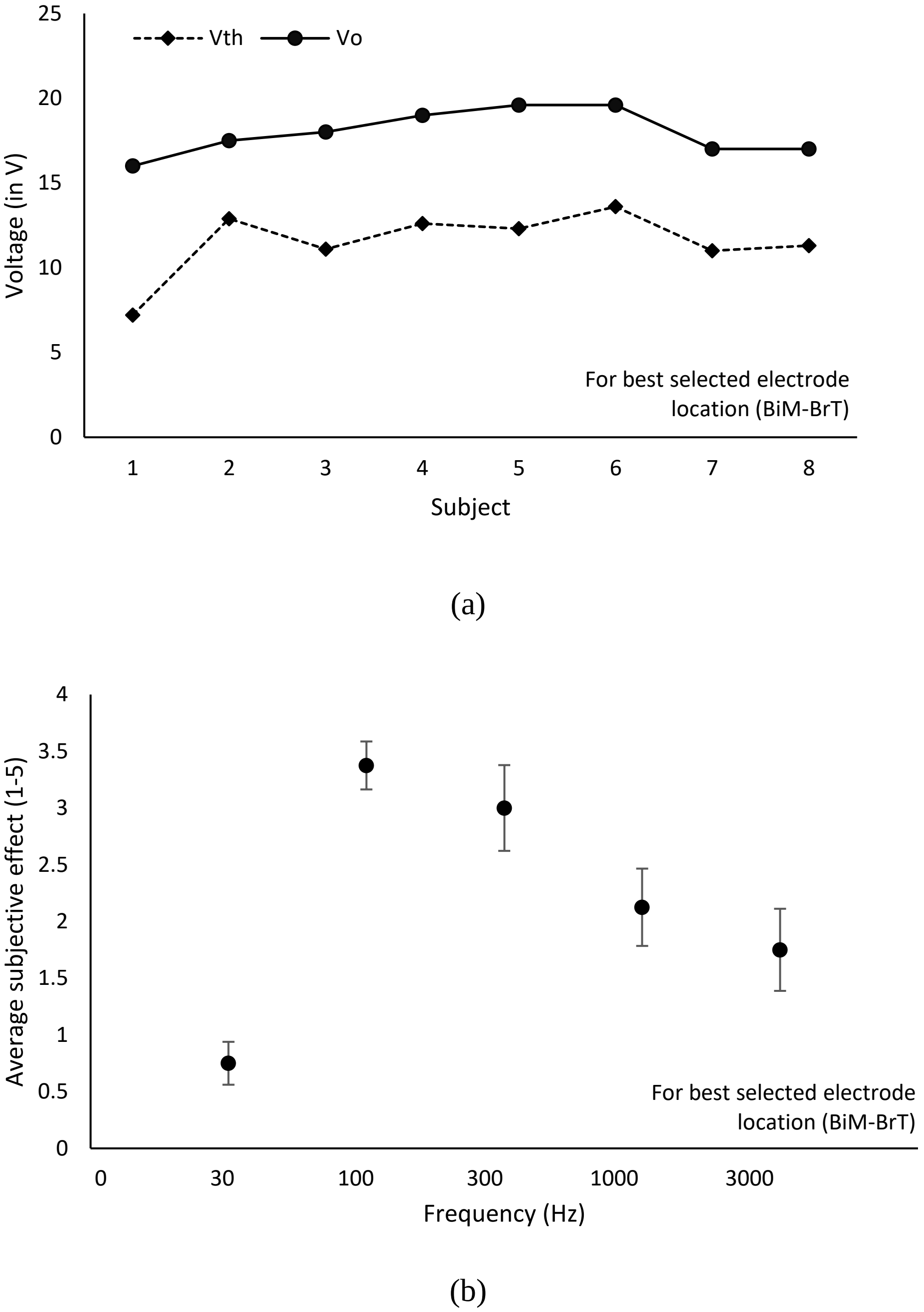


Figure 3.1 Average subjective effect for identified electrode locations for transcutaneous electrical stimulation for 3 initial subjects. Symbols used for electrode location, Bi: Biceps brachii, Br: Brachioradialis, M: Muscle belly, and T: Distal Tendon. For example, BiM – BrT, represents electrode located at Biceps brachii belly and Brachioradialis distal tendon.

3.3. Biphasic electrical stimulation with voltage amplitude 15-20V and frequency of 100 Hz was most effective on evoking proprioceptive illusion

In the experiment for identifying the appropriate electrical stimulation parameters for eliciting proprioceptive illusions, the identified optimal biphasic peak-to-peak voltage values were in range of 15-20 V for all subjects, shown in Fig. 3.2a. The electrical stimulation frequency was fixed at 100 Hz for identifying the above voltage amplitudes.



(a)

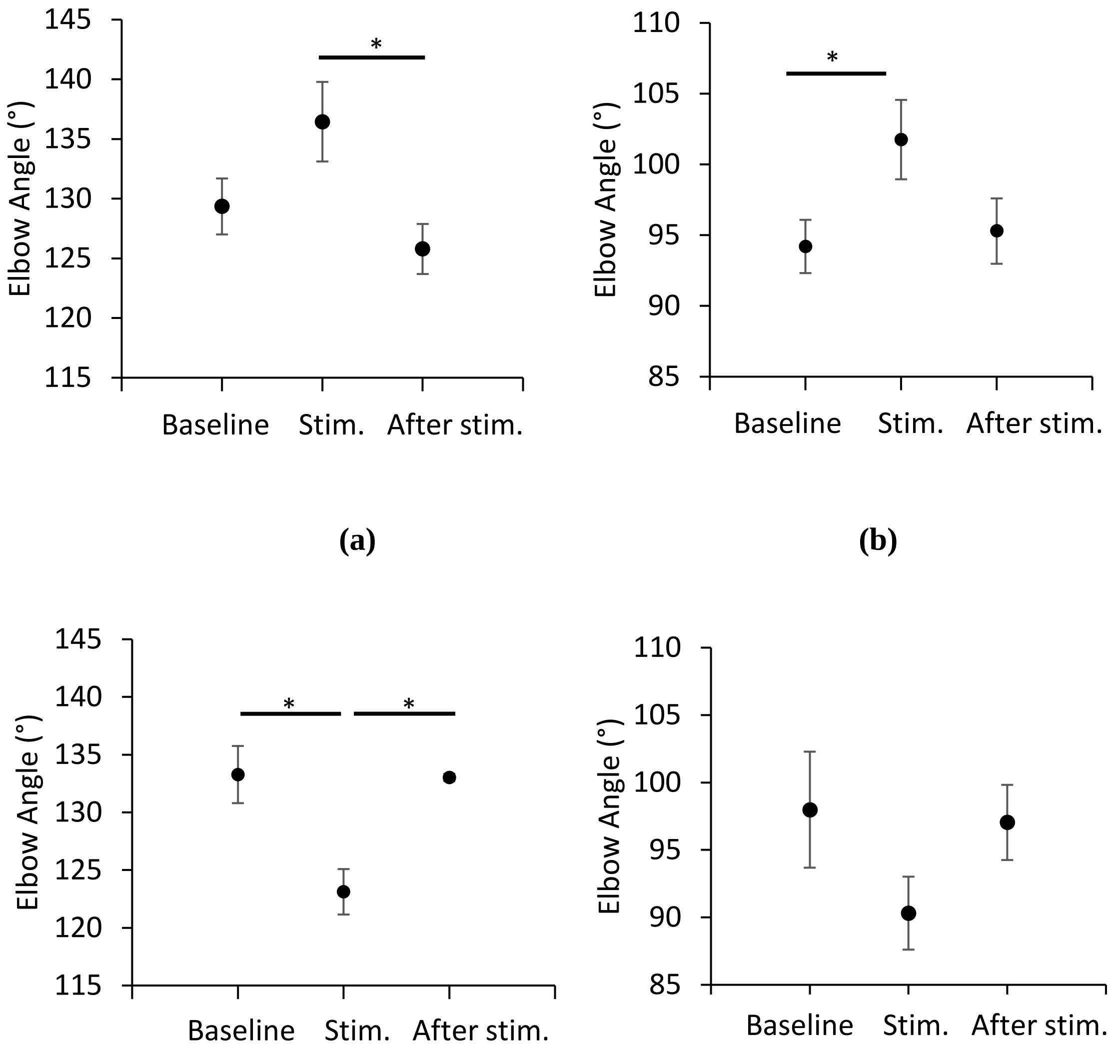
(b)

Figure 3.2 (a) Threshold peak-to-peak voltage levels for best electrode location (BiM-BrT) for biphasic electrical stimulation identified for all (8) subjects; and (b) Average subjective effect for different frequencies for transcutaneous electrical stimulation using the best electrode location (BiM-BrT) for all(8) subjects.

‘V_o’ (refer to Fig. 3.2a) voltage values identified in above experiment were further used to determine the best suitable frequency for electrical stimulation to induce maximum proprioceptive illusions. Subjects reported, lower frequencies in the range of 30-80 Hz resulted in low level of paresthesia and low level of proprioceptive illusion. The frequencies in range of 100-300 Hz resulted in low level of paresthesia and high level of proprioceptive illusion effect. For frequencies higher than 300 Hz, the subjects reported very high level of paresthesia along with low to medium proprioceptive illusion effect. In the range of 100-300 Hz, 100Hz provided the strongest proprioceptive illusion with average of 3.375 effect reported on 1-5 subjective scale over all the subjects, as shown in Fig. 3.2b and was used for further experiments.

3.4. Transcutaneous electrical stimulation evoked proprioceptive illusion is maximum for highest comfortable voltage above perception level

In the experiment for the characterization of perception evoked by electrical stimulation, subjects reported proprioceptive illusion above a perception threshold (V_{th}), and the proprioceptive illusion became stronger as the stimulation amplitude increased, before subjects felt discomfort along with paresthesia. In other words, the strongest proprioceptive illusion was observed at the maximum voltage level (V_o) just before discomfort feeling (i.e., comfort threshold), according to the subjects’ report of perception. Fig. 3.2a shows the V_{th} and V_o for all subjects.



(a) **(b)**

(c) **(d)**

Figure 3.3 Angular proprioceptive illusion for subjects in arm matching experiment, 2 trials per subject: (a) average for 6 subjects with arm extension illusion, 135° reference angle, (b) average for 6 subjects with arm extension illusion, 90° reference angle, (c) average for 2 subjects with arm flexion illusion, 135° reference angle, and (d) average for 2 subjects with arm flexion illusion, 90° reference angle. * represents samples with statistical significance ($p < 0.05$) for a two-tailed t test with 95% confidence.

3.5. Stimulation caused proprioceptive illusion of extension for 6 subjects and illusion of flexion for 2 subjects, but the effect was consistent within each of the 8 subjects

The raw data for two arm matching experiments, for two subjects, is shown in Figs. 2.5a and 2.5b as an example. Fig. 2.5a shows the raw elbow angle data recorded from one of the six subjects who reported proprioceptive illusion in the direction of elbow extension. The left elbow angle becomes larger than baseline when stimulation is turned on and decreased back to the level of baseline when stimulation is turned off. Fig. 2.5b shows the opposite case, from one of the two subjects who reported proprioceptive illusion in the direction of elbow flexion. The left elbow angle becomes smaller than baseline when stimulation is turned on and increased back to the level of baseline when stimulation is turned off. Fig. 3.3 shows the averaged left elbow joint angle over all subjects, before any stimulation was applied (baseline), when the stimulation was turned on, and after stimulation was turned off, for each of 90° and 135° reference angles. The data show that stimulation caused 5-10° angular displacement on average, in replicating the right elbow angle, for both reference angles. The direction of this angular illusion was either extension or flexion.

3.6. Pinocchio illusion was experienced by all subjects

All subjects reported Pinocchio illusion upon application of the electrical stimulation with the electrodes placed over biceps brachii belly and distal tendon of the brachioradialis. Subjects reported perception of either nose extension or shrinking, with the graphical representations shown to them (see Fig. 5). The subjects in extension group

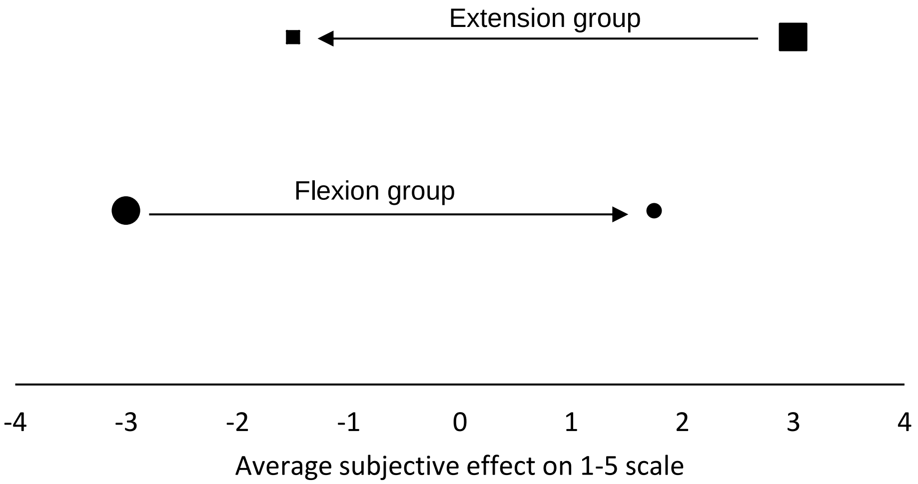


Figure 3.4 Average subjective effect and after-effect for Pinocchio illusion experiment, negative values represents the nose shrink and positive values are used to represent nose extension. Average for 6 subjects in extension group(felt nose extension on stimulation and nose shrink as after-effect) represented by square, and average for 2 subjects in flexion group(felt nose shrink as the effect of the stimulation and nose extension as after-effect) represented by circle.

(those who experienced elbow extension illusion by stimulation) reported nose extension on stimulation and nose shrink as an aftereffect. The subjects in flexion group (those who experienced elbow flexion illusion by stimulation) reported nose shrink on stimulation and nose extension as an aftereffect. As shown in Fig 3.4, flexion group reported nose shrunk to -3 on average, during the stimulation is applied, and nose extension to +1.75 on average, as an aftereffect. Extension group reported nose extension to +3 on average, during the stimulation is applied, and nose shrunk to -1.5 on average, as an aftereffect.

4. DISCUSSION

4.1. All subjects felt proprioceptive illusion, although the direction of illusion was not consistent

Research studies in past, using vibration, found that vibration did not induce proprioceptive illusion for part of the subjects [1,29,45-47]. Fuentes et al. reported that 10–20% of subjects did not feel proprioceptive illusion by the vibration [45] and Roll et al. also assumed the limited efficacy and restricted the subject group as previously successful participants [47]. In this study, all subjects experienced proprioceptive illusion although the direction of illusion was not consistent.

4.2. Stimulating muscle spindles in two synergistic elbow flexors together seems critical in transcutaneous electrical stimulation evoked proprioceptive illusions

We found that the location of electrodes is a critical factor for inducing proprioceptive illusion using transcutaneous electrical stimulation, as seen in prior work on tendon electrical stimulation for force feedback [40] . Based on our experiment, we found that the electrode pair with one electrode on biceps brachii muscle belly and other electrode at forearm on tendinous area of brachioradialis in proximity of tendon area of flexor carpi radialis provided much better result than the other locations (see Fig. 3.2). Interestingly, stimulating the spindle in one of the biceps brachii and brachioradialis was much less effective than stimulating the spindle in both muscles together. We expect that it is because elbow flexion is usually driven by change in length of both muscles, and contradictory information between two muscle spindles may suppress the gain of the proprioceptive feedback.

4.3. The effect of stimulation location and frequency on proprioceptive modulation needs to be further investigated

We were able to find the optimal stimulation voltage amplitude and frequency to maximize the proprioceptive illusion for elbow joint angle. Vibration-induced proprioceptive illusion is reported as being dependent on the frequency. According to the current understanding, vibration can selectively activate muscle spindle afferents according to the vibration frequency. For example, vibration with higher frequencies activates secondary (II) spindle afferent, and vibration with lower frequencies activates primary (Ia) spindle afferents (Roll et al. 1989, Taylor et al. 2017). Likewise, it would be interesting to explore the effect of frequency dependency of electrically induced proprioceptive illusion. As suggested by the subjective variations in our experimental results, the experiment should be conducted according to subject identified parameters, rather than using the single best parameter set for all subjects.

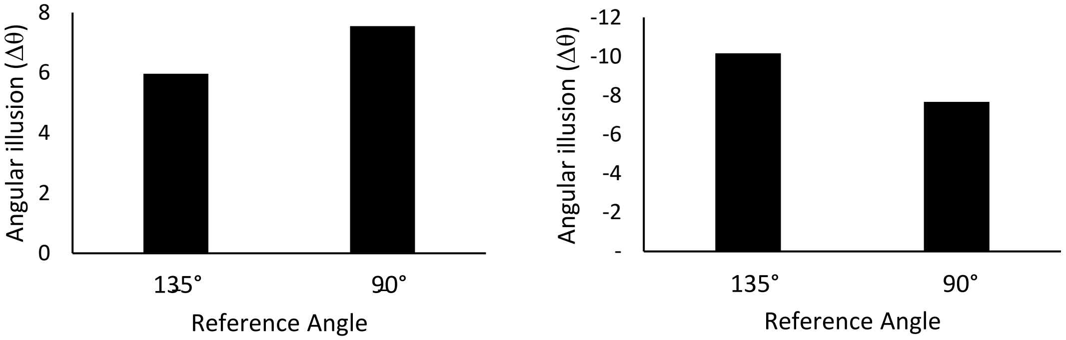
4.4. For 6 of 8 subjects who reported extension with the applied stimulation, we expect the stimulation augmented activity of muscle spindles on biceps brachii short head and brachioradialis

The experimental results from 6 of 8 subjects, who reported illusion in direction of extension, suggest that transcutaneous electrical stimulation over both biceps brachii and brachioradialis augmented the perception of the elbow extension. This result agrees with the hypothesis that transcutaneous electrical stimulation augmented the muscle spindle afferent signal from biceps brachii short head and brachioradialis (synergistic elbow flexors), and therefore, augmented the perception of the elbow extension. We expect that the identified electrode location of biceps belly and tendinous area of brachioradialis provided a proper current pathway to activate muscle spindle of both muscles.

4.5. For 2 of 8 subjects who reported flexion with the applied stimulation, we expect the stimulation either interrupted muscle spindle afferent signal or excited cutaneous receptors on the skin

For the 2 of 8 subjects who reported illusion in direction of flexion with transcutaneous electrical stimulation, we have two kinds of interpretation. First, we expect that the stimulation might have interrupted original muscle spindle afferent signal, instead of augmenting it. In other words, the transcutaneous electrical stimulation attenuated the spindle afferent signal corresponding to the stretch of elbow flexor muscles, which results in illusion of elbow flexion. Multiple prior works using vibration support this notion as vibration interrupted muscle spindle afferent signal, like adding a noise, and suppressed the effect of muscle spindle afferent signal [1-4,21]. Second, we cannot exclude the possibility that the electrical stimulation excited the cutaneous receptors on the skin. Previous studies on skin stretch showed that the proprioceptive illusions are enhanced when skin stretch is used along with the vibration [34] and other studies established cutaneous receptors also contribute to proprioception [49]. As studies have reported that the augmented tactile feedback on the joint area evokes the perception of skin contraction

[48], the transcutaneous electrical stimulation over the elbow joint area could have elicited the perception of elbow flexion.



(a) (b)

Figure 4.1 Average angular illusion (Δθ) (Stimulation left arm angle - baseline left arm angle) (a) for 6 subjects in extension group (who felt arm extension when stimulation was applied), and (b) for 2 subjects in flexion group (who felt arm flexion when stimulation was applied).

4.6. Different efficacy of proprioceptive modulation for different elbow joint angles, further support the idea of modulation of muscle spindle afferent signaling

For subjects who felt illusion in the direction of elbow extension, illusion at 90° elbow joint angle was stronger compared to that at 135° elbow joint angle (see Fig. 3.4 and Fig. 4.1). For the subjects who felt illusion in the direction of elbow flexion, illusion at 135° elbow joint angle was stronger compared to that at 90° elbow joint angle (see Fig. 3.4). As the biceps spindle is more stretched at 135° elbow joint angle than at 90° elbow joint angle. We expect that, when spindle is less stretched (90° elbow joint angle), it would be easier to augment the spindle afferent with stimulation. Conversely, when spindle is more stretched (135° elbow joint angle) with more afferent signaling, it would be easier to decrease the spindle afferent with noise. These observations further support our argument that the transcutaneous electrically induced proprioceptive illusion occurs by the modulation of muscle spindle afferent signaling.

4.7. Effect of the transcutaneous electrical stimulation on muscle spindle afferent is influenced by biological variation

We observed that the effect of transcutaneous electrical stimulation on elbow flexor muscles can be either extension or flexion, and the effect was consistent for each subject over duration of the trials. As seen in the previous paragraphs of discussion section, we interpret these contradictory results as the transcutaneous electrical stimulation can either augment or interrupt the original spindle afferent signal. In other words, the compound action potential evoked by the stimulation could work as either the effective signal or the noise. Although it is hard to clarify what exactly electrical stimulation changed in spindle afferent signal, it is clear that the effect of the stimulation can be much different among people and even opposite between them.

4.8. Transcutaneous electrical stimulation has advantages over the vibration-induced proprioceptive illusion, in terms of latency, consistency, and implementation

Transcutaneous electrical stimulation can potentially replace the vibration-induced proprioceptive illusion, which is currently the most widely accepted non-invasive method for inducing proprioceptive illusion. First, the latency issue observed in vibration-induced proprioceptive illusion [1,29] can be addressed by using the transcutaneous electrical stimulation. All subjects reported that the transcutaneous electrical stimulation caused proprioceptive illusion with minimal latency that they were not able to recognize. Second, the consistency of proprioceptive illusion can be improved by employing the transcutaneous electrical stimulation. Note that the biggest challenge for the vibration-induced proprioceptive illusion is the inconsistency of the effect [1,29]. Although the intersubject effect was not consistent with transcutaneous electrical stimulation, intrasubject effect was consistent for all subjects. Third, electrical stimulation allows for easy and simple system implementation, compared to the vibration-based approach. Fixation of the vibrator motor on a specific location of the arm is not easy because of the inherent properties of mechanical vibration resulting in mechanical deviation from the targeted location, and vibration reaching neighboring muscle groups. Also, the bulkiness of the mechanical vibration system makes it hard to implement the whole system as a small wearable. On the other hand, electrical stimulation-based approach can result in an easy to design, small sized, highly localized, consistent system without any mechanical deviation. Such electrical system will minimally disturb the natural arm/hand movements and allow easy translation of such approach to real-world applications.

4.9. Consistent after-effect illusion could be used for practical applications

We observed consistent after-effect proprioceptive illusion (refer to Fig. 8) when the stimulation is turned off, which is in the opposite direction to the direction of the proprioceptive illusion initially generated by turning on stimulation. These after-effects could be effectively used for providing proprioceptive information by using a sequence of stimulation on to stimulation off, instead of using the stimulation on effect to provide the proprioceptive information in just one direction. This could be highly effective for providing bidirectional proprioceptive information by stimulating one group of synergistic muscle pairs for various application.

4.10. Further study is needed to investigate the effect of the elbow joint angle on the induced proprioceptive illusion

Studies on vibration-induced illusion suggest that both static and dynamic state of muscle spindle (i.e., initial angle and thixotropy) have strong effects on proprioceptive illusions [1]. According to the current understanding, different elbow joint angles changes the effect of stimulation on muscle spindle activity, which determines the efficacy of transcutaneous electrical stimulation on proprioceptive modulation [1,29]. Our experimental result agrees with this, as we observed that the efficacy of the proprioceptive illusion depends on the elbow joint angle, as shown in Fig. 3.4 and Fig. 4.1.

5. CONCLUSIONS AND FUTURE RESEARCH

This study tested the novel approach of transcutaneous electrical stimulation to induce proprioceptive illusions. The observation and results strongly suggest that transcutaneous electrical stimulation is not just a viable option for proprioceptive modulation but a strong candidate to replace the current vibration-based proprioceptive modulation. However, for practical use of this new approach, there are many challenges and factors to be addressed. We need to further investigate the underlying principle of proprioceptive illusion elicited using transcutaneous electrical stimulation. We need to clarify the changes in the activities of muscle spindle and Golgi tendon organ by transcutaneous electrical stimulation. We also need to clarify the involvement of cutaneous receptors via electrical stimulation, as transcutaneous electrical stimulation can easily activate cutaneous receptor afferents on the skin. Future research in this direction could try to investigate the operating principles of the mechanism, and exact physiological changes associated with it. Upon the robust establishment of effective parameters and location for transcutaneous electrical stimulation to induce proprioceptive illusion, it has immense potential to be applied in virtual reality, teleoperations, neurorehabilitation, and neuroprosthetics.

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