Contributing Factors to Orofacial Somatosensory Sensitivity

by

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ABSTRACT

The brain uses the somatosensory system to interact with the environment and control movements. Additionally, many movement disorders are associated with deficits in the somatosensory sensory system. Thus, understanding the somatosensory system is essential for developing treatments for movement disorders. Previous studies have extensively examined the role of the somatosensory system in controlling the lower and upper extremities; however, little is known about the contributions of the orofacial somatosensory system. The overall goal of this study was to determine factors that influence the sensitivity of the orofacial somatosensory system. To measure the somatosensory system's sensitivity, transcutaneous electrical current stimulation was applied to the skin overlaying the trigeminal nerve on the lower portion of the face. After applying stimulation, participants' sensitivity was determined through the detection of the electrical stimuli (i.e., perceptual threshold). The data analysis focused on the impact of (1) stimulation parameters, (2) electrode placement, and (3) motor tasks on the perceptual threshold. The results showed that, as expected, stimulation parameters (such as stimulation frequency and duration) influenced perceptual thresholds. However, electrode placement (left vs. right side of the face) and motor tasks (lip contraction vs. rest) did not influence perceptual thresholds. Overall, these findings have important implications for designing and developing therapeutic neuromodulation techniques based on trigeminal nerve stimulation.

I dedicate this to those who have stood by my side from the beginning.

For the unwavering support, encouragement, and love you have given.

To my family who has shown me anything is possible.

Thank you for fostering my love of medicine and science.

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GLOSSARY

Term	Definition
Mechanotransduction	The conversion of mechanical stimulus to electrical or chemical signals that convey information about physical touch
Thermoreception	The perception of temperature
Nociception	The perception of pain
Interoception	The perception of the internal body and organs
Proprioception	The perception of movement and spatial orientation
Somatosensation	Relating to physical sensations of touch
Perceptual Threshold	The lowest level of stimulus intensity that can be detected
Extremities	Pertaining to the limbs of the body: arms and legs
Rheobase Current	Minimal amount of electrical current that causes excitation

CHAPTER 1

INTRODUCTION

Statement of Problem

The somatosensory system is a complex network consisting of neural pathways and peripheral receptors. These pathways and receptors assist people in identifying the world around them through mechanotransduction, thermoreception, nociception, interoception, and proprioception (Richardson & Collins, 2001; Kandel et al., 2014; Bhatnagar, 2013). The somatosensory system relies on the primary (first), secondary (second), and tertiary (third) neurons to convey efferent and afferent information (Kandel et al., 2014). This system is vital as it controls the person's ability to process somatosensory information (McCance & Huether, 2014). Understanding the functions of the somatosensory system is essential for developing potential treatments for many sensory and movement disorders. While there is a fairly large body of research on somatosensation, the orofacial regions have historically been ignored in favor of the extremities. When using a well-known technique that has not been studied on a region of the body, several considerations must be made to ensure the that the protocol can be easily replicable and produce sound results.

Considerations of Study

The first consideration was the electrical stimulation parameters, electrode configuration, and surface space of the stimulation region. Electrical stimulation parameters here forward, termed stimulation factors, are explained best by the Weiss-Lapicque strength and duration relationship formula (Lapicque, 1909; Weiss, 1901). The strength and duration relationship formula explains how charge (Q), pulse length (t), current (I), charge as stimulation reaches zero (k), and charge as stimulation reaches infinity (b) interact with each other to cause an action potential (Prausnitz, 1996).

$$Q = k + bt$$

Equation 1. Weiss-Lapicque strength and duration relationship formula part 1.

$$I = \frac{k}{t} + b$$

Equation 2. Weiss-Lapicque strength and duration relationship formula part 2.

It is essential to keep in mind that, when an action potential occurs due to stimulation, the change in electrical potential allows for ion exchanges to occur between the intracellular and extracellular spaces of the cell membrane. If the threshold reaches a critical level during this period, it will allow the sodium channels to become flooded, bringing the intracellular potential to over 50 mV (millivolts). During this period, the cell membrane goes into an absolute refractory period known as depolarization. When depolarization occurs, the cell membrane can no longer receive stimulation until the relative refractory period, but only at substantially more current than that at which initial depolarization occurred (Seikel et al., 2016). There must be a minimum charge on the stimulated surface to induce the excitation of a nerve and produce an action potential when the stimulation factor is shorter than the charging time of the stimulated surface. When the stimulation factor is exceedingly longer than the pulse length, a rheobase current is required for the excitation of the nerves. This differs when the stimulation factor meets or exceeds the stimulated surface, as the stimulated surface will depolarize; thus, more charge is required for stimulation of the nerves to cause an action potential. The configuration of the stimulation factors is prominent, as multiple pulses can cause an increased sensation, while sequential pulses can reduce sensation, and frequency can change the quality of stimulation (Prausnitz, 1996).

Specific electrode configurations and placements can produce different somatosensory sensations. If stimulation occurs on a larger surface space, it will produce a sensation felt deeper in the skin and will be non-painful until the electrical current reaches a high intensity. The opposite is found when stimulation occurs in more localized or smaller surface space; the electrical currents will be localized, provoking nociception (Richardson & Collins, 2001). Gate control theory of pain plays a role in the electrode configuration because sensory thresholds increase when exposed to painful stimulation (Apkarian et al., 1994; Prausnitz, 1996). As the orofacial region has a small surface space, 2-point discrimination theory should also be considered as a factor that could influence perception of stimuli. Two-point discrimination is the ability to differentiate and distinguish stimulation occurring on two different locations in a similar region as two distinct points rather than one. As such, 2-point discrimination is lost when painful stimuli are detected (Kauppila et al. 1998). Considering that the surface area of the orofacial region is not as large as when stimulating the extremities and the consistent use of stimulation, there were concerns regarding increasing sensitivity levels due, with participants unable to detect both areas of stimulation to each individual having an individualized pain threshold or tolerance.

The second consideration was regarding resting state and voluntary motor movement. Generally, resting and moving states have been well-studied in the somatosensory system. Sensory transmission is known to have impairments when conducting stimulation and or motor movement. The velocity of motor movement can impact the suppression of the somatosensory sensation. Movement causes a decrease in acuity, which is linked to the suppression of somatosensory evoked potentials, thus causing the suppression of sensations (Rauch et al., 1985). Similarly, voluntary muscle contraction superimposed on transcutaneous peripheral electrical stimulation of the medial nerve decreases somatosensory evoked potentials compared to the resting state (Takahara et al., 2020). Voluntary motor movement (force generation) and resting state (force relaxation) were found to have similar effects in decreasing somatosensory evoked potentials on the median nerve. Although both conditions had the same force production during the phase, somatosensory evoked potentials were smaller in the force generation task (Wasaka & Kakigi, 2012). The reduction in somatosensory evoked potentials suggests that the somatosensory system is suppressed during movement and somatosensory stimuli are less likely to be detected or felt by the individual.

The last consideration was accounting for hemispheric lateralization and its effects on the stimulation site. Hemispheric lateralization occurs in three forms contralateral (opposite side), ipsilateral (same side), and bilateral (both sides). For the purpose of this study, we primarily examined the somatosensory system of the orofacial region, but we also examined effects of somatosensation during movement; meaning that activation of the motor cortex and facial muscles were involved. There are three main tracks of the trigeminal system that effect somatosensation which include the spinal trigeminal track, ventral trigeminothalamic tract, and dorsal trigeminothalamic tract (Price & Daly, 2022; Bhatnagar, 2013). The first order sensory fibers are associated with the cell bodies in the Gasserian ganglion which enter the pons targeting the chief sensory nucleus and terminating at the spinal trigeminal track. The second order sensory fibers form the ventral trigeminothalamic tract and consist of the ventral and dorsal secondary ascending tracts, which eventually become the third-order fibers that project to the primary sensory cortex (Bhatnagar, 2013). The ventral trigeminothalamic tract crosses contralateral to the ventral posteromedial nucleus of the thalamus which conveys information on thermoreception and nociception. The dorsal trigeminothalamic tract remains uncross and conveys information of mechanotransduction and proprioception ipsilaterally to the ventral posteromedial nucleus of the thalamus (Price & Daly, 2022; Bhatnagar, 2013). The lower third portion of the primary motor cortex is responsible for movement of the head and facial muscles. The motor cortex primarily innervates contralaterally to the cranial nerves. While contralateral innervation is the norm, for skilled movements there is sensory feedback from the sensorimotor cortex, until that skilled movement has been mastered (Bhatnagar, 2013).

The effects of hemispheric lateralization are well known regarding stimulation of the extremities and motor control of speech. Previous studies, such as Eickhoff et al. (2008), reported that stimulation to either the right or left side of the face had both a contralateral and ipsilateral activation in the cortex. However, ipsilateral activation was 5.8% lower than contralateral activation. Functional magnetic resonance imaging has also been used to detect that the cortex produces bilateral activation during normal and perturbed stimuli (Behroozmand, 2015). A study focusing on which areas of the cortex are associated with simple speech motor control in four conditions (speech spoken aloud, mouthed speech, unarticulated speech, and internal speech), found bilateral activation when comparing the different conditions (Murphy et al., 1997).

Chosen Protocol and Incidentals

For this study, electrical stimulation was chosen to elicit somatosensory information to the orofacial region targeting the orbicularis oris. Somatosensory electrical stimulation focuses on low-intensity electrical currents to detect sensitivity or perceptual thresholds. An electrical stimulus protocol allows numerous variables to be easily utilized while ensuring no differences in reproducing the protocol when subjects complete the experiment. The somatosensory electrical stimulation should only generate somatosensory information without any visible effects of involuntary muscle contraction. While visible effects cannot be detected, somatosensory stimulation that occurs to the head or face will elicit a multitude of components stemming from the composition of musculature to the neurons that transmit information between the cortex and nervous system.

Aims of Study

This thesis aimed to investigate and further expand knowledge on the effects of somatosensory electrical stimulation on sensitivity levels (perceptual threshold) when applied to the orofacial region, explicitly targeting the orbicularis oris muscle or the medial mandible. This study assessed interactions of stimulation factors between laterality (stimulation site) and motor task (resting and voluntary movement) to determine sensitivity levels. This study's findings helped improve and build on existing knowledge of somatosensory electrical stimulation, create a replicable baseline protocol of somatosensory stimulation of the orofacial region, and help propose recommendations for future studies using the techniques based on this experimental protocol. Overall, the goal of this study was to determine the sensitivity of the somatosensory system to experimental manipulation of electrical stimulation (parameter), electrode configuration (laterality), and task (motor task). For this purpose, we used the perceptual threshold of detecting electrical stimulation to measure somatosensory sensitivity.

CHAPTER 2

METHODS

Participants

Fifteen adults (14 right-handed, 12 women, 3 men) with an age range of 20-33 years (M=22.65 years, SD=3.29 years) participated in this study. The inclusion criteria were as follows: self-reported survey stating the absence of (a) neurological disorders, (b) psychological disorders, and (c) speech-language disorders. Before partaking in the experimental session, each participant signed a written consent form. Arizona State University's institutional board approved all study protocols.

Apparatus

Figure 1 shows the apparatus of the experiment. Participants were seated in front of a monitor with a keyboard and asked to adjust the keyboard within comfortable reach. The experimental session took place in a silent room with minimal distractions that could take attention away from electrical stimulation.

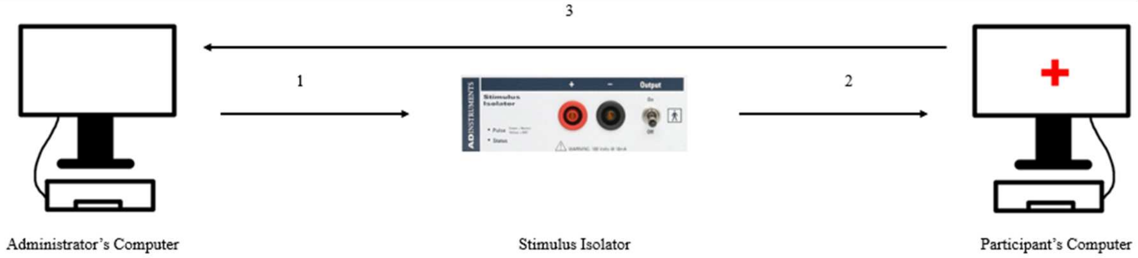

Figure 1. Schematic of the Experimental Setup.

To apply electrical stimulation, we used ADInstruments Stimulus Isolator. Electrical stimulation was applied using a transcutaneous technique. Four 3cm COVIDIEN foam conductive adhesive hydrogel electrodes and four 185cm snap electrical lead wires were placed on the inferior portion of the orbicularis oris. Electrodes were placed as anode and cathode pairs on the left and right sides of the inferior orbicularis. Figure 2 displays the electrode configuration on the mandible. The left and right side of the inferior orbicularis oris was distinguished by the mental protrusion of the mandible, with the anode positioned medially and the cathode positioned laterally.

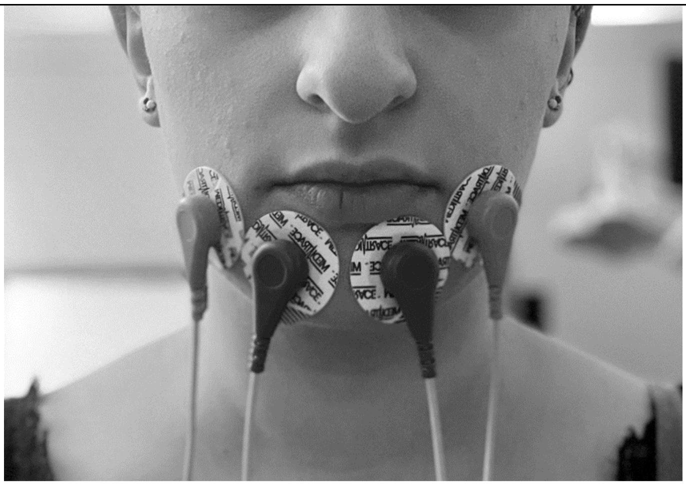

Figure 2. Electrode Configuration on the Mandible. The anode electrode was positioned medially, and the cathode electrode was positioned laterally in reference to the mental protuberance.

Before placing electrodes and leads, we used BRIEMARPAK 70% alcohol skin cleaning swab to optimize conduction between the epidermis and electrodes. For participants with facial hair, we used EASYCAP high-chloride (10%) abrasive electrolyte gel prior to the alcohol skin cleaning swab to assist in lowering impedance. Before each experimental session, the electrodes, equipment, and software were tested to ensure that everything functioned adequately, thus avoiding delays and concerning mishaps.

To compile recorded data for perceptual threshold, we used a custom-written MATLAB script that tracked participants' responses from the keyboard and reaction times to perceived and nonperceived stimulation. The keyboard's left and right arrow keys were used to record sensitivity levels (perceptual threshold). Entry of the left arrow key signified that stimulation was perceived [YES], and entry of the right arrow key signified that stimulation was not perceived [NO]. ADInstruments LabChart 8 was used to establish a sampling frequency at 10kHz/s and tracked each time electrical stimulation was delivered to the inferior orbicularis oris.

Procedure

The experiment lasted 1.5 hours and was completed in one session. All participants completed an electrical stimulation training task prior to the commencement of electrical stimulation tasks. One participant elected to complete the experiment in two sessions, one week apart, by choice due to time constraints. The participant that took two sessions to complete the experimental protocol did not repeat the training task.

Training Task

The goal of the training task was to ensure that participants became accustomed to the experimental setup and electrical stimulation. Each participant completed a training task that consisted of 40 trials and lasted approximately 3.5 minutes. Each trial commenced with a visual indicator of a red plus sign, which was followed by a green plus sign to signify the end of the trial. Between the presented visual indicators electrical stimulation was applied at a random time interval to reduce anticipation of when stimulation would occur. Once the trial was completed, participants were shown a prompt of 'YES' and 'NO' with a 2-second wait period to receive input from the left or right arrow key. Before the subsequent trial commenced, participants were given a 1.25-second rest period. Participants were trained to use active and passive measures during the training task. The active measure was defined as gently contracting lips as if producing the phoneme /m/on the first visual indicator and releasing muscle contraction on the second indicator. The passive measure was defined as resting with no lip movement. Participants were instructed to alternate between the active and passive measures during the training task to become accustomed to the procedure during stimulation. None of the participants struggled with the training task or measures, and therefore, we did not need to repeat the training task.

Stimulation Tasks

The goal of the electrical stimulation task was to find which stimulation factor and configuration are best suited for perceptual threshold. Each participant completed 16 conditions: 4 stimulation parameters (Single Pulse Width, Pulse Width, Pulse Frequency, Pulse Repetition), 2 levels in each stimulation parameter, 2 laterality (left vs. right), 2 motor tasks (active vs. rest). Each condition consisted of 40 trials that examined two parameters, Factor A [20 trials] and Factor B [20 trials]. Table 1 and 2 display the parameters of Factors A and B. The order of the conditions was randomized to reduce anticipation of stimulation patterns and sight. The design of the conditions was similar to the training task, except that the participants were verbally informed which measure [active or passive] should be used throughout the condition before beginning.

	Pulse Width	Pulse Frequency	Pulse Number	Initial Current	Step Size	Initial Step Size
Single Pulse Width	1 ms	n/a	1	1 mA	0.1 mA	0.2 mA
Pulse Width	1 ms	50 Hz	10	0.75 mA	0.05 mA	0.1 mA
Pulse Frequency	1 ms	25 Hz	10	1 mA	0.1 mA	0.2 mA
Pulse Repetition	1 ms	50 Hz	5	1 mA	0.1 mA	0.2 mA

Table 1: Configuration for Each Condition: Factor A. Pulse Width was measured in milliseconds (ms) and Pulse Frequency in hertz (Hz). Initial current, step size, and initial step size were all measured in milliamperes (mA). Pulse Number indicates the number of pulses used in the condition.

	Pulse Width	Pulse Frequency	Pulse Number	Initial Current	Step Size	Initial Step Size
Single Pulse Width	2 ms	n/a	1	1 mA	0.1 mA	0.2 mA
Pulse Width	2 ms	50 Hz	10	0.5 mA	0.025 mA	0.05 mA
Pulse Frequency	1 ms	100 Hz	10	0.75 mA	0.05 mA	0.1 mA
Pulse Repetition	1 ms	50 Hz	20	0.75 mA	0.05 mA	0.1 mA

Table 2: Configuration for Each Condition: Factor B. Pulse Width was measured in milliseconds (ms) and Pulse Frequency in hertz (Hz). Initial current, step size, and initial step size were all measured in milliamperes (mA). Pulse Number indicates the number of pulses used in the condition

We used a custom-written MATLAB script that automatically adjusted based on the imputed responses to find the lowest intensity [perceptual threshold] a participant could detect. Perceptual threshold detection was found by using an adaptive staircase method. We used a two-down/one-up fixed step size with the presumed ratio target Δ-

/Δ+= 0.54 that converges to 80.35% correct points (or accuracy) (Garcia-Perez, 1998). Kauppila et al. (1998) used a similar method by increasing the distance of the 2-point discrimination task by 2mm (millimeters) until participants reached 80% accuracy. The adaptive staircase method in this study, differs than Kauppila et al. (1998) study, as we presumed participants detect 80% of stimulations presented. Figure 3 shows how Single Pulse stimulation factors utilized the adaptive staircase method. The fixed step size was chosen to maximize the collection of data while keeping participants from becoming disengaged from a more extended experimental design.

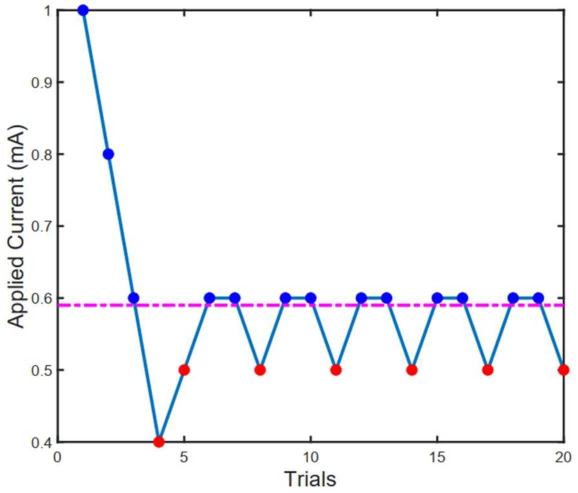

Figure 3. Adaptive Staircase Model. The Adaptive Staircase Method was used to estimate the perceptual threshold in each experimental condition. Stimulation was presented at a current level and followed by the participant responding : [YES] (blue circles) or [NO] (red circles).

Data Analysis

Data analysis was conducted using a custom-written MATLAB script to inspect sensitivity levels. As mentioned earlier, the goal is to establish if participants' perceptual thresholds change as a function of laterality, stimulation factors, and measures or interactions therein; therefore, we did not investigate the participant's reaction times in this paper. The first ten trials of Factor A and Factor B were discarded to establish perceptual thresholds, only using the last 20 trials of perceived [YES] and nonperceived [NO] responses. The rationale for excluding the first 10 trials was based on the configuration of the stimulation factors beginning at a higher ampere enabling the participant to feel the stimulation distinctly (refer to Table 2 and Table 3; initial current). Removing the first 10 trials allowed for increased accuracy in measuring sensitivity levels once participant responses had stabilized. We calculated the averaged perceptual threshold by taking the sum of the last 20 trials divided by 20 at the individual and group level.

Statistical Analysis

All statistical analyses were completed using version 28.0.1.0 of IBM SPSS Statistics. The goal of the statistical analysis was to compare the responses among the variations per condition to determine significance; thus, for this experiment, we conducted one-way repeated measures ANOVAs for each dependent variable in this experiment. Due to 73% of participants being right-handed women (11 right-handed women out of 15 participants), we elected to forgo group-by-interaction analysis and treat all participants as one group. Factor [A/B], laterality [stimulation site], and measures [active & passive] were used as dependent variables in ANOVA for the repeated measures within Conditions (Single Pulse Width, Pulse Width, Pulse Frequency, and Pulse Repetition)

CHAPTER 3

RESULTS

The computed individual and group averages per tested condition are shown in Figures 4–8 and Tables 3–6.

Single Pulse

The Single Pulse data showed a statistically significant main effect of Factor, ($F(1,16) = 102.392$, $p < 0.001$) and Measure ($F(1,16) = 4.857$, $p = 0.043$), but not for Laterality ($F(1,16) = 0.0626$, $p = 0.441$). The effect of Factor was associated with needing a slightly higher current to be perceived in Factor A ($M = 1.06858$, $SD = 0.49571$) than Factor B ($M = 0.87928$, $SD = 0.46676$). The effect of the Measure was associated with needing a slightly higher current when active ($M = 1.00135$, $SD = 0.49994$) than passive ($M = 0.94651$, $SD = 0.4799$). The two-way interaction analysis showed no significant interactions between Factor and Laterality ($F(1,16) = 1.107$, $p = 0.308$), Factor and Measure ($F(1,16) = 0.176$, $p = 0.68$), and Laterality and Measure ($F(1,16) = 0.091$, $p = 0.767$). The three-way interaction analysis showed no significant three-way interaction effect ($F(1,16) = 0.013$, $p = 0.912$).

Table 3: Results for Repeated Measures of ANOVA: Single Pulse

	DF1	DF2	F-Value	P-Value
Main Effect				
Factor	1	16	102.392	**<0.001**
Laterality	1	16	0.0626	0.441
Measure (task)	1	16	4.857	**0.043**
2-way Interaction				
Factor x Laterality	1	16	1.107	0.308
Factor x Measure	1	16	0.176	0.68
Laterality x Measure	1	16	0.091	0.767
3-way Interaction				
Laterality x Measure x Factor	1	16	0.013	0.912

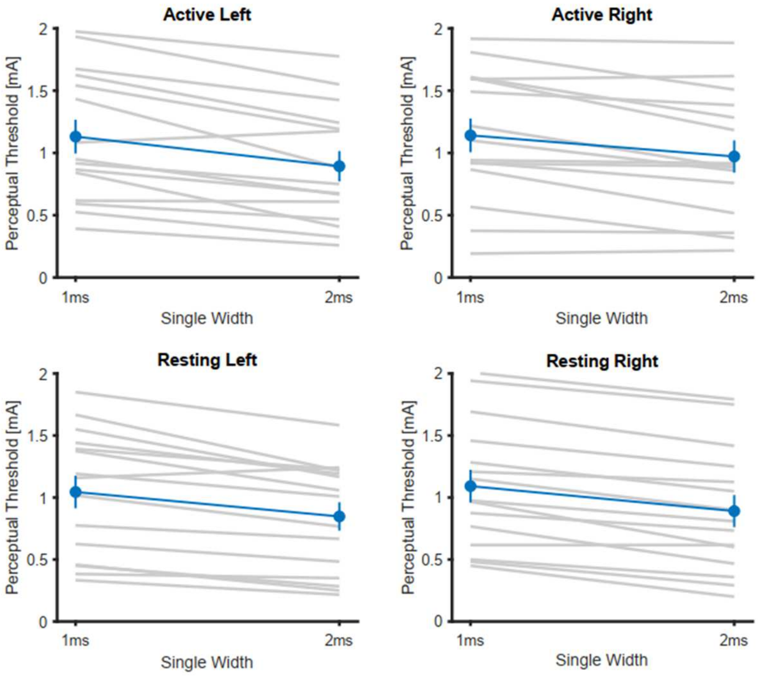

Figure 4. Averaged Sensitivity Levels of Individual and Group: Single Pulse. Graph A displays stimulation to the left side of the orofacial region during voluntary motor movement. Graph B displays stimulation to the left side of the orofacial during the resting state. Graph C displays stimulation to the right side of the orofacial region during voluntary motor movement. Graph D displays stimulation to the right side of the orofacial region during the resting state.

Pulse Width

The Pulse Width data showed a statistically significant main effect of Factor, (*F*(1,18) = 60.954, *p* < 0.001), but not for Laterality (*F*(1,18) = 0.238, *p* = 0.632) or Measure (*F*(1,18) = 0.059, *p* = 0.881). The effect of Factor was associated with needing a slightly higher current to be perceived in Factor A (*M* = 0.6642, *SD* = 0.35688) than Factor B (*M* = 0.458607, *SD* = 0.458607). The two-way interaction analysis showed no significant effects between Factor and Laterality (*F*(1,18) = 1.403, *p* = 0.252), Factor and Measure (*F*(1,18) = 0.327, *p* = 0.574), and Laterality and Measure (*F*(1,18) = 0.152, *p* = 0.701). The three-way interaction analysis showed no significant three-way interaction effect (*F*(1,18) = 0.346, *p* = 0.564).

Table 4: Results for Repeated Measures of ANOVA: Pulse Width

	DF1	DF2	F-Value	P-Value
Main Effect				
Factor	1	18	60.954	**<0.001**
Laterality	1	18	0.238	0.632
Measure (task)	1	18	0.059	0.881
2-way Interaction				
Factor x Laterality	1	18	1.403	0.252
Factor x Measure	1	18	0.327	0.574
Laterality x Measure	1	18	0.152	0.701
3-way Interaction				
Laterality x Measure x Factor	1	18	0.346	0.564

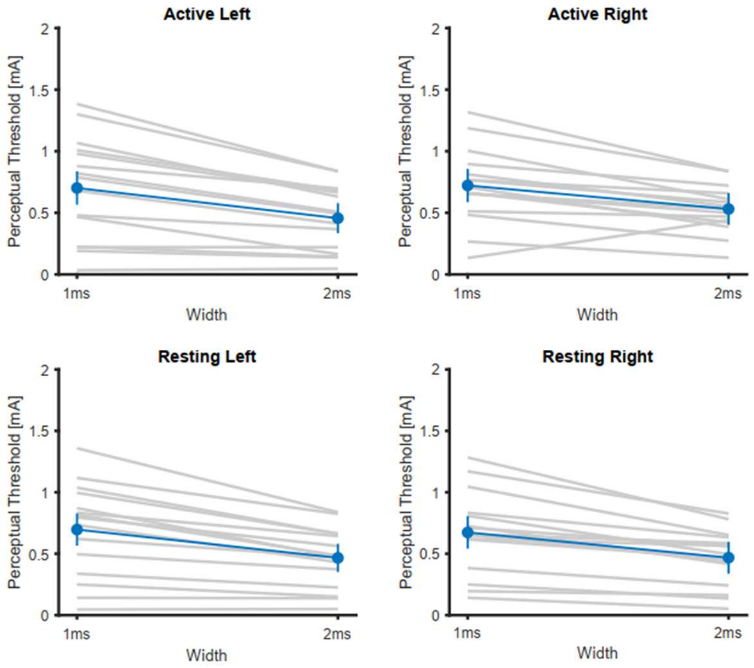

Figure 5. Averaged Sensitivity Levels of Individual and Group: Pulse Width. Graph A displays stimulation to the left side of the orofacial region during voluntary motor movement. Graph B displays stimulation to the left side of the orofacial during the resting state. Graph C displays stimulation to the right side of the orofacial region during voluntary motor movement. Graph D displays stimulation to the right side of the orofacial region during the resting state.

Pulse Frequency

The Pulse Frequency data showed no statistically significant main effect of Factor (*F*(1,17) = 0.672, *p* = 0.424), Laterality (*F*(1,17) = 0.318, *p* = 0.58), or Measure (*F*(1,17) = 0.055, *p* = 0.818). No statistical significance was found for the two-way interactions between Factor and Laterality (*F*(1,17) = 0.204, *p* = 0.657), Factor and Measure (*F*(1,17) = 0.01, *p* = 0.922), or Laterality and Measure (*F*(1,17) = 0.066, *p* = 0.80). The three-way interaction effect was not statistically significant (*F*(1,17) = 1.784, *p* = 0.199).

Table 5: Results for Repeated Measures of ANOVA: Pulse Frequency

	DF1	DF2	F-Value	P-Value
Main Effect				
Factor	1	17	0.672	0.424
Laterality	1	17	0.318	0.58
Measure (task)	1	17	0.055	0.818
2-way Interaction				
Factor x Laterality	1	17	0.204	0.657
Factor x Measure	1	17	0.01	0.922
Laterality x Measure	1	17	0.066	0.80
3-way Interaction				
Laterality x Measure x Factor	1	17	1.784	0.199

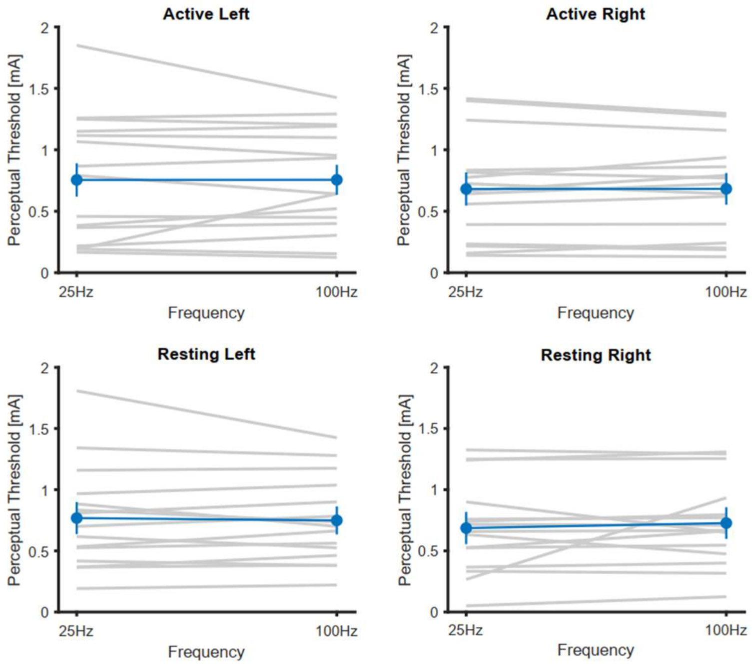

Figure 6. Averaged Sensitivity Levels of Individual and Group: Pulse Frequency. Graph A displays stimulation to the left side during movement. Graph B displays stimulation to the left side during the resting state. Graph C displays stimulation to the right-side during movement. Graph D displays stimulation to the right side during the resting state.

Pulse Repetition

The Pulse Repetition data showed a statistically significant main effect of Factor ($F(1,16) = 38.166$, $p < 0.001$) but not for Laterality ($F(1,16) = 0.272$, $p = 0.609$) or Measure ($F(1,16) = 0.804$, $p = 0.383$). The effect of Factor was associated with needing a slightly higher current to be perceived in Factor A ($M = 0.83074$, $SD = 0.43237$) than Factor B ($M = 0.6795$, $SD = 0.36456$). The two-way interaction analysis showed no significant effects between Factor and Laterality ($F(1,16) = 0.271$, $p = 0.61$), Factor and Measure ($F(1,16) = 2.593$, $p = 0.127$), or Laterality and Measure ($F(1,16) = 0.268$, $p = 0.612$). The three-way interaction was not statistically significant ($F(1,16) = 1.319$, $p = 0.268$).

Table 6: Results for Repeated Measures of ANOVA: Pulse Repetition

	DF1	DF2	F-Value	P-Value
Main Effect				
Factor	1	16	38.166	**<0.001**
Laterality	1	16	0.272	0.609
Measure (task)	1	16	0.804	0.383
2-way Interaction				
Factor x Laterality	1	16	0.271	0.61
Factor x Measure	1	16	2.593	0.127
Laterality x Measure	1	16	0.268	0.612
3-way Interaction				
Laterality x Measure x Factor	1	16	1.319	0.268

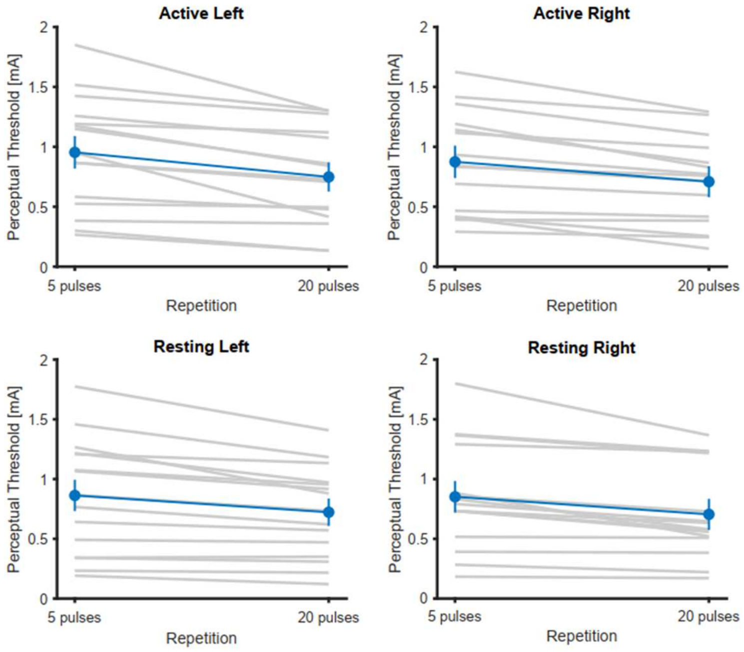

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Figure 7. Averaged Sensitivity Levels of Individual and Group: Pulse Repetition. Graph A displays stimulation to the left side during movement. Graph B displays stimulation to the left side during the resting state. Graph C displays stimulation to the right-side during movement. Graph D displays stimulation to the right side during the resting state.

CHAPTER 4

DISCUSSION

Summary of Results

The goal of this study was to determine (a) how stimulation factors affect sensitivity levels, (b) how laterality affects the detection of stimuli, and (c) how resting and voluntary motor movement affects the perception of somatosensory electrical stimuli.

Stimulation factors showed to be essential for stimulus detection. Simulation factors of Single Pulse, Pulse Width, and Pulse Repetition were shown to be the most effective for evoking somatic sensation and determining a baseline sensitivity level of the orofacial region. Though this may be the case for three of the four conditions, Pulse Frequency was shown to be ineffective in eliciting somatic sensation. The findings of Pulse Frequency indicate that manipulating frequency in the stimulation factors is inconsequential and may not play a significant role in determining sensitivity levels or provoking a somatic response of the orofacial region.

Laterality, or stimulation site, was found not to significantly affect sensitivity levels for all four conditions. Stimulation on the right or left side of the orofacial region demonstrated that the stimulation site of the orofacial region is negligible when conducting somatosensory electrical stimulation; thus, a somatic response could be generated from stimulation of either the left or right side of the orofacial region. Resting and voluntary motor movement displayed a response that was not anticipated. Resting and voluntary motor movement only showed significant effects in the Single Pulse condition, which is contrary to results of previous studies displaying that somesthetic suppression occurs during voluntary motor movement (Rauch et al., 1985; Takahara et al., 2020; Wasaka & Kakigi, 2012). This indicates that there may have been issues in how voluntary motor control was conducted in this experiment, or that the cranial nerves may react differently than the peripheral nerves during rest and motor state. Results displayed that stimulation parameters, such as pulse, frequency, and duration influence perceptual thresholds, but that electrode placement and motor tasks did not influence perceptual threshold. Overall, these findings have important implications for designing and developing therapeutic neuromodulation techniques based on trigeminal nerve stimulation.

Laterality: Left and Right-Side Stimulation

Hemispheric lateralization has been thoroughly studied on different body parts to determine how the cortex works in motor movement. This study looked at the differences in left and right-side stimulation of the inferior face during resting and voluntary muscle contraction (motor movement). Original hypotheses in this study are that (a) laterality will not affect the detection of stimuli and (b) that equal levels of stimulus sensitivity will be found in both left and right-side are supported by the results in this study. . These results support findings from previous studies that there is no indication of contralateral or ipsilateral lateralization, more so that motor control of the face occurs bilaterally and causes bilateral activation (Eickhoff et al., 2008; Behroozmand, 2015; Murphy et al., 1997).

Measures: Active and Passive

Considering that Active [voluntary motor movement] and Passive measures have been thoroughly studied in the trunk and the extremities, we expected that the results would display significance between the active and passive measures, but preliminary results did not find significance. Original hypotheses in this study were that (a) voluntary motor and muscle activation of the orofacial region will decrease the perception of stimuli, and (b) stimuli presented in a resting state will be more easily perceived with an outcome of higher sensitivity levels. Both of these were not supported by the results for most of the conditions tested. From the four conditions, only the main effect of Single Pulse Width had a significant difference, signifying that participant needed a higher amperage (or amplitude in the current) to detect stimulus when conducting voluntary muscle contraction. Based on previous findings, arguments could be made that that all conditions assessed in the Active condition would have suppression somesthetic sensation, thus meaning that the active measure would need a higher current to be detected (Rauch et al., 1985; Takahara et al., 2020; Wasaka & Kakigi, 2012). While results did not align with previous studies, this lends an observation that the cranial nerves may react, and function differently than the nerves found in the extremities.

There are several possible reasons why the results did not align with expectations, which begin with the protocol. The experimental protocol required voluntary muscle contraction to begin muscle contraction on the visual indicator and holding until the second visual indicator is displayed. Although participants were trained on this method, during the conditions, participants may not have been able to endure the consistent onset and offset (40 continuous trials for eight conditions), of voluntary muscle contraction, due to muscle or repetition fatigue skewing the statistical analysis results. The skewed result could have also occurred from incorrect timing of voluntary muscle contraction if participants did not hold contraction from the beginning of the visual indicator until the second visual indicator stimulation could have occurred during the participant's resting state of that trial.

Similarly, problems could have occurred with the experimental design and how we defined voluntary muscle contraction as "gently contracting lips as if producing the phoneme /m/." The amount of pressure used during voluntary muscle contraction may not have been substantial to suppress somatosensory sensation, thus producing inconsequential results in three of the four conditions. If this study were to be repeated to determine the effects of resting and voluntary muscle contraction of the orofacial region, an occlusal force meter could be used to account for pressure differences in the orofacial muscles (Serra & Manns, 2013). A modified occlusal force meter could assist in determining the amount of force needed to cause somatic suppression of the orofacial muscles. The modified occlusal force meter could present a study in self to determine the pressure of the orofacial muscles under different conditions. Additional other products such as one developed form Phidgets like the Spatial Precision or the Differential Airpressure Sensor could be modified and used to assist in determining the amount of force and acceleration is needed to suppress somatosensory sensation of the orofacial region.

Parameters: Stimulation Factors

The main goal of this study was to determine how stimulation factors affect somatic sensation and sensitivity levels in the orofacial region. Original hypotheses for this research question were that: (a) stimulation factors will not affect the outcome of sensitivity levels, and (b) multiple stimulation factors can be used to elicit a somatosensory response of the orofacial region. These hypotheses were partially supported by the results in conditions tested. Three of the four conditions tested demonstrated that stimulation factors were inconsequential in provoking somatic sensations with similar sensitivity levels. Pulse Frequency was the only stimulation factor that did not have statistically significant differences. These results align with findings that frequency of the stimulus could change the quality of sensation, thus reasoning as to why this condition could have been insignificant (Prausnitz, 1996). Different frequencies can be manipulated in future experiments to determine whether different frequencies could be prominent as a stimulation factor and what frequency levels are needed to produce significant effects in the orofacial region under a similar condition.

Implications

An exhaustive understanding of how the cranial nerves function serves an essential purpose not only to scientists and medical professionals but to individuals with clinical abnormalities. Somatosensory electrical stimulation protocols and experimental protocols have been thoroughly studied on the trunk and extremities of the body. Though those experiments have given insights into the somatosensory process, they have not been studied or not studied thoroughly on the inferior face. The cranial nerves investigated in this study serve many purposes, including sensory and motor innervation. This includes pain, touch, temperature, and motor movement (mastication, facial expression, etc.). However, not thought about as often are the additional functions these nerves perform, such as communication through speech [facial motor movement] and non-verbal communication [facial expressions] (Seikel et al., 2016).

This study offered novel insights into executing an experimental protocol to study how the inferior face and surrounding cranial nerves react when stimulated using transcutaneous somatosensory electrical stimulation. The protocol design from this experiment may be used as a reference for further studies to continue building a baseline protocol for somatosensory stimulation or combining other techniques to gather more information on neuroscience and clinical abnormalities of the orofacial region. Future studies can examine the effects somatosensory stimulation in different age groups and how sensation of the orofacial region changes as aging occurs. Similarly, this protocol can also be used to determine if there are differences in sensitivity levels between sexes. More complex studies can use the baseline protocol with transcranial magnetic stimulation to discern the effects of cortical excitability and somatosensory stimulation of the inferior face. The baseline protocol can also be used within itself to produce cortical excitability and paired with an electroencephalogram (EEG) to determine cortical excitability and areas of activation in the cortex.

Anatomy and Clinical relevance

Electrical stimulation to the inferior face influences the skeletal and muscular system and the cranial nerves. One of the major components being stimulated is the trigeminal system. The trigeminal consist of three major nerve divisions that work to supply sensory and motor innervation: ophthalmic, maxillary, and mandibular nerves. The nerves unit at Meckel's cave in the middle cranial fossa forms the Gasserian ganglion, where they travel towards the pons, separating into four nuclei and two categories: mesencephalic nucleus, principal sensory nucleus, spinal trigeminal nucleus, and motor nucleus. The mandibular division is the largest nerve of the trigeminal and the only branch of the trigeminal system to contain afferent and efferent nerves (Walker, 1990; Sanders, 2010; Seikel et al., 2016). Due to our parameters, the mandibular division received the most input from the electrical stimuli. The somatic stimulation supplies sensation to the mandible, mandibular teeth, mucous membranes of the mouth & two-thirds of the tongue, and the temporomandibular joint.

The secondary cranial nerve being stimulated is the facial nerve. The facial nerve has both a sensory and motor root, making this a mixed nerve that consists of three nuclei: the main motor nucleus, sensory nucleus, and parasympathetic nuclei. Unlike the trigeminal, the facial nerve has five major branches: temporal, zygomatic, buccal, marginal mandibular, and cervical. The main responsibilities include providing motor innervation to the facial muscles [facial movements], secretions of the submandibular, sublingual, and lacrimal glands, and sensation of taste. Due to our parameters, the marginal mandible nerve received the most input from the electrical stimuli. Somatic stimulation works to stimulate the depressor labii inferioris, depressor anguli oris, orbicularis oris, and the mentalis muscles (Seneviratne & Patel, 2021; Sanders, 2010; Seikel et al., 2016).

Clinical abnormalities and relevance to both facial and trigeminal nerves are noted and hold limitations. This study accounted for typical subjects. The results of this study may have been skewed by undiagnosed clinical abnormalities affecting the subject pool or could produce different results in atypical subjects.

Walker (1990) explained that the trigeminal has several sources that can lead to denervation and cranial neuropathy. Prominently, trigeminal neuralgia affects the third division of the trigeminal system by causing intense pain to the individual. Central lesions of the somatosensory cortex have a known effect on raising nociception and thermoreception ipsilateral to the lesion site. Similarly, unilateral midpontine lesions can cause ipsilateral paralysis in the muscles of mastication and decrease tactical perception (Walker, 1990). Seneviratne and Patel (2021), explain that lesions of the upper or lower neurons can cause abnormalities in the facial nerve. Clinical abnormalities such as herpes simplex, varicella-zoster, and human immunodeficiency viruses can attack the motor axons of the facial nerve. Other conditions such as neurovascular compression, fractured facial bones [including other injuries/trauma], and neoplasms significantly interfere with the facial nerves. Damage of the motor axons or other clinical abnormalities can cause denervation and cranial neuropathy (Seneviratne & Patel, 2021).

The somatosensory system is extremely complex and something that individuals utilize every day to process their surroundings. While there has been extensive interest of the somatosensory system, there is a deficit of understanding how it functions in the orofacial region. By appropriately acknowledging and recognizing clinical relevancies of the facial skeletal muscular system and the cranial nerves we were able to create a baseline protocol. The developed protocol in this study assist in gauging sensitivity levels of the orofacial region using transcutaneous electrical current stimulation to determine what factors influence perception in a meaningful manner.

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BIOGRAPHICAL SKETCH

Maya Elie Khoury was born in Mesa, Arizona on February 17, 2000. She received her secondary education at Mesquite Highschool. In 2017, Maya entered Arizona State University, where she completed her bachelor's in Speech and Hearing Science with a minor in English Literature. During her undergraduate education she was an active member in the Child Language and Literacy Lab and the Speech and Brain Research Laboratory. In January 2021, she began her master's degree in Auditory Language Neuroscience at Arizona State University. Maya continued working in the Speech and Brain Research Laboratory during her graduate education, alongside being an assistant teacher for her advisor at the university.