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Evoked haptic sensations in the hand via non-invasive proximal nerve stimulation

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Abstract

Objective. Haptic perception of a prosthetic limb or hand is a crucial, but often unmet, need which impacts the utility of the prostheses. In this study, we seek to evaluate the feasibility of a non-invasive transcutaneous nerve stimulation method in generating haptic feedback in a transradial amputee subject as well as intact able-bodied subjects. *Approach.* An electrode grid was placed on the skin along the medial side of the upper arm beneath the short head of the biceps brachii, in proximity to the median and ulnar nerves. Varying stimulation patterns were delivered to different electrode pairs, in order to emulate different types of sensations (Single Tap, Press-and-Hold, Double Tap) at different regions of the hand. Subjects then reported the magnitude of sensation by pressing on a force transducer to transform the qualitative haptic perception into a quantitative measurement. *Main results.* Altering current stimulations through electrode pairs on the grid resulted in repeatable alterations in the percept regions of the hand. Most subjects reported spatial coverage of individual fingers or phalanges, which can resemble the whole hand through different pairs of stimulation electrodes. The different stimulation patterns were also differentiable by all subjects. The amputee subject also reported haptic sensations similar to the able-bodied subjects. *Significance.* Our findings demonstrated the capabilities of our transcutaneous stimulation method. Subjects were able to perceive spatially distinct sensations with graded magnitudes that emulated tapping and holding sensation in their hands. The elicitation of haptic sensations in the phantom hand of an amputee is a significant step in the development of our stimulation method, and provides insight into the future adaptation and implementation of prostheses with non-invasive sensory feedback to the users.

Keywords: sensory feedback, electrical stimulation, peripheral nerve stimulation, haptic sensations

S Supplementary material for this article is available online

(Some figures may appear in colour only in the online journal)

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Introduction

Haptic perception is an important aspect of the human experience that exerts substantial influence on our interactions with the world around us. Upper limb amputation results in a loss of both motor and sensory function [1]. While recent technological advancements have resulted in substantial improvements in the mechanics and control of prosthetic devices, incorporating sensory feedback into these systems remains a largely unmet need [2]. A lack of sensory feedback to the users can drastically impact the usability of a prosthetic limb or hand. As a result, users typically rely extensively on visual feedback when interacting with an object, and therefore cannot reliably use the prosthesis without constant observation and focus. An increasing number of recent studies have attempted to tackle this problem of sensory deficit through various modalities of feedback [3, 4]. The stimulation methods are either an activation of sensory receptors through mechanical/electrical tactile input or a direct activation of the sensory nerves, and the resultant sensation is either non-somatotopically matched (i.e. substitution) or somatotopically matched with the sensation on the phantom limb.

Sensory substitution is a relatively straightforward, non-invasive means of providing proportional feedback using mechanical/vibratory [5–9] or electrotactile [10–15] stimulations. Although these methods do not always restore the same qualitative nature of the intended feedback, they can nonetheless provide a valuable means to relay sensory information from a prosthesis. However, differences in the perceived location of the feedback and the actual intended sensation can still limit the performance and increase response time [16, 17]. When the feedback is also somatotopically matched, studies have shown promise in providing more intuitive sensory information, which reduces the cognitive load of the induced perceptions by evoking sensations in specific regions of the phantom hand or fingers [18–23]. Different somatotopic matching techniques range widely between non-invasive to invasive studies, each with their merits and costs. Non-invasive somatotopic methods mainly involve the utilization of the natural remapping of phantom sensation onto the residual limb. After identification of these locations on the amputee's residual limb, stimulation of the sensory receptors beneath the skin at the labelled locations can result in perceived sensation of the phantom limb [16, 19]. One limitation of this type of feedback is that the continuous phantom mapping only presents itself in a limited number of amputees, and an exhaustive searching and labelling of the locations are typically required [24]. An extension of the sensory remapping is in the targeted sensory reinnervation where the residual nerves are surgically redirected to innervate a different location of the body, leading to a larger area of the phantom map [25].

Recent studies of somatotopic feedback for prosthetic users involve increasing focus on peripheral nerve interfaces using implanted electrodes. Various groups have shown that electrical stimulation of the afferent pathways contained in the ulnar and median nerves is able to induce referred sensations in the hand with varying quality and degrees of spatial resolution [20–23], which can also be incorporated into a prosthetic device. For example, Raspopovic *et al* developed a bidirectional implanted electrode setup which provided sensory feedback of a prosthetic hand's finger forces by stimulating the median and ulnar nerves [21]. Similarly, modular sensory percepts were demonstrated in a bidirectional setup by Davis *et al* by utilizing an implanted microelectrode array in the peripheral nerves of the upper arm [22]. Tan *et al* also demonstrated repeatable, stable sensory responses in two human amputee subjects [23, 26], by using a peripherally implanted cuff electrode. In these setups, numerous different locations in the phantom hand could be stimulated, and allowed the amputee to 'feel' different types of sensations (tapping, pressure, light touch, vibration).

Despite these examples of successfully induced haptic sensations, the main drawbacks of these methodologies are the invasive surgery procedure to implant the electrodes, the extensive post-surgery care, and the long-term stability issues of the implanted electrodes partly due to scar tissue accumulation and/or system failure [27, 28]. To overcome these limitations, the purpose of this study was to investigate the feasibility of a highly specific transcutaneous nerve stimulation method in eliciting localized and graded haptic sensations in the hand. Similar to the aforementioned peripheral nerve stimulation methods, this study aims to activate the afferent fibers in the proximal nerve bundles to induce referred sensations of the hand, but only via non-invasive transcutaneous nerve stimulation. A recent work by D'Anna *et al* applies transcutaneous stimulation to the median and ulnar nerve bundles in the distal stump of amputee subjects, with a single monopolar electrode targeting a particular nerve [29]. In our current study, we applied biphasic stimulation to the nerves of the proximal upper arm through a custom electrode array placed on the surface of the skin. Electrical current delivered through different pairs of closely-spaced electrodes can induce a highly specific electrode field, which has the potential to activate different nerve fibers innervating different regions of the hand. The results of this study demonstrated the functionality of this method in one amputee and seven able-bodied subjects. All subjects reported haptic sensations in varying regions of their hand, and could perceive varying amplitudes of haptic sensations corresponding to different stimulation patterns. This system has the potential to aid in the development of future non-invasive sensory feedback systems that can provide somatotopically matched sensation to prosthetic users, and could enhance user embodiment of prostheses.

Methods

Subjects

This study recruited seven able-bodied subjects (six male, one female, 20–34 years of age) and one female transradial amputee (Age: 23, two years since amputation). The amputee subject had no reported phantom limb pain, and regularly uses a myoelectric prosthetic hand. All subjects had no known neurological disorders. Each subject had modulated electrical stimulation delivered transcutaneously to the median and ulnar nerves, which induced haptic sensations in the palmar side of

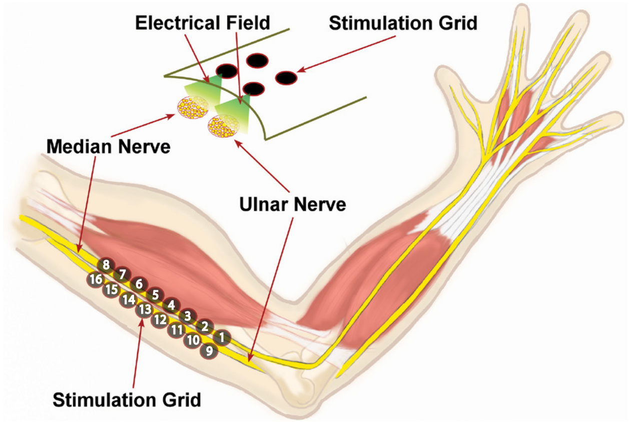

Figure 1. Diagram of stimulation electrode array placement. The electrode array was placed on the skin near the biceps where the median and ulnar nerves are most superficial. Varying the electrode pairs used to deliver the electrical current theoretically produces a variable electrical field which could preferentially activate different axons in the nerve bundles.

their hands. Prior to any testing, subjects gave informed consent (approval number: 16-1852) approved by the Institutional Review Board of the University of North Carolina at Chapel Hill.

Experimental setup

The subjects were seated in a chair with both of their arms resting comfortably on a table. In order to activate different portions of the nerve fibers in the median and/or ulnar nerve bundles innervating different regions of the hand, a 2×8 grid of electrodes were placed along the medial side of the upper arm = beneath the short head of the biceps brachii (figure 1). This location was chosen for its superficial access to the median and ulnar nerve bundles. The median nerve innervates the index, middle, and part of the ring finger while the ulnar nerve innervates the pinky and part of the ring finger. Depending on the pairs of electrodes used in the grid, different groups of neurons in the nerve bundles could be activated based on their position in the imposed electric field, leading to percepts produced in different areas of the hand. Each individual electrode was a ~1 cm wide disk cut from standard Ag/AgCl gel electrodes (Kendall H59P Cloth Electrodes, Covidien, Mansfield, MA, USA). Prior to the electrode grid placement, a bar electrode (3 cm inter-electrode distance, Cadwell Concave Bar, Cadwell, Kennewick, WA) was used to validate the general location of the median and ulnar nerves, which can help optimize the grid placement later. Specifically, the concaved space below the bulge of the biceps muscle was palpated by the experimenter to feel for the brachial artery, which anatomically runs parallel to the ulnar and median nerve bundles. The bar electrode was initially placed and manually held over this area on the medial side of the upper arm. Brief pulses of electrical stimulation (1 s duration, 3 mA, 200 μs pulse width, and 150 Hz) were delivered transcutaneously with minor adjustments to the held position to verify subjects could feel some sensations in their hand (or phantom hand).

Following the initial verification, the grid electrodes were placed over the same region and generally aligned parallel to the direction between the medial epicondyle of the humerus and the center of the axilla. Each of these electrodes were connected to the columns of a switch matrix (Agilent Technologies, Santa Clara, CA), the rows of which were connected to the anode and cathode of a stimulator channel. A custom MATLAB (version 2016b, MathWorks Inc., Natick, MA) interface was used to activate any of the switches so that the anode or cathode could be connected to any pairs of the 16 electrodes. Two such electrodes could then be dynamically chosen to change the stimulation location. Safety protocols were enforced within the program so that only one connection to the anode and cathode could be made at any given time.

Stimulation pattern generation

A multi-channel programmable stimulator (STG4008, Multichannel Systems, Reutlingen, Germany) was used to deliver electrical stimuli to the subjects. Charge-balanced biphasic square-wave stimulus current from the stimulator was controlled using a custom-made Matlab interface which could freely modulate the stimulation current output with a temporal resolution of 20 μs, a current resolution of 2 μA, and a current maximum of 16 mA. Within these limits, the pulse amplitude, width, and frequency could be modulated programmatically to fit any desired parameter. Different increasing or decreasing stimulus patterns could also be generated which allowed for a change in a specific current pulse parameter over time while others remained constant. Although any of the stimulation parameters could be modulated, the pulse width was chosen as the main parameter to change whilst the pulse frequency and current amplitude were kept constant during each trial. In this study, three main patterns were utilized and named based on their overall appearance. The 'Triangle' pattern involved a linear increase and an immediate decrease of the pulse width, whereas the 'Trapezoid' pattern, as the name suggests, had a linear increase to a held plateau followed by a linear decrease of the pulse width. Lastly, the 'Two-Peaks' pattern involved a linear increase and short decrease to a mid-level plateau, back up to the same initial peak value as before then followed by a linear decrease of the pulse width. The patterns were selected to emulate different types of haptic sensations: Triangle as a single tap, Trapezoid as a press-and-hold, and the Two-Peak as a double tap in rapid succession. These patterns were determined based on initial pilot testing, and were chosen as a way to test the sensitivity of the different referred sensations in the hand to different rising, falling, and constant intensities of stimulation. Examples of these patterns are later shown with the results in figure 5.

Sensation matching and recording

In order to quantify the subjective sensation of the stimulation, the subjects were asked to match the magnitude of the haptic sensations felt in one hand by pressing on a force transducer (LCM201-100N, Omega Engineering Inc., Stamford, CT, USA) with the other hand. The subjects were also asked to verbally report the regions where the sensation was localized in the hand. The subjects were stimulated on their right arm or the amputated side, and matched the haptic sensations with their left or intact hand. During the stimulation, if the subject felt nothing in their hand, they were asked to completely lift their finger/palm from the force transducer. The force signal was sampled at 1 kHz, and was synchronized with the stimulation. In addition to the sensation magnitude, the localized region of the sensation in the stimulated hand was verbally reported by the subject using a reference drawing of a labelled hand which was displayed in front of the subject (supplemental figure S1 (stacks.iop.org/JNE/15/046005/mmedia)). The subject described the regions of the hand where the sensation was perceived based on the labels or simply in their own words (e.g. 'Index finger, segment 1 and 2', 'All of the index and middle', 'Left side of the palm', etc). Subjects were also encouraged to subdivide the suggested finger regions into left and right halves or even quartiles depending on the perceived specificity of the referred sensation. These locations were then recorded by the experimenter using an interface in Matlab which allowed selection of specific regions on the image of the hand displayed to the subjects. A final visual confirmation from the subject was requested prior to saving the region data.

Procedures

After the electrodes were placed, a custom vice was used to apply mild pressure to the electrodes, ensuring stable skin contact. Different pairs of electrodes were then probed with a short, constant stimulus train (1 s duration, 3 mA, 200 μs pulse width, and 150 Hz) while the subject was asked to report if they perceived any sensations in the hand. Once an electrode pair with a consistent referred sensation was found, the corresponding electrode pair was noted along with the general region of sensation. An electrode pair was chosen based on its unique region of sensation as well as a minimization of local, in-place, sensations at the upper arm. In sensory perception, it has been well documented that selective attention can amplify (or selectively process) sensory neural responses for the relevant signal, while suppressing irrelevant responses [30–33]. During our experiment, when the subject did report sensations at the upper arm, we also instructed the subjects to focus on the sensation in the hand and ignore the sensation at the upper arm, and the subjects reported that they could phase out the sensations in the arm. A constant stimulation train with a current amplitude of 3 mA, pulse width of 200 μs, and pulse frequency of 150 Hz was then used as a starting point to determine each subject's upper bound of stimulation for the specified electrode pair. During this portion of examination, the current amplitude was manually raised or lowered in increments of 0.1 mA until the current was just below the value which caused motor activation in the finger muscles. For the amputee subject, this value was selected to be below any noticeable twitching of the muscles in the residual limb. The current amplitude just below the motor threshold was then used for all the different stimulation patterns in a specific subject. Then the pulse duration was varied for the modulation of the charge density in different stimulation patterns. The maximum pulse width was set at 200 μs, which was selected based on the comfort of the subject during pilot testing, as larger pulse widths often induced more noxious sensations at the electrode locations. Given that the maximum stimulation current for sensory response was used to explore the different possible hand regions that can be sensed through different electrode pairs, and also due to time constraints, the minimum current level signifying the sensory threshold was not identified. Instead, the minimum pulse width of 20 μs (the resolution of the stimulator, presumably below the sensory threshold) was used for each stimulation pattern (see the Limitation section for this procedure).

For the Two-Peaks pattern, the middle plateau value was set at 160 μs (80% of maximum). The 80% maximum was determined based on a pilot testing with a range of values from 20% to 80%, such that with a 20% of charge reduction, the subjects could perceive a decline of the haptic sensation, and, meanwhile, most subjects could still feel some low level sensations (i.e. above the sensory threshold). Each of the stimulation patterns was repeated 15 times with 2 s of resting. The order of each set of stimulations was randomized between the different patterns. At the start of each stimulation train, the subjects were asked to match the magnitude of the sensation as best as possible, and were then asked to report the location of sensation immediately upon completion of the trial. The same procedure was repeated in other stimulus electrode pairs that could elicit a different sensation region, and typically four to six unique regions were found for each subject.

Data processing

Of the 15 repeated patterns for each trial, only the last ten repetitions were used for further analysis, in order to exclude the initial variability that was present at the start of each trial as the subject became familiarized with the sensation matching task for the new pattern. This force trace was then partitioned into ten separate traces with an additional 1 s before and after the stimulation. As each matched force had a variable amount of lag between the timing of stimulus input and the response of the subject, the force of each trace was shifted in time based on its correlation with a given stimulation pattern. After time-alignment, the average of the ten force traces was calculated for that trial. Once the sensation-matched force average for each pattern was obtained, force values from each force trace were extracted as summary values for each trial. This process is illustrated in figure 2.

In order to compare the stimulation input and force output, the average force trace of each pattern was normalized to its own maximum, and the sensation input was also normalized to the maximum pulse duration used across all trials. The root-mean-squared-error (RMSE) between the normalized stimulus intensity and the normalized average force were then calculated to quantify the degree of match. All of these values were then grouped by stimulation pattern type and by subject, and averaged to obtain an RMSE average for the three patterns

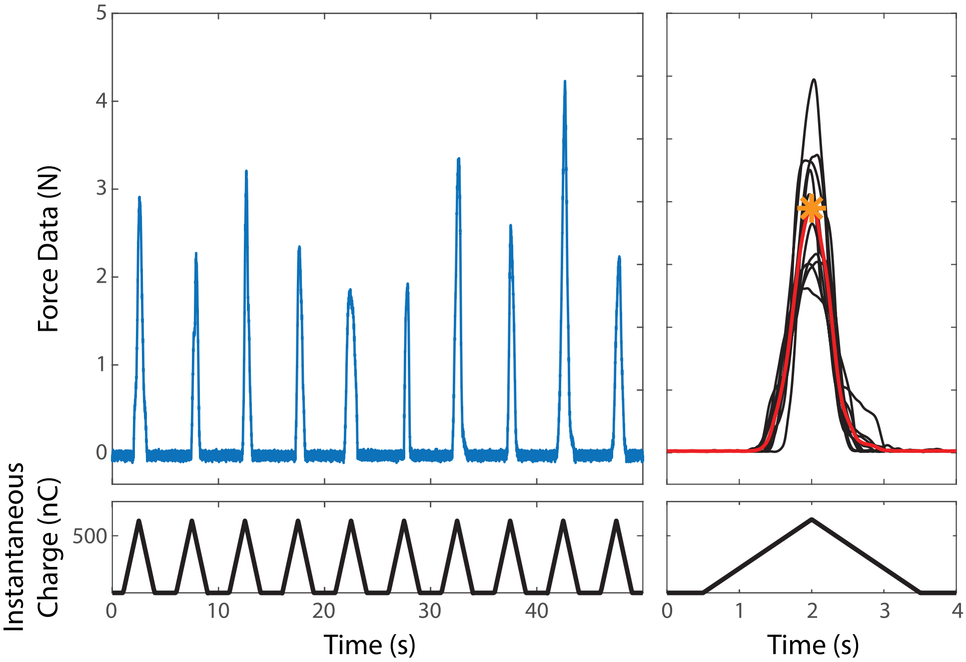

Figure 2. Sensation-matched force trace split. Force values remain unnormalized for sample purposes. Left: blue trace indicates the last ten sensation-matched forces in a trial. Right: red trace indicates the average force of the individual the time-correlated forces (black). Bottom plots contain a sample of the instantaneous charge envelope of the stimulation train delivered. In this example of the Triangle pattern, the absolute peak force (indicated by the orange asterisk) was extracted and saved prior to normalization.

for each subject. A One-Way Repeated Measures analysis of variance (ANOVA) was used to investigate if there was a significant difference in the RMSE values between the stimulation pattern types, in order to evaluate whether the tasks with different extents of dynamic components of varying current levels have an impact on the performance. Specifically, the Trapezoid pattern has the least dynamic component, while the Triangle and Two-Peak patterns have more dynamic components. A post-hoc pairwise comparison with Bonferroni adjustment for multiple comparisons was used to further elucidate the matching differences between patterns.

Results

Regions of sensation in the hand

All subjects qualitatively described the stimulation-induced sensations as a vibration, a pulse, or a fast tapping of the skin localized to specific regions of the hand. During a single set of stimulation locations, the localized regions of sensation did not vary noticeably between different stimulation pattern types. Therefore, the reported sensation locations elicited from each electrode pair were combined so that each set of stimulation trials could be represented by a single region of the hand. Each of these regions was then combined to map the different sensation locations for each subject. Figure 3 displays the individual sensation regions for all the subjects. Each shaded color represents a single stimulation set from a specific electrode pair. Regions with multiple overlapping colors indicate areas of the hand that the subject reported the stimulation sensation across different stimulation sets. Although the electrode pairs during the experiment were selected based on those which elicited strong unique sensations, some overlap was inevitable. The electrode grid below each sensation map are the color-coded electrode pairs which were used to induce the corresponding sensations. Each numbered circle corresponds to the electrode grid placement in figure 1, and circles with multiple colors indicate that single channels were used in multiple different anode-cathode combinations. Specificity of the anode and cathode has been ignored as previous preliminary tests did not result in any noticeable differences in the sensation felt.

Figure 3(A) represents the haptic sensations reported in the phantom hand of the amputee subject. Across the different sets of stimulation locations, all the five fingers were reported to have sensation at least once. Multiple different electrode locations reported sensations in the middle, ring, and little fingers with varying proportions focused on each finger. In one stimulation set, the amputee subject also explicitly reported a sensation in the thumb localized to both the palmar and dorsal sides of the hand. All the able-bodied subjects also reported multiple sensation regions (figure 3(B)), but some did not experience sensations in all of their fingers. None of the selected electrode pairs that were reported involved any sensations on the dorsal side of the hand, so these have been excluded. Depending on the stimulation intensity and electrode pair, some subjects (e.g. C1, C3) also reported a highly localized sensation to a portion of their finger segments. Although a large majority of reported sensations were localized to the fingers themselves, a number of subjects (C3, C4, C5, C6, C7) reported some sensations in palmar regions of the hand. Overall, the electrically elicited haptic sensations typically followed the anatomical innervations of the ulnar and median nerves. All multi-finger sensations were reported

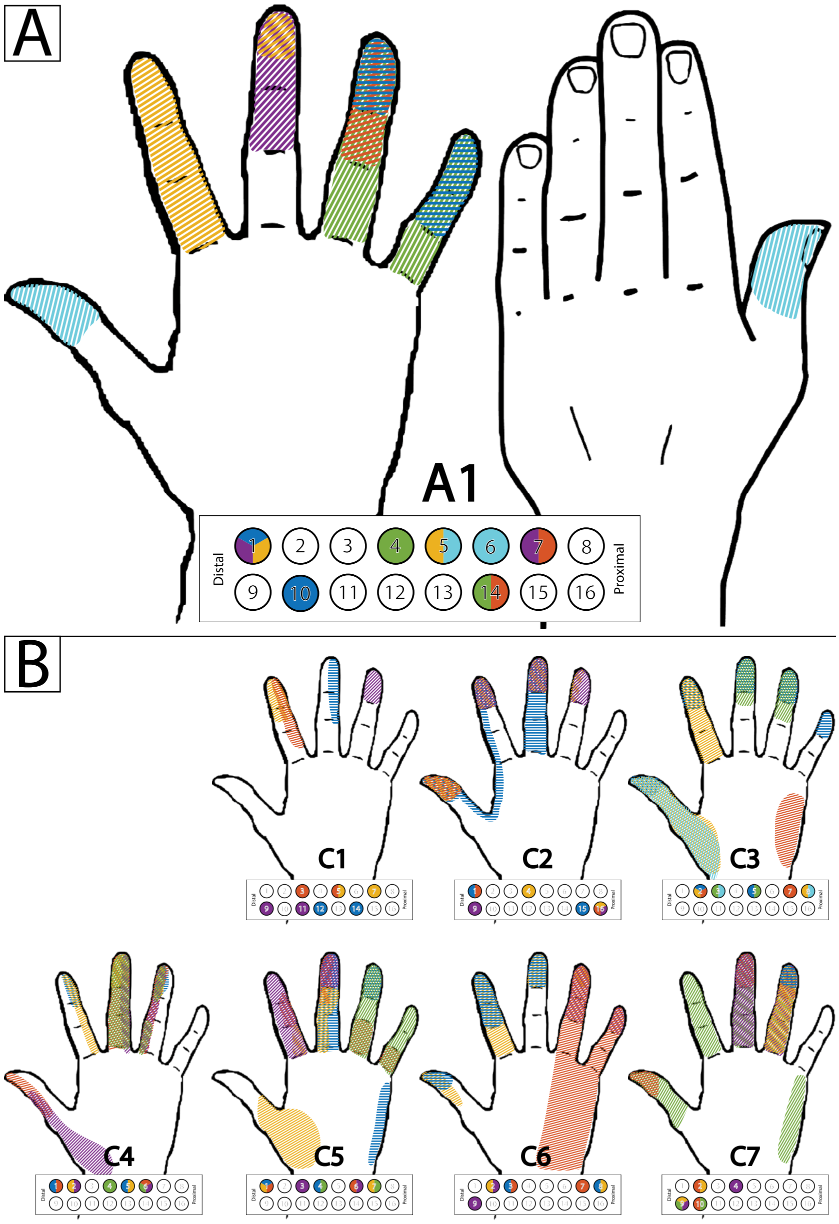

Figure 3. Subject hand map. (A) Enlarged view of amputee subject. (B) Palmar view of all able-bodied (control) subjects. Each shaded region of a specific color represents the reported region of sensation for a single electrode location. Colors between subjects have no correlation to each other or to any specific electrode pair.

with adjacent finger regions, with no non-adjacent sensation regions reported concurrently by the subjects.

In a general overview of the electrode pairs used, no directly obvious pattern between the stimulation location and the induced sensation region is visible. Although at the macro level, we placed the electrode grid in similar locations between subjects, the overall anatomical variability between subjects would likely lead to different electrode pairs that can activate similar sensation regions. One notable occurrence is the repeated overlap of certain single channels across different trials. Additionally, three of the able-bodied subjects (C3, C4, C5) also only had effective electrodes in the first row, potentially due to the anatomical variations of the subject or electrode placement variations.

Sensation-matched force

Figure 4 shows a set of data from the amputee subject with the regions of sensation and the three stimulus pattern matching tasks. The current amplitude for the amputee subject was set at 2.2 mA and the absolute reported force values were 2.3 ± 1.4 N across all the trials. Figure 4(A) displays the sensed regions of the missing hand that were reported by the subject. Each of the colored regions represents a single electrode pair which was chosen for the given trial, which also matches the colors of the reported sensation magnitude. The shaded region corresponds to the combined regions of sensation for all three stimulation patterns. Figures 4(B)–(D) illustrate the normalized sensation-force (solid line) overlaid by the normalized charge delivered

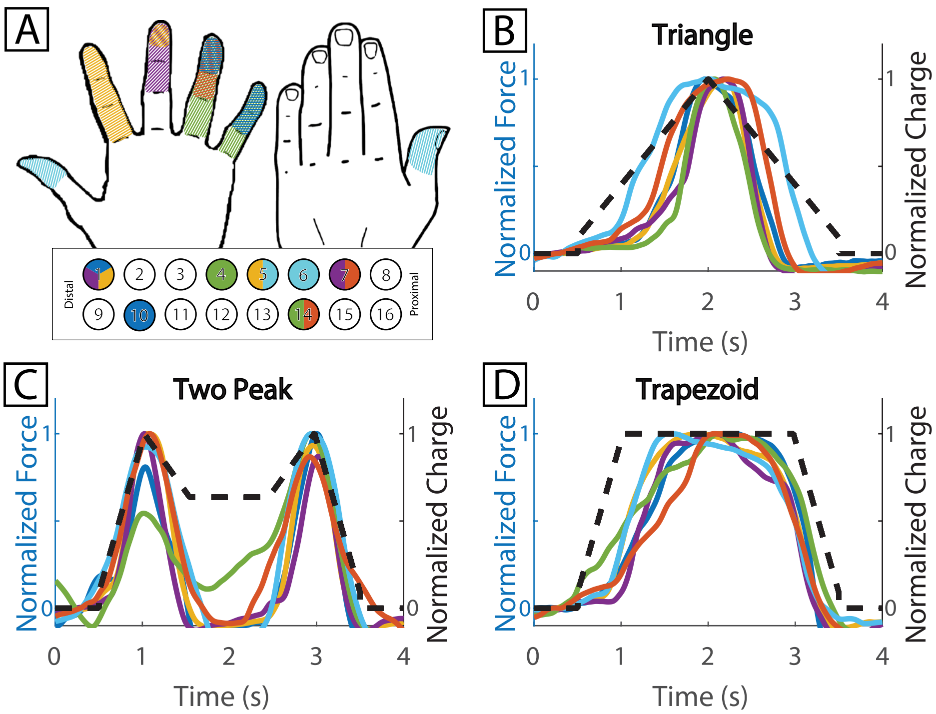

Figure 4. Sensation matching trial data (A1). (A) Multiple overlaid regions of sensation across the three reported patterns. Also shown in figure 3. The included grid uses the color coded trials to indicate which electrode pairs were chosen for the stimulation. (B)–(D) Overlaid charge input and sensation-matched force output corresponding to each pattern type. All traces have been normalized to its own maximum.

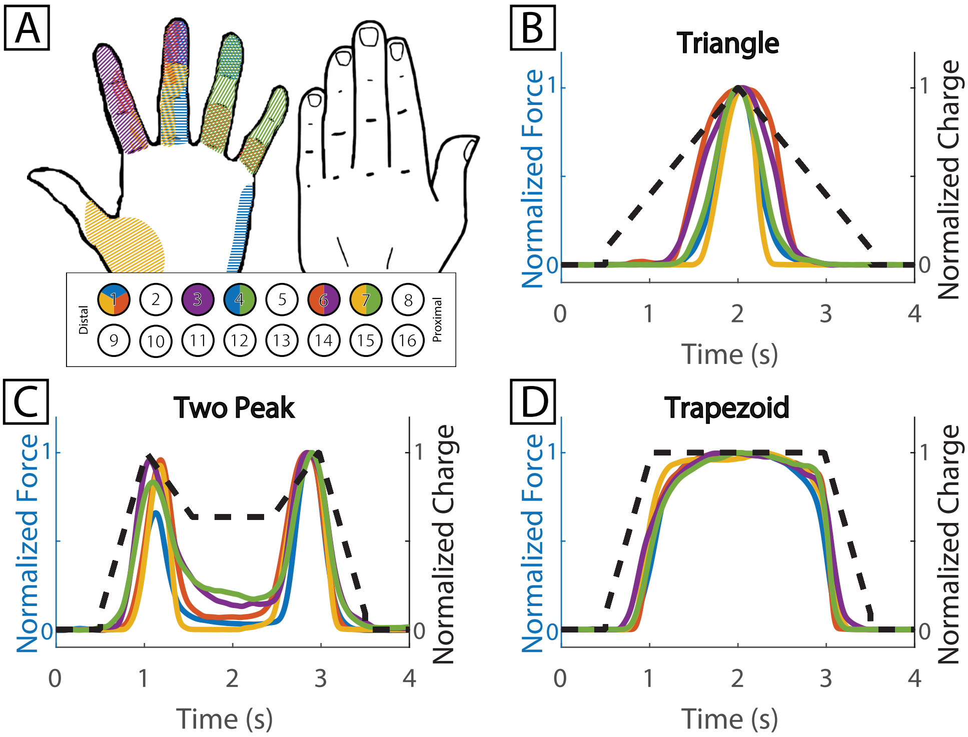

Figure 5. Sensation matching trial data (C5). (A) Multiple overlaid regions of sensation across the three reported patterns. Also shown in figure 3. The included grid uses the color coded trials to indicate which electrode pairs were chosen for the stimulation. (B)–(D) Overlaid charge input and sensation-matched force output corresponding to each pattern type. All traces have been normalized to its own maximum.

over time (dash line) for each of the stimulation patterns. Figure 5 demonstrates the similar results of a representative able-bodied subject with sensed regions across all the fingers. A condensed display of all the matched force patterns for each subject is available in supplemental figure S2.

As shown in figure 4, the majority of stimulus-sensation trials for the amputee subject followed a similar general response shape for each pattern. For the Triangle Pattern, sensation was typically not reported in the lower intensity ranges at the start and end of the stimulus pattern, but only in the

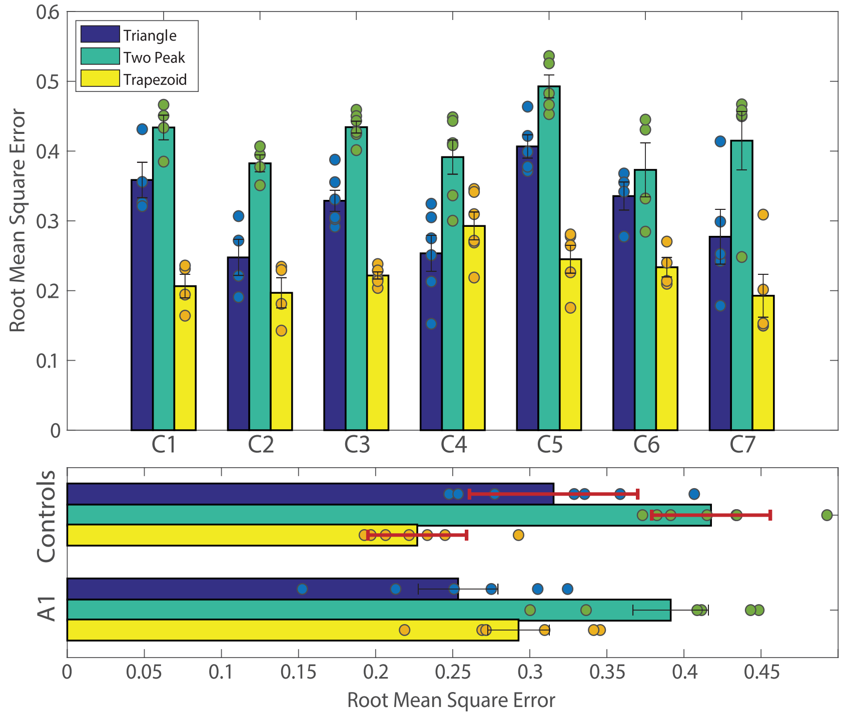

Figure 6. Grouped RMSE summary. (Top) individual RMSE for all trials/locations from able-bodied control subjects. Dots indicate RMSE of each pattern matching trial. Thin black error bars are standard error for each pattern. (Bottom) the means of each able-bodied subject was calculated and grouped to represent the total able-bodied subject's RMSE range. Thick red error bar represents the 95% CI of the able-bodied group. A1 is the data from the amputee subject.

center when the current intensity was at a higher value, largely due to the sensation threshold effect. For the Two-Peak pattern, no sensation was reported in the middle plateau with lower charge in all but one trial, also likely due to the fact that the stimulus was below the sensation threshold. Lastly, the Trapezoid pattern typically led to a reported sensation similar to the Triangle, but with a prolonged center plateau which matched the duration of the held stimulation level. All able-bodied subjects exhibited similar overall sensation-forces in response to the three stimulation patterns. The grand mean of the able-bodied subject's absolute peak forces was 6.5 ± 5.9 N (Mean $\pm$ Std. Dev). However, most of the able-bodied subjects (six out of seven) reported some non-zero force during the middle plateau region in the Two-Peak pattern, as shown in figure 5(C), indicating that the middle plateau stimulation was above the sensation threshold for those subjects.

Group summary of matching errors

The RMSE between the stimulus current charge and the response force was calculated to quantify the matching error of each stimulus pattern for each subject (figure 6). As mentioned previously, the Trapezoid pattern exhibited the lowest error across all able-bodied subjects (0.23 ± 0.013) as shown in figure 6, while the Two-Peak pattern had the highest error across both subject groups (0.42 ± 0.16). The Triangle pattern fell between the other two patterns at 0.32 ± 0.022. A One-Way Repeated Measures ANOVA showed a significant effect on the stimulation pattern [$F = 42.7$, $p = 3.49 \times 10^{-6}$]. The subsequent post hoc analysis revealed that the RMSE of the different stimulus patterns all differed from each other (Triangle versus TwoPeak: $p = 0.0012$; Triangle versus Trapezoid: $p = 0.041$; TwoPeak versus Triangle: $p = 0.00024$). The group summary of the able-bodied subjects was then compared with the amputee subject. The 95% confidence interval (CI) of the matching errors of the three stimulus patterns are (0.26, 0.37) for the Triangle pattern, (0.38, 0.46) for the Two-Peak pattern, and (0.20, 0.26) for the Trapezoid pattern, respectively. The mean matching error of the amputee subject for the three stimulus patterns are 0.25, 0.39, and 0.29 respectively. Only the Two-Peak RMSE fell into the 95% CI of the able-bodied subjects, indicating no difference between the able-bodied and amputee subjects for that pattern condition. The Triangle pattern RMSE for the Amputee lies just below the 95% CI of the able-bodied subjects, indicating the subject was significantly different, but in this case means there was a lower error. Contrastingly, the Amputee's Trapezoid pattern RMSE lies above the able-bodied subject 95% CI, signifying that the amputee subject was significantly different and had a higher error for this pattern.

Discussion

This study focused on exploring the efficacy of a transcutaneous proximal nerve stimulation method on the graded and localized generation of haptic sensations in the hand. Using a grid of small stimulation electrodes, several unique percept locations were able to be found and consistently activated. Variations of the stimulation location via changes in active electrode channel pairs on the grid allowed for repeatable alterations in the percept locations. Different patterns of stimulation were also utilized to emulate different types of touch sensations such as tapping or holding. Our results show that our non-invasive stimulation method is capable of providing both selective and differentiable sensory feedback to the subjects. These outcomes demonstrate the feasibility of this stimulation approach to be used for future prosthetics development.

Spatial coverage and resolution

Our stimulation method elicited both single-finger and multi-finger sensory feedback across all of the five fingers in most of the subjects, and in at least three fingers in all the subjects. In contrast, other comparative invasive studies with implanted cuff electrodes are limited by whichever percept regions are available to the user after implantation and do not typically have the freedom to find other locations [20, 21, 34]. As previously mentioned, the different stimulation regions found in this study were consistent with the physiological regions of innervation of the ulnar and median nerves. In a recent study, D'Anna *et al* have purposefully targeted one or both of the distal branches of the ulnar and median nerves near the distal end of the residual limb to activate different sensory regions of the hand [29]. Compared with this study, our results showed similar spatial coverage of the hand across the fingers and the palm, but our experimental design differs in several aspects compared with the previous one. First, instead of using a single electrode with a monopolar stimulation mode, our high-density electrode grid with bipolar stimulation allows us to impose more focal electrical fields, which has the potential to dynamically target different regions of the hand. Although precise quantitative comparison is difficult, the regions of the sensation induced in the D'Anna *et al* study were generally limited to inducing sensations in large regions of the hand including the palm and several fingers. In our present study, we were able to induce more localized sensations in single or multiple fingers. Second, although the D'Anna *et al* work can lead to a self-contained compact prosthesis, in our approach, there are also several practical advantages of targeting the proximal bundle rather than the distal branch. Specifically, the skin contact and the relative position of the stimulation electrodes at the proximal segment are less likely to be interfered by the socket of the prosthetic hand. In addition, the proximal nerve stimulation may also induce relatively smaller stimulation artifacts to the electromyogram recordings for myoelectric control. These different aspects are important for future applications of this method in bi-directional prostheses with combined motor control and sensory feedback.

Accessibility of inducing referred sensations across the whole hand was a key point of interest in the current study. Using a microelectrode array, Davis *et al* showed that the coverage of percept areas were directly correlated to the physiological organization of the targeted nerve with electrode implant [22]. Although intuitively obvious, this physiological limitation suggests that any nerve stimulation technique targeting haptic sensations across the whole hand must be able to electrically activate both ulnar and median nerves. Our technique demonstrates mixed success in this regard. Figure 3 shows that the subject who reported sensations in only three fingers (C1) had the index, middle, and ring fingers with evoked sensations. It is possible that the electrode array setup for that subject was only able to activate the median nerve. Subjects C2 and C4 also displays a similar percept coverage that suggests only the median nerve was activated. Despite palpating for the nerve location as well as using anatomical landmarks, these cases are indicative of the subject variability and overall sensitivity to the electrode placement inherent in our current study. However, the overall success in spanning all the fingers for the rest of the subjects shows promise in the ability of the electrode array to target both of the adjacent median and ulnar nerves. For future development, smaller individual electrodes and a denser electrode grid can potentially improve the spatial coverage and resolution to the same overall area, allowing higher probability of an electrode pair, which could activate both of the desired nerve bundles.

In addition to the overall spatial coverage across the stimulation trials, the spatial resolution of the individual sensation trials also varied across subjects. The sensory percepts were typically refined enough for the subject to identify specific phalanges, or even specific regions of a single phalanx. However, a few subjects reported large percept areas that included a wide region on the palm of the hand. In previous studies utilizing implanted electrodes, the sensory regions were typically limited to small regions in the palms or fingers. For example, using an implanted cuff electrode, Tan *et al* showed channel-specific percept areas that ranged in size between just the tip of the thumb to an area crossing one or two joints [23]. Comparatively, our transcutaneous method and that of D'Anna *et al* [29]. have relatively larger percept areas, with a range from single phalanxes to single or multiple fingers. Despite this difference in resolution, the method presented in this study is novel in that it has the advantage of dynamically choosing the desired area by searching through the different electrode pairs. The relatively larger percept area of our results could be explained by our modulation of pulse width, or effectively charge density. Recent literature suggests that increases in the charge per pulse can increase both the recruited population size (total area of sensation) and the perceived intensity [35] As we varied the pulse width over time, it is possible that we induced changing percept areas within each short stimulation pattern, while only the most prominent region paired with the maximum level was reported. . It is necessary to further test the spatial resolution using lower current intensities and different parameters in further studies.

Differentiation of different stimulation patterns

Although only a few sample figures were provided, all subjects were able to sense and differentiate between different stimulation patterns and amplitudes. Despite the thresholding effects seen in the Triangle and Two-Peak patterns, both the able-bodied and amputee subjects demonstrated differences in sensation from the modulated charge delivered with stimulation patterns. As a general overview, all subjects reported an increasing and decreasing sensation-matched force which correlated to the amount of charge delivered for the Triangle pattern. The amputee subject did not sense any difference between the center plateau and zero in the Two-Peak pattern, as a result of the current density of the center plateau being below the sensation threshold. Most of the able-bodied subjects were able to differentiate between the two, and depending on their relative threshold, subjects showed that a 40 μs decrease in the pulse width delivered could be sensed.

Sensation type, quality, and force-matching

It is important to note that although the stimulation method in this study was able to induce somatotopically matched referred sensations in the hand, the quality or type of the sensation can differ in modality compared to true natural sensations. Subjects reported the stimulation sensation in their hand often times as a vibration or pulsing which qualitatively differed from normal pressure or touch, although fingertip tapping sensations have also been reported. However, these differences in sensation modality are common across studies of somatotopic sensory feedback, especially with electrical stimulation [19, 23, 29]. Implanted nerve electrode studies have reported more natural perceptions of force [21, 26], which was achieved based on the modulation of the stimulation parameters. Further investigation of the temporal stimulation parameters is necessary to understand if more natural modalities of sensation can be generated through our peripheral nerve stimulation.

In sensory perception, the magnitude or intensity of a sensation is one of the simplest dimensions to internalize and report [36]. Despite the inherent differences between our stimulation sensation and the matched pressure in the other hand, there may not be significant biases in the quantitative conversion of this subjective qualia. However, one potential source of error is that the magnitude of the stimulation sensation is much stronger than that of a typical sensation of touch or pressure involved in object manipulation. One related observation is that the absolute value of the matched forces were around 6.5 N, which is relatively large in comparison to the forces needed for normal activities of daily living (<5 N) [37]. Assuming that the subjects were matching the relative magnitude of the induced sensation as instructed, this may indicate that subjects were experiencing sensations which were larger than those normally encountered. Further investigation on the relative scaling of the haptic sensations is also needed to better provide a more accurate quantification of magnitude for future prosthetic integration.

Non-invasive stimulation and adaptability

The major benefit of the proposed haptics stimulation method lies in its non-invasive implementation. Many recent electrical stimulation methods for somatotopic sensory feedback have involved implanted electrodes which require surgery, post-surgery care, and specialized system maintenance. Other non-invasive electrical stimulation methods have been developed which utilize projected hand maps on the residual limb of amputees to induce referred sensations of the phantom hand [17, 19]. Other methods of non-somatotopic sensory substitution is also a common approach to inducing haptic feedback [1]. In principle applying a mechanical or electrical perturbation on a different area of the body is technically simple to implement because there only needs to be a direct matching of sensation intensity. Studies have shown that comparable performance between somatotopic and non-somatotopic methods can be achieved after sufficient training [15]. However, despite the simplicity and benefits of sensory substitution methods, a non-invasive somatotopic feedback method is still a valuable and potentially more universal approach to provide sensory feedback for amputee subjects without significant involvement of subject training. Although our current study did not include any direct functional tasks, the ability of all subjects to immediately translate and report the magnitude of sensation at a specific region of their hand provides insight into its ease of use and adaptability. Combined with the consistent anatomical placement of the electrode grid and ability to rapidly switch between electrode pairs to search for different percept regions, our methodology requires minimal initial risk and experimental investment for potential users.

Limitations

One limitation of our method is that the relative location of the electrodes over the skin and the underlying nerve bundles can change if the subject has substantial movement. This change can be overcome since multiple redundant electrode locations typically exist within the array, which can activate similar percept regions. An automatic system to catalogue the electrode pairs and their finger locations could be used to better register the activation and make up for any changes in the sensation region during an experiment. Another limitation inherent in the transcutaneous stimulation is that the exact position of the nerves is unknown. Even with anatomically guided electrode positioning, effective stimulation of both the ulnar and median nerves is not assured. As mentioned previously, targeting both nerves is crucial for complete coverage of the hand. This limitation can be better controlled by using a grid with a larger number of smaller electrodes that covers a denser area surrounding the nerves, improved electrophysiological modeling of the upper arm, as well as imaging techniques that can determine the best positioning of the electrodes. An additional factor to consider in our results is the potential confounding of the in-loco sensation magnitude and the sensations in the hand. Although subjects attested to ignoring any sensations at the stimulation site, the true separation of the two qualia is unknown. Lastly, since eliciting haptic sensations across the whole hand was a central focus of the current study, a maximum current below the motor threshold was used, and the sensory threshold was not identified for each electrode pair. As a result, when the current increased from minimal value to the maximum value, a certain section of the electrical profile was subthreshold, which could influence the estimated errors between the reproduced force and the current input, especially in the Two-Peak pattern.

Conclusions

In summary, this study demonstrated graded and selective haptic sensations in the hand elicited through a non-invasive transcutaneous stimulation array. Subjects were able to report different sensation profiles which emulated tapping, holding, and variable touch sensations in the finger tips. Especially of note are the similar haptic sensations elicited in the phantom hand of a subject with a transradial amputation, in comparison with able-bodied subjects. Future development of this stimulation method could not only improve upon adaptation and control of prosthesis, but could also have wider uses in the clinical setting as a non-invasive electrical stimulation paradigm.

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