Published in final edited form as:

IEEE Trans Biomed Eng. 2019 October ; 66(10): 2761–2767. doi:10.1109/TBME.2019.2895575.

Evoked Haptic Sensation in the Hand with Concurrent Non-Invasive Nerve Simulation

Luis Vargas,
Joint Department of Biomedical Engineering at University of North Carolina-Chapel Hill and NC State University

Graham Whitehouse,
Joint Department of Biomedical Engineering at University of North Carolina-Chapel Hill and NC State University

He Huang,
Joint Department of Biomedical Engineering at University of North Carolina-Chapel Hill and NC State University

Yong Zhu,
Mechanical and Aerospace Engineering Department at NC State University

Xiaogang Hu
Joint Department of Biomedical Engineering at University of North Carolina-Chapel Hill and NC State University

Abstract

Objective: Haptic perception is critical for prosthetic users to control their prosthetic hand intuitively. In this study, we seek to evaluate the haptic perception evoked from concurrent stimulation trains through multiple channels using transcutaneous nerve stimulation.

Methods: A 2x8 electrode grid was used to deliver current to the median and ulnar nerves in the upper arm. Different electrodes were first selected to activate the sensory axons, which can elicit sensations at different locations of the hand. Charge-balanced bipolar stimulation was then delivered to two sets of electrodes concurrently with a phase delay (dual stimulation) to determine whether the evoked sensation can be reconstructed from sensations of single stimulation delivered separately at different locations (single stimulation). The temporal delay between the two stimulation locations were altered to evaluate potential interference. The short-term stability of the haptic sensation was also evaluated.

Results: The evoked sensation during dual stimulation was largely a direct summation of the sensation from single stimulations. The delay between the two stimulation locations had minimal effect on the evoked sensations which was also stable in the short-term.

Conclusion: Our results indicated that the haptic sensations at different regions of the hand can be constructed by combining individual stimulation locations directly. The interference between stimulations were minimal.

correspondence : xiaogang@unc.edu.

Significance: The outcomes will allow us to construct specific haptic sensation patterns when the prosthesis interacts with different objects, which may help improve user embodiment of the prosthesis.

Keywords

Electrical Stimulation; Haptic Sensation; Transcutaneous Nerve Stimulation; Embodiment

I. Introduction

HAPTIC perception is essential to successfully interact with the environment. Upper limb amputations result in a loss of motor function while at the same time removing their ability to receive sensory feedback [1]. In recent years, prosthetic devices have advanced greatly in mechatronics, nearly replicating the degrees of freedom of the human hand. Unfortunately, the utility of these advanced devices has been limited, partly due to a lack of direct sensory feedback to the users [2], [3]. In recent years, various techniques have been developed to reduce the sensory deficiency of amputees [1]. These approaches provide a resultant sensation that is either somatotopically or non-somatotopically matched with the sensation on the phantom limb.

Non-somatotopically matched sensation can be produced by visual, auditory, or tactile cues. For example, tactile cues are delivered using electrotactile or mechanical devices that can deliver force/angle information using a proportional stimulus [4]–[6], which can benefit object interactions, such as recognizing object stiffness [7], [8]. However, the modality and locational difference in the sensation often results in increased response times due to mismatched internal representations [9], [10]. Although training can improve the performance, the response time is still greater compared with the somatotopically-matched technique [8], [10].

Alternatively, somatotopically matched feedback can evoke spatially similar and modality matched sensation through direct peripheral nerve or cortical stimulation. These methods can potentially reduce the cognitive burden. Electrical stimulation of the peripheral nerve using implanted electrodes can induce haptic sensation with varying degrees of spatial resolution, intensity, and types of sensation [11]–[14]. Direct cortical stimulation in the somatosensory area can also produce various types of sensory perception [15], [16]. Although these invasive approaches have been successful in research settings, several concerns could still limit wide application such as the need for surgery, secondary procedures after interface damage, and long-term stability issues [17]–[19].

Non-invasive nerve stimulation approaches have been developed to address these limitations. For example, remapping of the phantom sensation onto the residual limb of the amputee has been investigated [20]. Unfortunately, sensory remapping can be cumbersome, due to relatively random reinnervation [21]. Transcutaneous nerve stimulations targeting the proximal bundle or distal branches are non-invasive alternatives that can elicit somatotopically matched haptic sensation [22]–[24]. Spatially distinct haptic sensations with controllable intensity can be induced in the hand by activating different axons of the median and ulnar nerves. Similar results have been shown in both able-bodied individuals and an

amputee through proximal nerve bundle stimulation [23], although a study on the stimulation of distal nerve branch failed to show sensations of phantom digits [24], potentially due to subtle cortical reorganization after digit amputation [25].

Despite all these developments, electrically evoked sensation has been limited to only a single stimulation location at a time, which can elicit sensations in a particular region in the hand. However, when prosthetic hands interact with different objects, spatially distributed or highly specific haptic sensations may be needed. To evoke spatially controlled haptic sensation, axons innervating distributed hand regions need to be activated simultaneously, which requires concurrent stimulation trains across multiple electrodes. Specifically, with the spatial location of haptic sensations in individual stimulations mapped out, more specific haptic sensation patterns can then be constructed through multichannel stimulations. Essentially, the individual haptic sensations at different regions can be combined to form a desired composite sensation with a spatial distribution matching the pressure distribution sensed by the prosthetic hand. However, it is not clear whether the individually evoked sensations can be superimposed directly. In addition, given that charge-balanced current is typically used, potential interference between concurrent stimulation pulse trains could occur, depending on the temporal delay between pulse trains.

To address these issues, we compared the spatial patterns of sensation during single and dual stimulations. In this context, concurrent stimulation described the concurrently perceived sensation by the subject with two interleaved simultaneous stimulus trains.. Different delays between the two stimulation pulse trains were also evaluated to quantify the potential interference of the electric field around the nerve, generated by the two stimulation trains. The short-term stability of the dual stimulation was also evaluated. Our results demonstrated that the evoked sensations during dual stimulation largely represented a direct summation of the sensations evoked from single stimulations. The temporal delay also showed minimal effect on the evoked sensation. Lastly, the dual stimulation also revealed stable sensations in the short-term. Our findings indicate that spatially complex haptic sensations during object manipulations can be constructed directly by superimposing individual sensations during single stimulations, in that the single stimulation can be considered as building blocks for more complex concurrent multichannel stimulations. The outcomes can allow us to provide spatially realistic haptic sensation for prosthetic hand users when they interact with a variety of objects.

II. Methods

A. Subjects

This study recruited seven neurologically intact subjects (6 Male, 1 Female, 20-35 years of age). All subjects had no known neurological disorders. An earlier study has shown that intact subjects demonstrated similar haptic sensations in response to nerve stimulation as in amputated individuals [23]. Each subject gave informed consent via protocols approved by the Institutional Review Board of the University of North Carolina at Chapel Hill.

B. Experimental Setup

Each subject was seated in a chair with one arm resting comfortably on a table. A grid of 2x8 electrodes was placed on the medial side of the upper arm just beneath the short head of the biceps brachii (Figure 1). The concave space below the bulge of the bicep muscle was palpated by the experimenter to identify the brachial artery, which runs parallel to the median and ulnar nerve bundles. After the artery pulses have been located, the electrode array was placed over the region, and were aligned parallel to the direction between the center of the axilla and the medial epicondyle of the humerus (Figure 1A). The electrode array allows for the activation of distinct portions of the medium and/or ulnar nerve bundles that each innervate different regions of the hand. The placement along the upper arm provides the maximum superficial access to the median and ulnar nerve bundles. Different combinations of electrode pairs in bipolar configurations can generate electric potential field around different groups of axons in the nerve bundles that produced distinct percepts at different regions of the hand.

This study used Ag/AgCl gel electrodes with approximately 1 cm in diameter (Kendall H59P, Covidien, MA). Each electrode was first connected to the columns of a switch matrix (Agilent Technologies, Santa Clara, CA), while the rows of the matrix were connected to the anode and cathode of a stimulator. A custom MATLAB (version 2016b, MathWorks Inc, Natick, MA) interface controlled the switches so that any two (for single bipolar electrodes) or four (for two bipolar electrodes) of the 16 electrodes could be connected to the cathode or anode. During dual stimulation involving two stimulation channels concurrently, the switch can select an anode and cathode electrode for stimulation channel 1, while simultaneously selecting an anode and cathode for stimulation channel 2.

A multi-channel fully programmable stimulator (STG4008, Multichannel Systems, Reutlingen, Germany) was used to deliver the single and dual electrical stimuli. Using a custom-made MATLAB interface, charge-balanced biphasic square-wave stimulus current (Figure 1C) from the stimulator was programmed. A hand map MATLAB interface was used to record the location of sensation with a total of 108 hand regions labeled, (Figure 1B). These regions were selected based on the known innervation mapping of the median and ulnar nerves. During the experiment, the subjects were asked to identify the locations of the sensation, and the sensation strength according to a three-point scale. Green regions indicated sensation of low strength, yellow regions of moderate strength, and red regions high strength. Some subjects also associated the sensation strength with the certainty of the sensation at a particular hand region.

C. Procedures

Once the electrodes were placed, a vice was used to apply mild inward pressure onto the electrodes to ensure a secure skin contact. Subjects were asked to confirm that they were not feeling discomfort or experiencing restrictive blood flow throughout the experiment. The experiment began by searching through the electrode grid for bipolar electrodes that induced haptic sensation in the hand. This form of stimulation was termed as the single stimulation. A constant pulse frequency of 150 Hz and pulse width of 200 μs per phase were used throughout the experiment, and these parameters were selected based on an earlier study

[23]. The current amplitude was dependent on the subjects, their anatomical characteristics, and electrode grid placement. The current amplitude was above the sensory threshold and below their motor threshold, and ranged from 2 to 4 mA across subjects, but was kept constant throughout the study for a given subject. The specific current amplitude was determined after bipolar electrodes that can elicit haptic sensation were identified. A current amplitude that evoked a moderate level of spatial distribution was selected, which evoked uniquely localized sensation, allowing for a better subsequent spatial analysis. A train of current pulses was delivered with a stimulation duration of 2 s. In a stimulation trial, a total of 10 batches of 2-s stimulation trains were delivered with a rest duration of 1 s between each stimulation train. After each trial, subjects were asked to report any sensations along the hand/arm, but only sensations (location and strength) in the hand were recorded using the hand map interface.

Random bipolar electrodes were then explored using the switch matrix. If the bipolar electrodes evoked sensation in the subject's hand, the electrodes were documented for future use. Among the 2x8 grid, approximately 8-12 bipolar electrodes were identified that could elicit spatially distinct sensation regions. The identified bipolar electrodes were then used to construct 5 unique sets of dual stimulation electrodes (Figure 2). Five random sets were sufficient to include different combinations of spatial regions that can cover the entire palmer side of the hand. The dual stimulation protocol involved three blocks of tests. The first examined the spatial patterns of evoked sensation during single versus dual stimulations. The second determined if altering the delay between the two stimulation trains during dual stimulation affected the haptic sensation. Lastly, the third block identified the short-term stability of the elicited sensations over 30 to 60-minute time intervals. A flowchart displaying the stimulation protocols is shown in Figure 3.

Specifically, the first block evaluated how two current pulse trains evoked the combined haptic sensations regarding both spatial location and strength. The two pulse trains were delivered to two pairs of previously identified electrodes, each producing unique regions of sensation. A delay of 3.33 ms between the two stimulation trains were used to avoid potential interference in the electric potential field. Five sets of dual stimulation locations were performed for each subject, and each set was repeated twice for a total of 10 dual stimulations. The single stimulations were also repeated for comparison, resulting in 30 total trials. The order of all the 30 trials was randomized (with a minimum 30-minute interval between the same dual stimulations) for each subject. A minimum of 1-minute rest time was provided between each set to avoid potential interference from previous sets.

The second block quantified how the delay between two pulse trains influenced the evoked sensations, because two biphasic current pulses may cause potential interference in the electric potential field, and the delay between two pulses may alter the sensation. Specifically, six delays (0.5, 1.0, 1.5, 2.0, 2.5, or 3.0 ms) were tested, with one for each trial. The order of the trials was also randomized for each subject.

The third block evaluated whether the dual stimulation could produce consist haptic sensations over time. The dual stimulation protocol, involving the 5 dual stimulation sets, was repeated once in a random order, with a minimum 30-minute interval between the same

set. The dual stimulation trials from the first block were also used for the later analysis. The average time interval between stimulations of the same electrode configuration was approximately 30 and 60 minutes.

D. Data Processing

To evaluate the degree of agreement between the elicited sensation regions, the kappa coefficient [26]–[28] was used to quantify the similarity between two hand maps (or two images in general). The kappa coefficient measures inter-rater agreement between qualitative observations. By evaluating individual sensation regions across two trials, categorical similarities can be assessed based on the location and intensity, using a contingency table. From the table, Cohen's kappa coefficient calculates the percentage of agreement while accounting for expected agreement due to chance. Prior to the calculation, the individual hand regions were digitized into a 4-level strength map. 1, 2, or 3 were used to describe the given sensation strength (low, moderate, or high), and a zero was used with no perceived sensation. The kappa coefficient can describe the level of agreement using categorical bounds proposed by Landis and Koch [27]. Kappa coefficients between 0.01-0.20 indicate slight agreement, 0.21-0.40 indicate fair agreement, 0.41-0.60 indicate moderate agreement, 0.61-0.80 indicate substantial agreement, and 0.81-0.99 indicate a near perfect agreement. Poor agreement is denoted by any kappa value less than zero.

The perceived strength of sensation was based on the subjective interpretation of low, moderate, and high for a given trial, and the level of perception may change across trials. To account for this potential subjective bias, the kappa coefficient was also calculated solely based on whether a region had sensation (denote as 1) or not (denote as 0).

To determine the similarities between single and dual stimulation, the two digitized hand maps corresponding to the single stimulation were summated. If a value above three in the summated map was identified, the value was normalized to three. The summated map was then subtracted from the dual stimulation map, indicating the potential difference in sensation between the single and dual stimulations. A zero value indicated no change in sensation in a particular region. A negative value indicated that the sensation region was weakened or lost during the dual stimulation. A positive value indicated that a new region was sensed or the sensation became stronger during the dual stimulation. A histogram was used to quantify the changes in sensation. The probabilities of new regions, lost regions, regions of increased/decreased sensation strength, and regions of no change were also calculated. The kappa coefficient was also calculated to evaluate the similarity between the summated map in the single stimulation and the sensation map in the dual stimulation.

To evaluate the effects of delay between two stimulation trains, 15 distinct kappa coefficient values from any possible pairs of delay configurations were calculated. A 6x6 upper triangular matrix summarized the kappa coefficients, and the median kappa value was calculated for each subject.

To evaluate the short-term stability of the evoked sensations from the dual stimulations, any two of the three repeated trials with identical stimulation parameters were used for the kappa coefficient calculation, yielding 15 total kappa values for all 5 dual stimulation locations. A

3x3 upper triangular matrix was also constructed for the three repeated dual stimulation trials. The median kappa coefficient value was calculated across a particular dual stimulation and across the 5 sets of dual stimulations as well.

III. Results

A. Single vs. Dual Stimulation Comparison

We first quantified whether the resulting sensations of dual stimulations could be constructed by directly summating single stimulation sensations. Figure 2 displays the sensation perceived by a representative subject during single and double stimulations. The hand maps located on the left and right correspond to the evoked sensation during single stimulation, while the center hand map shows the sensation during dual stimulations. The sample hand maps revealed similarities in both the spatial location and strength of sensations between the summated individual stimulations and the dual stimulation. The results indicated that little interference occurred between the two stimulation locations.

For each subject, all the dual stimulations were compared with their corresponding single stimulations, to determine the change in sensation. Figure 4 illustrates the change in sensation for a representative subject across all single versus dual stimulation trials. The histogram describes the number of instances in which there was an increase or decrease in sensation intensity between single and dual stimulation perceptions at a given region. A decrease in sensation level or deletion of a sensation region resulted in a negative value, while an increase or appearance of a new sensation region resulted in a positive value. The results suggested that the majority of sensation regions remained unchanged during dual stimulation when compared with the single stimulations.

Table I summarizes the results across all subjects. Over all, approximately 87.04 percent of the sensation regions were unchanged when comparing single and dual stimulations. The regions that showed altered sensations were below 4%. The degree of changes in sensation, including increased or decreased sensations levels of zero and non-zero regions, were limited to around one sensation level, which could be a result of the subjective identification of the intensity at a given time. The kappa coefficients between the sensations during dual stimulation and the summed sensation during corresponding single stimulations were calculated, and the median values were higher than 0.6, indicating a substantial agreement between the single and dual stimulation perceptions.

B. Variation in Stimulation Delay

A representative example of the sensations across the different delay conditions are shown in Figure 5A. As shown in the hand maps, the sensation regions and intensities were similar throughout the different delay conditions. The results indicated that the delay had minimal effect on the haptic perception for a given set of electrodes.

The confusion matrix (Figure 5B) shows the kappa coefficient values calculated for the sensation regions between different temporal delays. The resulting kappa coefficients revealed moderate to substantial levels of agreement. The median kappa coefficients across subject are summarized in Figure 6. The median kappa coefficient were greater than 0.4, the

lower bound of moderate agreement, when the sensation levels were considered. The median kappa coefficients were higher than 0.6, the lower bound of substantial agreement, when only regions were considered. Table II summarizes the probabilities associated with the temporal delay results across all subjects.

C. Short-term Stability of Sensation

Lastly, the short-term stability of the sensation was evaluated. Representative hand maps indicating the evoked sensations during dual stimulation over time is shown in Figure 7A. The hand maps revealed similar sensation patterns with the majority of the sensation regions remaining constant. A change in the sensation regions at 51 minutes were largely low-level sensations (shown in green). The confusion matrix summarizing the kappa coefficient values between different time points are shown in Figure 7B. The kappa coefficients revealed that there were moderate to substantial levels of agreement among the sensation regions, indicating that the haptic sensation regions were stable in the short-term.

Figure 6 shows the median kappa coefficient values across subjects. The median kappa coefficients were greater than 0.4, when the sensation levels were considered, which indicated a moderate agreement over time. The median kappa coefficient were higher than 0.6, when only regions were considered, which indicated a substantial agreement over time. Table II summarizes the probabilities associated with the stability results across all subjects.

IV. Discussion

This study sought to quantify the spatial distribution of haptic sensations during concurrent nerve stimulation over two bipolar channels, which can activate different sensory axons and elicit sensations at different locations of the hand. Overall, the results showed that the haptic sensations at different regions of the hand can be represented largely by combining individual stimulation locations directly with minimal stimulation interference. The outcomes indicated that, with the spatial locations of haptic sensation in individual stimulations, different desired haptic sensation patterns can be constructed through multichannel stimulations. The results suggest that it is possible to elicit haptic sensations with realist spatial distribution when the prosthesis interacts with different objects, which can help further improve user embodiment of the prosthesis.

Our dual stimulation results showed that there was a substantial strength of agreement when comparing combined sensation of separate single stimulations with the sensations of the dual stimulation. These results suggest that the sensory axons from sensory receptors of different hand regions, which are activated through the single stimulations, are also activated concurrently through the dual stimulation. This spatial summation of the sensation is consistent with the findings of a previous study where multi-finger perceptions were represented and identified when multiple concurrent stimulations were delivered [29].

In our study, there were indeed some instances (although low percentage) with either an addition or subtraction of perceived location, or a change in the magnitude of the sensation during dual stimulation. Several mechanisms can contribute to these changes. First, the addition of new sensory regions could potentially be explained by the recruitment of

neighboring axons which was only depolarized to sub-threshold levels during single stimulations. Specifically, these sub-threshold axons could be experiencing overlapping excitation from the dual stimulation, causing new action potential generation along these axons. A spatial subtraction could alternatively be explained by colliding depolarization which interfere with one another, and result in a net loss of action potential generation. Second, the changes in the perceived sensation magnitude may also be due to overlapping axonal depolarization which would effectively double the stimulation frequency. As has been demonstrated using a nerve cuff stimulation [30], the perceived magnitude of a sensation is dependent on both the frequency and amplitude of the stimulation. Third, this change may have been caused by a drift in an individual's subjective perception as they attempt to perform a classification of sensation strength over time.

Altering the temporal delay between the two stimulation trains was tested to evaluate the effect of potential electric field interference. By decreasing the temporal delay between 0.5 and 3.0 milliseconds, more stimulation trains can theoretically be delivered simultaneously increasing the possibility of interference. However, our results revealed substantial agreement in the spatial distribution of haptic sensation, which suggest that the temporal delay had little to no effect on the sensations evoked for a given dual stimulation. Although this result seems counter-intuitive, an alternate interpretation is that the two selected electrode pairs for each subject were unique and activated minimal overlapping axons. Therefore, it is possible that the delay can still induce interference if the two stimulation trains activated similar sets of axons. Nevertheless, the insensitivity of the temporal delay is important practically, as it allows the stimulation parameters to be altered without causing substantial interference at different sensation regions in the hand.

Lastly, we also evaluated the short-term temporal stability of the haptic perception evoked during concurrent transcutaneous nerve stimulation. Comparisons between the haptic sensations of dual stimulations showed consistent sensation regions, with a moderate agreement in sensation magnitude and a substantial agreement in the sensation regions. The results suggest that both the electrode positioning as well as the sensory summation of the dual stimulation is mostly stable in the short-term throughout the experimental session. The changes in sensation over time are largely a change in the sensation level. These differences in the sensation agreement is likely due to a shift of the electrode relative to the nerve bundle, or the subjective variability in reporting the most noteworthy sensations locations and levels. Clearly, further study evaluating longer term stability of the evoked sensation is necessary.

Limitations and Future Work

Limitations of this study include the lack of amputee subjects, analysis at different current amplitudes, and the absence of the evaluation of sensory adaptation that may occur over continuous stimulation. The use of neurologically-intact individuals to represent the haptic sensation perceived by amputees has been supported by results shown previously [23]. Namely, controllable levels of haptic sensation evoked were found to be similar in both amputee and neurologically-intact individuals, which suggests that the results from intact individuals can be representative and translatable to amputees. Others using more distal

nerve stimulation, but still proximal to the wrist, also showed sensation in the phantom digits in amputee subjects [22]. A different study, using stimulation of distal nerve branches at the palm, did not elicit sensation in the phantom finger [24]. Further study involving arm amputees is necessary to evaluate the spatial distributions of haptic sensations during multichannel stimulations. The evaluation of the potential sensory adaptation over time is essential for determining how the haptic sensation alters with continuous stimulation. Implanted electrode stimulation have been shown to have similar adaptation to that of mechanical stimulation [31]. However, the investigation on sensory adaptation have yet to be performed using non-invasive nerve stimulation approaches. We plan to evaluate the sensory adaption that occurs during continuous single and dual stimulations. The outcomes can help us to better understand the stability of evoked sensations, and help us to determine the necessary stimulation adjustment to accommodate the adaptations.

Our current study evaluated the spatial summation of sensation regions with two bipolar stimulations at a fixed stimulation amplitude. Direct representation of more complex percepts in an individual's hand may be achievable through the utilization of a larger number of concurrent stimulation trains at different current levels. Future work will be performed to determine if our findings are generalizable across higher number of stimulation sources and at different stimulation current amplitudes.

Conclusions

Overall, our results showed that haptic sensations at different locations of the hand can be reconstructed by combining sensation locations evoked during individual stimulation directly, with minimal stimulation interference. The outcomes indicated that different desired haptic sensation patterns can be constructed directly reflecting the haptic information experienced by the prosthetic hand. The haptic sensation can provide individuals with a substantial amount of sensory information that can be used to produce better control of the prosthetic hand. By producing a better replication of sensations as perceived by a biological hand, the sensory information can also increase the embodiment, and improve the user experience of a prosthetic limb.

Acknowledgments

This study was supported by the National Science Foundation (Grant #: IIS-1637892)

References

[1]. Schofield JS et al. "Applications of sensory feedback in motorized upper extremity prosthesis: a review," Expert Rev. Med. Devices, vol. 11, no. 5, pp. 499–511, Jun. 2014. [PubMed: 24928327]

[2]. Tyler DJ, "Neural interfaces for somatosensory feedback: bringing life to a prosthesis," Curr. Opin. Neurol, vol. 28, no. 6, pp. 574–81, Dec. 2015. [PubMed: 26544029]

[3]. Saunders I, Vijayakumar S, "The role of feed-forward and feedback processes for closed-loop prosthesis control," J. Neuroeng. Rehabil, vol 8, pp. 60, Oct. 2011. [PubMed: 22032545]

[4]. Cipriani C et al. "A miniature vibrotactile sensory substitution device for multifingered hand prosthetics," IEEE Trans. Biomed. Eng, vol. 59, no. 2, pp. 400–8, Feb. 2012. [PubMed: 22042125]

[5]. Kaczmarek KA et al. "Electrotactile and vibrotactile displays for sensory substitution systems," IEEE Trans. Biomed. Eng, vol. 38, no. 1, pp. 1–16, Jan. 1991. [PubMed: 2026426]

[6]. Strbac M et al. "Integrated and flexible multichannel interface for electrotactile stimulation," J. Neural Eng, vol. 13, no. 4, Aug. 2016.

[7]. Stepp CE et al. "Repeated training with augmentative vibrotactile feedback increases object manipulation performance," PLoS ONE, vol. 7, no. 2, pp. 1–6, Feb. 2012.

[8]. Witteveen HJB et al. "Stiffness feedback for myoelectric forearm prostheses using vibrotactile stimulation," IEEE INS-RE, vol. 22, no. 1, pp. 53–61, Jan. 2014.

[9]. Antfolk C et al. "Artificial redirection of sensation from prosthetic fingers to the phantom hand map on transradial amputees: vibrotactile versus mechanotactile sensory feedback," IEEE Trans. Neural Syst. Rehabil. Eng, vol. 21, no. 1, pp. 112–120, Jan. 2013. [PubMed: 23033439]

[10]. Zhang D et al. "Somatotopical feedback versus non-somatotopical feedback for phantom digit sensation on amputees using electrotactile stimulation," J. Neuroeng. Rehabil, vol. 12, pp. 44, 5 2015. [PubMed: 25929589]

[11]. Davis TS et al. "Restoring motor control and sensory feedback in people with upper extremity amputations using arrays of 96 microelectrodes implanted in the median and ulnar nerves," J. Neural Eng, vol. 13, no. 3, Jun. 2016.

[12]. Raspopovic S et al. "Restoring natural sensory feedback in real-time bidirectional hand prostheses," Set Transl. Med, vol. 6, no. 222, pp. 222, Feb. 2014.

[13]. Tan DW et al. "Stability and selectivity of a chronic, multi-contact cuff electrode for sensory stimulation in a human amputee," J Neural Eng, vol. 12, no. 2, pp. 859–862, Jan. 2015.

[14]. Tan DW et al. "A neural interface provides long-term stable natural touch perception," Set Transl. Med, vol. 6, Oct. 2014.

[15]. Flesher SN et al. "Intracortical microstimulation of human somatosensory cortex," Sci. Transl. Medicine, vol. 8, pp. 361, Oct. 2016.

[16]. Collins KL et al. "Ownership of an artificial limb induced by electrical brain stimulation," PNAS, vol. 144, no. 1, pp. 166–171, Jan. 2017.

[17]. Christensen MB et al. "The foreign body response to the Utah Slant Electrode Array in the cat sciatic nerve," Acta Biomater, vol. 10, no. 11, pp. 4650–4660, Nov. 2014. [PubMed: 25042798]

[18]. Sharma A et al. "Long term in vitro functional stability and recording longevity of fully integrated wireless neural interfaces based on the Utah Slant Electrode Array," J. Neural Eng, vol. 8, no. 4, Aug. 2011.

[19]. Svensson P et al. "A review of invasive and non-invasive sensory feedback in upper limb prostheses," Expert Rev. Med. Devices, vol 14, no. 6, pp.439–447, Jun. 2017. [PubMed: 28532184]

[20]. Chai G et al. "Characterization of evoked tactile sensation in forearm amputees with transcutaneous electrical nerve stimulation," J. Neural Eng, vol. 12, no. 6, Dec. 2015.

[21]. Kooijman CM et al. "Phantom pain and phantom sensations in upper limb amputees: an epidemiological study," Pain, vol. 87, no. 1, pp. 33–41, Jul. 2000. [PubMed: 10863043]

[22]. D'Anna E et al. "A somatotopic bidirectional hand prosthesis with transcutaneous electrical nerve stimulation based sensory feedback," Sci. Rep, vol. 7, no. 1, pp. 1–15, Sep. 2017. [PubMed: 28127051]

[23]. Shin H et al. "Evoked haptic sensations in the hand via non-invasive proximal nerve stimulation,"/. Neural Eng, vol. 15, no. 4, Aug. 2018.

[24]. Alonzo M et al. "Electro-cutaneous stimulation on the palm elicits referred sensations on intact but not on amputated digits," J. Neural Eng, vol. 15, no. 1, Feb. 2018.

[25]. Kaas JH et al. "The reorganization of somatosensory cortex following peripheral nerve damage in adult and developing mammals," Annu. Rev. Neurosci, vol. 6, pp. 325–356, Mar. 1983. [PubMed: 6340591]

[26]. Cohen J, "A coefficient of agreement for nominal scales," Educ. Psychol. Meas, vol. 20, no. 1, pp. 37–47, Apr. 1960.

[27]. Koch G, Landis J, "The measurement of observer agreement for categorial data," Biometrics, vol. 33, no. 1, pp. 159–177, Mar. 1977. [PubMed: 843571]

[28]. Sousa S et al. "Assessment of map similarity of categorical maps using Kappa statistics," ISEGI, Jan. 2002.

[29]. Li M et al. “Discrimination and recognition of phantom finger sensation through transcutaneous electrical nerve stimulation,” Front. Neurosci, vol. 12, Apr. 2018.

[30]. Graczyk EL et al. “The neural basis of perceived intensity in natural and artificial touch,” Sci. Transl. Med, vol. 8, pp. 362, Oct. 2016

[31]. Graczyk EL et al. “Sensory adaptation to electrical stimulation of the somatosensory nerves” J. Neural Eng, vol. 15, no. 4, Aug. 2018.

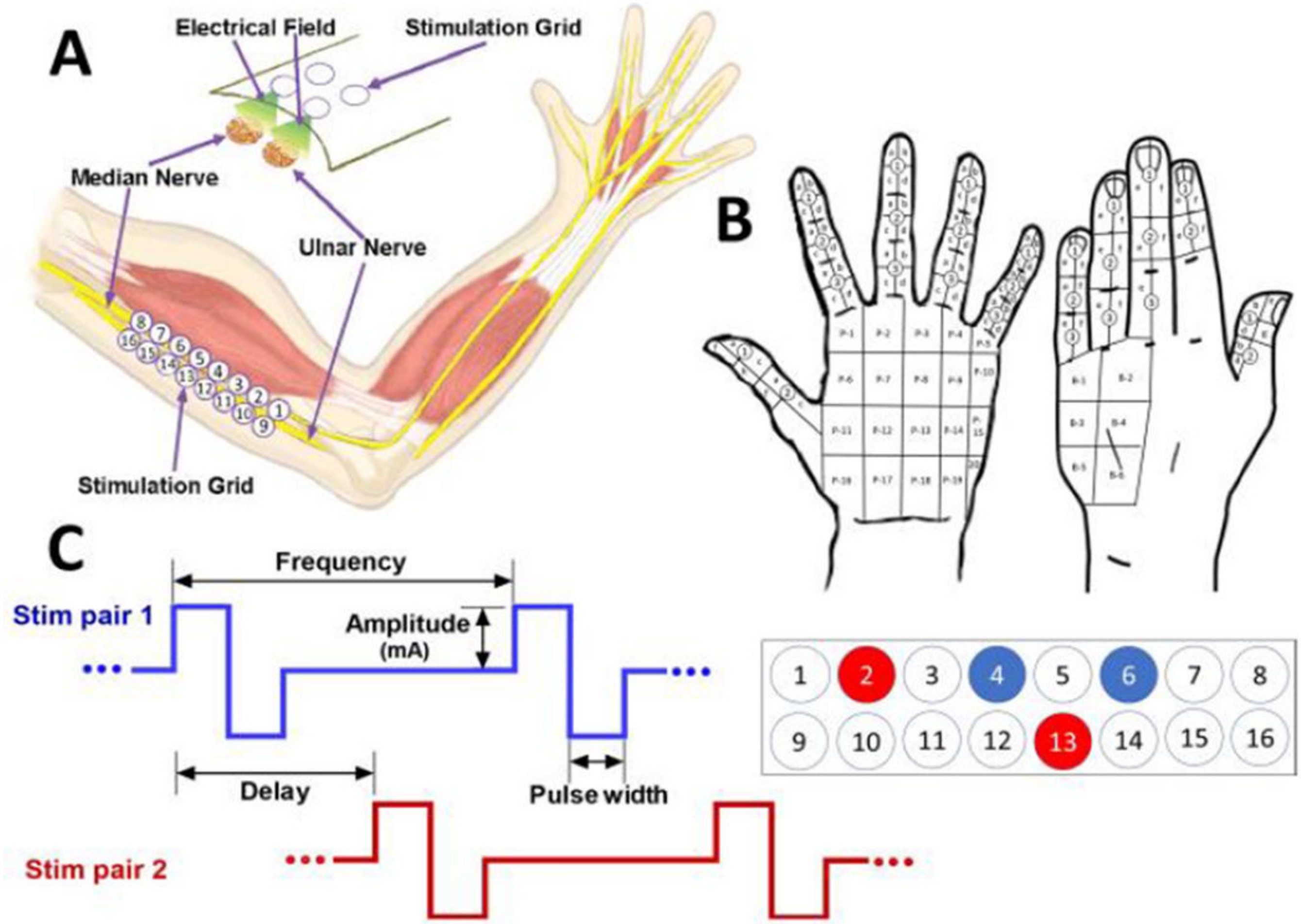

Fig. 1.

Diagram showing the placement of the electrode grid along the upper arm (A), hand map used to record the location and corresponding strength of the perceived sensation evoked during each stimulation trial (B), and stimulation train of two pairs of electrodes and its adjustable parameters, including a temporal delay between stimulation pairs (C).

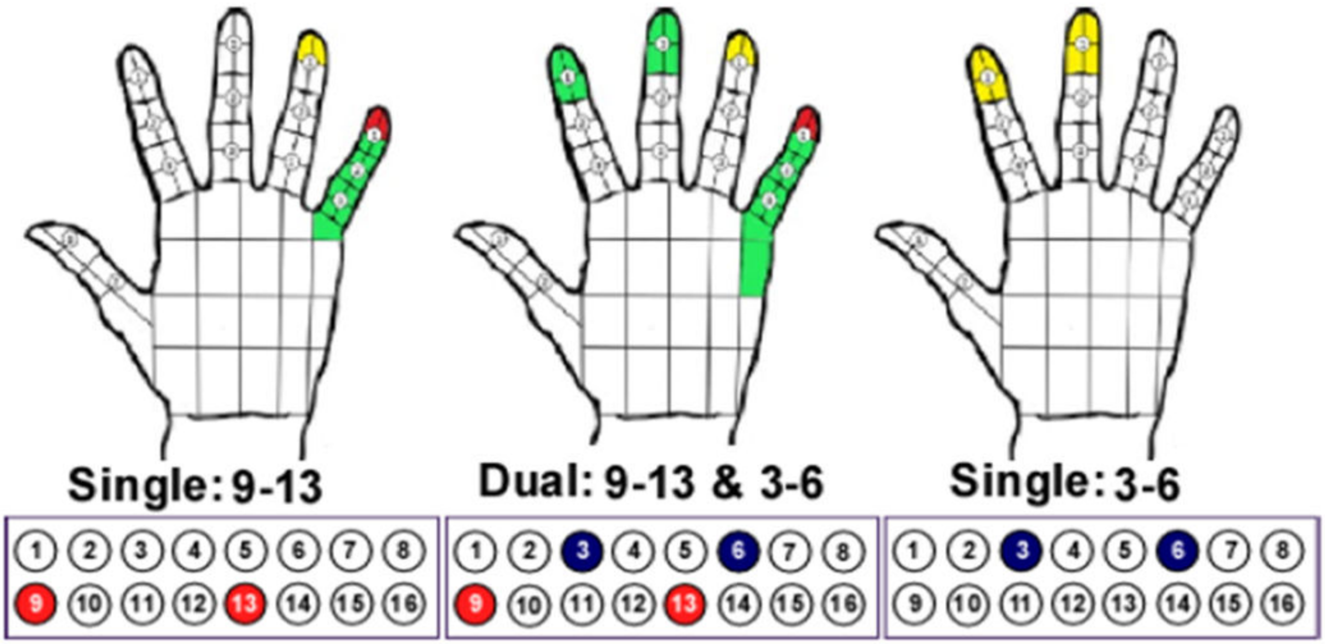

Fig. 2.
Hand maps showing the sensation perceived when a given single or dual set of electrodes are stimulated. Colors indicate sensation strength: green: low, yellow: moderate, and red: high.

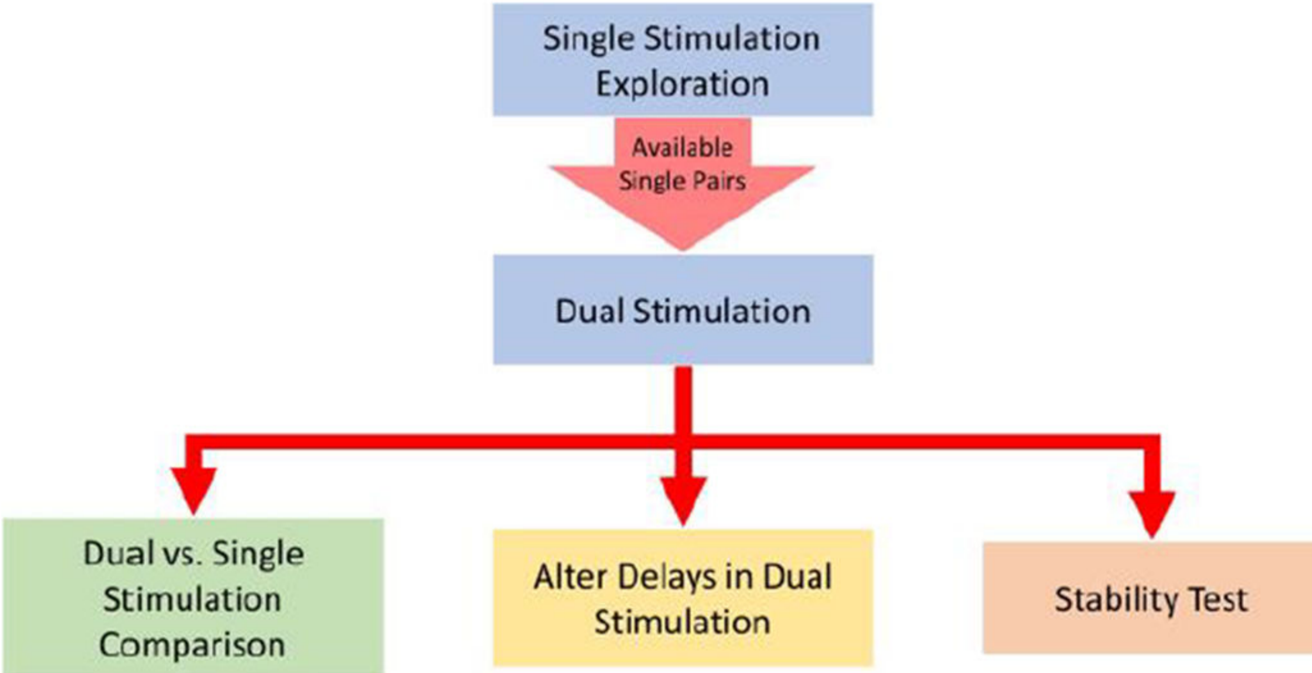

Fig. 3.
Diagram illustrating the protocol used during this study in order to evaluate the effects of concurrent stimulation on haptic sensation.

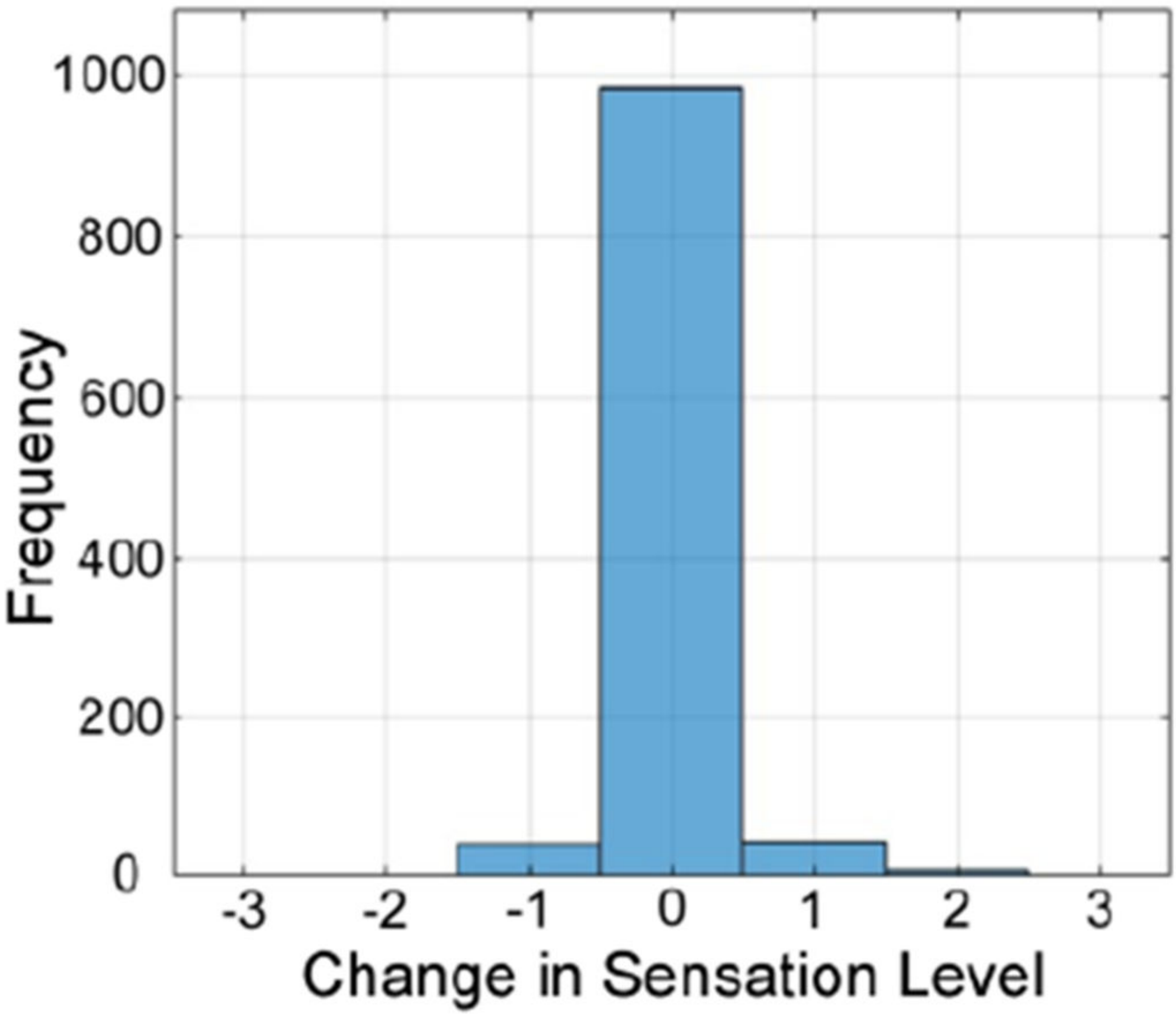

Fig. 4.
Change in the sensation strength when comparing single vs dual stimulation of a single subject.

Author Manuscript
Author Manuscript
Author Manuscript

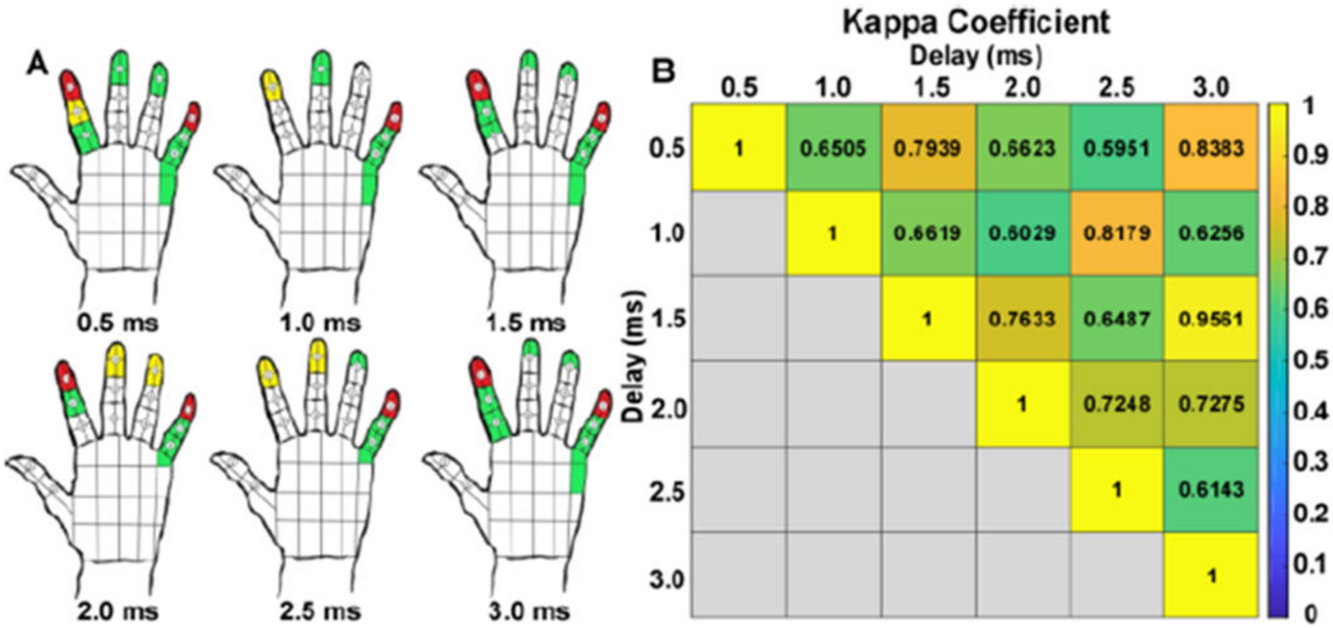

Fig. 5.

Haptic sensation of concurrent stimulations over different delays between stimulation locations (A), and confusion matrix showing the strength of agreement between temporal delay conditions from A (B).

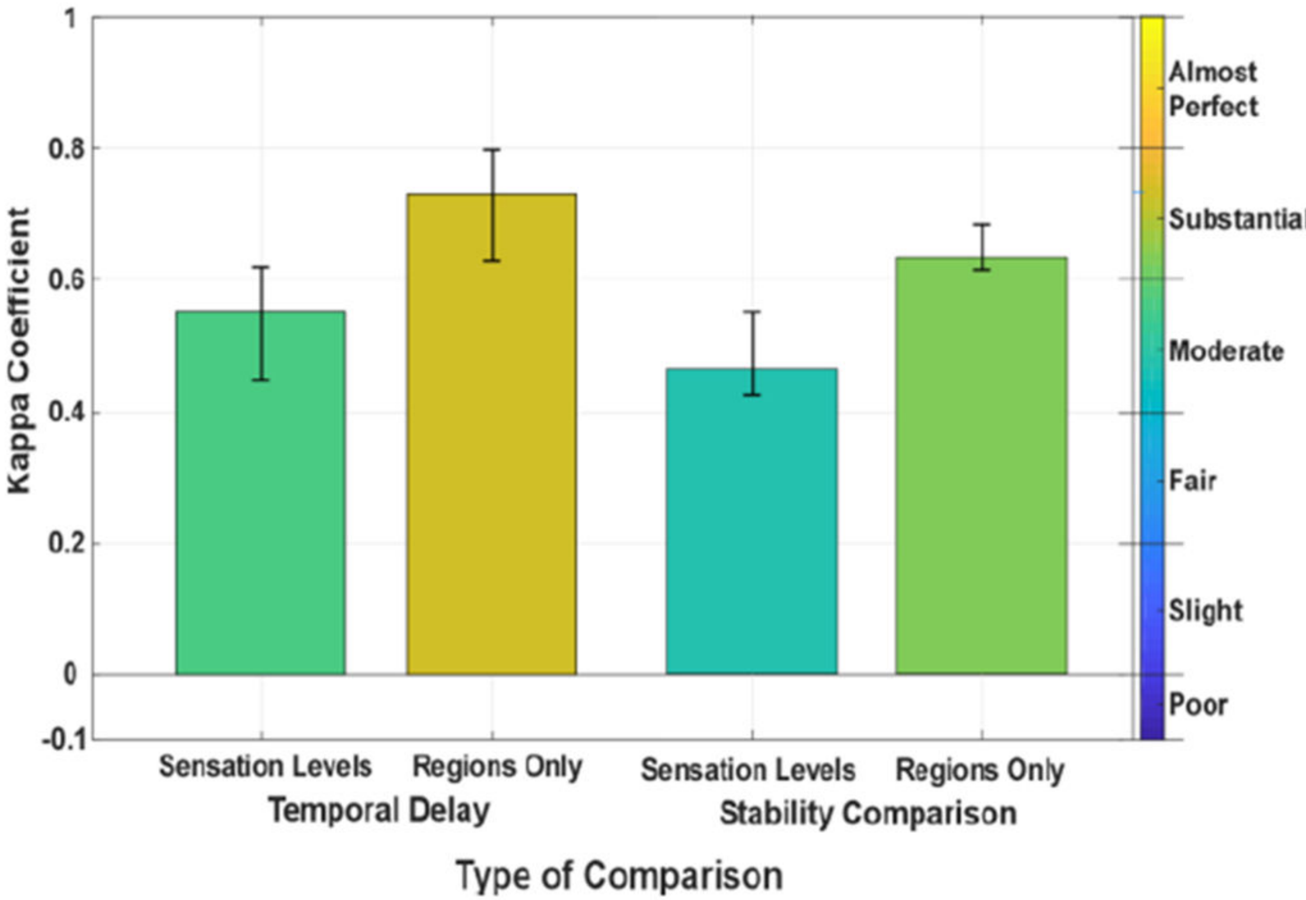

Fig. 6.

Median kappa coefficient between different temporal delay conditions and short-term stability recordings across all subjects. Error bars indicate interquartile range.

Author Manuscript
Author Manuscript
Author Manuscript

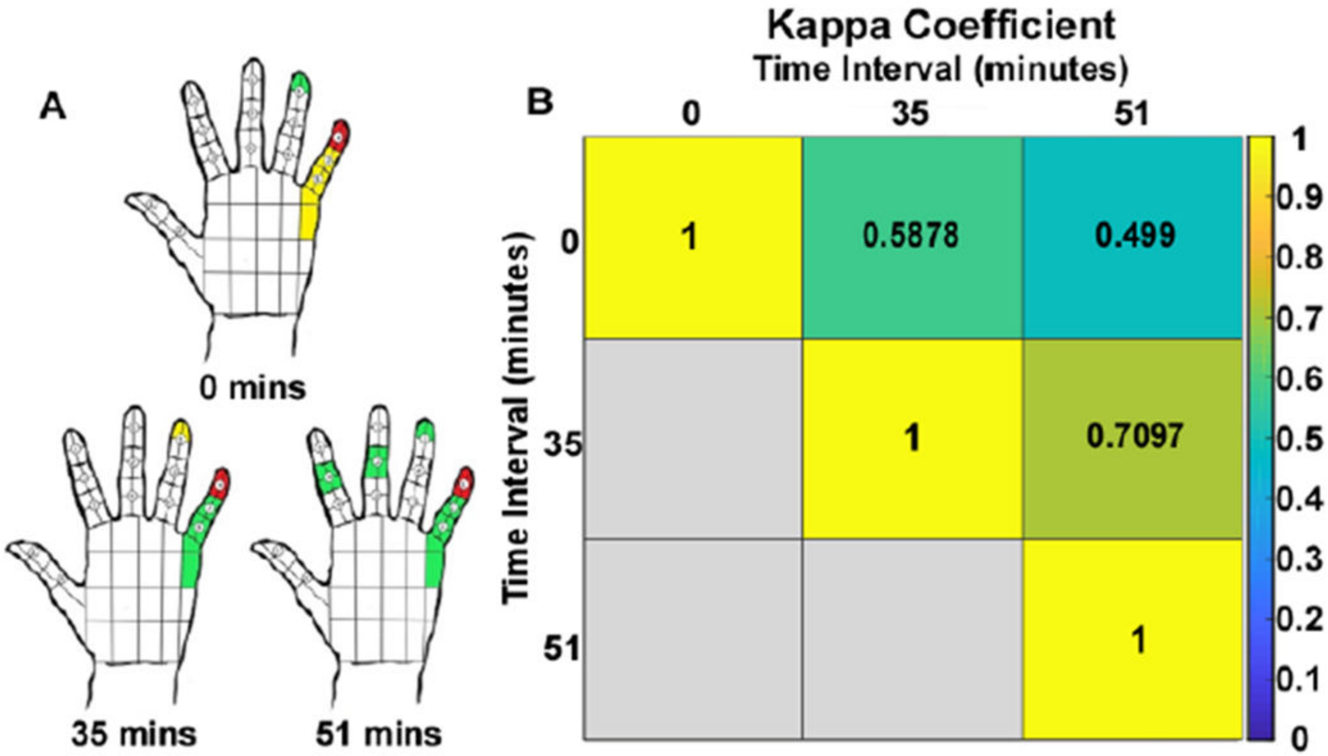

Fig. 7.

Sensation of concurrent stimulations over different stimulation instances (A), and confusion matrix showing the strength of agreement between different stimulation instances (B).

TABLE I

Single vs. Dual Stimulation Results across Subjects

	Median (IQR)
% No Change	87.04 (85.8-91.5)
% Deleted Regions	2.41 (2.13-4.12)
% New Regions	3.06 (2.41-3.89)
% Increased Sensation Level	3.70 (2.36-3.85)
% Decreased Sensation Level	1.48 (0.98-2.46)
Absolute Change in Sensation Level	0.955 (0.85-1.02)
# of Non-Zero Regions per Trial	20.5 (16-25.75)
Kappa Coefficient	0.62 (0.60-0.67)

TABLE II

Temporal Delay and Stability Results across Subjects

	Median (IQR)	
	Delay	**Stability**
% No Change	86.11 (82.00-90.74)	87.04 (83.33-90.74)
% New/Deleted Regions	8.33 (5.00-11.11)	8.33 (4.63-12.96)
% Change in Sensation Level	5.56 (3.00-7.41)	3.70 (0.93-7.41)
Absolute Change in Sensation Level	1.32 (1.18-1.44)	1.24 (1.22-1.44)
# of Non-Zero Regions per Trial	24 (18-28)	21 (16-27)