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Electrically-evoked referred sensations induce embodiment of rubber limb

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Abstract

Introduction: Electrical stimulation is increasingly relevant in a variety of medical treatments. In this study, the quality of referred sensations evoked using surface electrical stimulation was evaluated using the rubber hand and foot illusions.

Methods: The rubber hand and foot illusions were attempted under 4 conditions: (1) multi-location tapping; (2) one-location tapping; (3) electrical stimulation of sensation referred to the hand or foot; (4) asynchronous control. The strength of each illusion was quantified using a questionnaire and proprioceptive drift, where a stronger response suggested embodiment of the rubber limb.

Results: 45 able-bodied individuals and two individuals with amputations participated in this study. Overall, the illusion evoked by nerve stimulation was not as strong as illusions evoked by physically tapping but stronger than the control illusion.

Conclusion: This study has found that the rubber hand and foot illusion can be performed without touching the distal limb of the participant. Electrical stimulation that produced referred sensation in the distal extremity was realistic enough to partially incorporate the rubber limb into a person's body image.

Keywords

Rubber hand illusion, neurorehabilitation, sensation simulation/restoration, electrical stimulation, amputation

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Introduction

Phantom limb pain is a post-amputation phenomenon involving pain and/or extreme discomfort in the missing limb. Phantom limb pain occurs in a majority of people with amputated limbs, including over half of people with upper extremity amputations and significantly reduces quality of life.^{1–4} Pharmacological treatments provide variable relief and often come with intolerable side effects.^{5,6} Some non-invasive, non-pharmaceutical treatments are being investigated such as mirror therapy,⁷ virtual reality,⁸ and acupuncture.⁹ We are developing a potential non-pharmaceutical treatment involving referred sensations. Surface electrical stimulation can be used to evoke a variety

of referred sensations, or sensations felt in a location different than the stimulation.^{10,11} These referred sensations in the missing hand and foot can also be evoked in people with amputations.¹¹ The purpose of this paper is to investigate the authenticity of these electrically-evoked sensations using perceptual embodiment of a rubber limb.

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Embodiment of an artificial limb can be induced in most individuals using a technique known as the rubber hand (or foot) illusion.^{12,13} In this illusion, a rubber or artificial limb is placed in an anatomically appropriate location and the person's real limb is hidden from view. This illusion was first performed with simultaneous stroking on the dorsal surface of both the participant's hidden hand and the visible rubber hand. Participants reported feelings of ownership towards the rubber hand when the stroking was at the same time and location between the two hands.^{14,15} A stronger illusion was evoked when the sensation seen and felt were more similar and the illusion failed when the visual and the tactile information did not occur simultaneously (asynchronous condition). In the present study, the authenticity of the sensations evoked using surface electrical stimulation were quantified using this illusion. The hypothesis of this study is that the rubber hand or foot illusion can be achieved using electrically evoked referred sensation, suggesting that the stimulated sensations feel similar to the physical touch being seen.

Methods

Able-bodied participants were recruited from the Hope College campus community; participants with limb amputations were recruited through Mary Free Bed Rehabilitation Hospital. The protocol was approved by the Hope College Human Subjects Review Board and all participants gave written informed consent. Each study session lasted from 45 to 90 min and participants were compensated for their time.

The rubber hand and foot illusion evoked using nerve stimulation of referred sensation was compared to illusions evoked by physically tapping in different locations on the hand or foot (multi-location condition) and a control trial where the physical tapping was shifted in time between touching the rubber limb and the actual limb (asynchronous condition). Since traditional illusions consisted of touching in multiple locations and stimulation was only a single location, one additional condition was tested, where

synchronous physical tapping occurred in one location on the hand or foot (one location condition). The success of the illusion was quantified using a written questionnaire and a pointing task (proprioceptive drift).

Illusion details

The participants were not told how the rubber hand or foot illusion worked prior to the experimental session. They were told that participation in this experiment would help decide how normal the stimulation felt. For rubber hand illusion trials, the participants sat in an upright chair and placed their left arm supine on the table in front of them. For rubber foot illusion trials, participants placed their left foot on an inclined platform. In both cases, the distal extremity was then hidden from view and a light skin tone rubber hand or foot was placed next to the hidden one (or in the location of the phantom for participants with amputations). A ruler was placed across both limbs (Figure 1) and a baseline measurement was taken for proprioceptive drift.

Prior to starting the illusion, the participant put on noise canceling headphones to mask the sound of the robot moving. Each illusion was performed for 2 min and the participant was instructed to watch the tapping occur on the rubber extremity. Following each trial, the participant completed a questionnaire and repeated the measurement for proprioceptive drift three times. Each illusion condition is described in detail below:

- Multi-location condition: Simultaneous tapping with a reflex hammer or index finger of the experimenter was performed at 1–2 Hz at varying locations in both the rubber and hidden extremity.
- One-location condition: Simultaneous tapping with a reflex hammer or index finger of the experimenter was performed on the tip of the index finger or the base of the big toe of both the rubber and hidden extremity.
- Stimulation condition: Surface electrical stimulation was performed on the median, ulnar or peroneal nerve

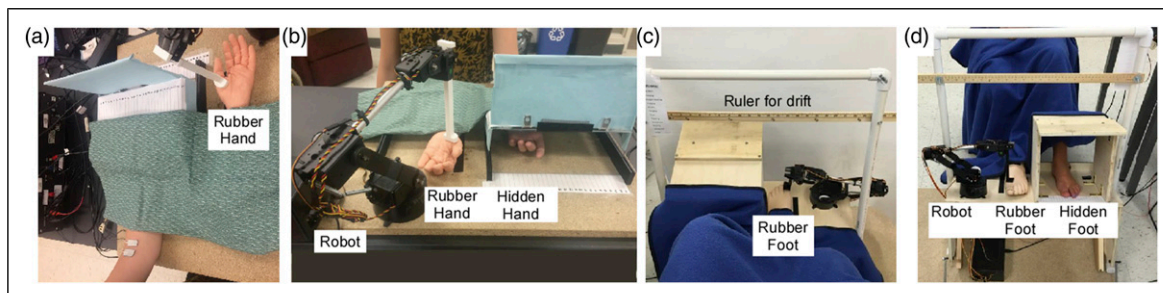


Figure 1. Experimental Setup. (a and b) Rubber hand illusion setup where the subject's left hand is hidden and the rubber hand is placed within view. (c and d) Rubber foot illusion setup where the subject's left foot is hidden and the rubber foot is placed within view. Tapping can be performed by an experimenter or by the robot.

to evoke a tapping sensation in the distal extremity while a robot tapped on a similar location of the rubber hand or foot at a synchronous time.

- Asynchronous condition: Similar to the multi-location condition, but tapping on the rubber and hidden extremity (performed by the experimenter) was staggered in time by up to a half second. This was the control condition that was not intended to evoke an illusion.

The illusions were performed in two blocks. The first block consisted of the illusions involving physical tapping and the second consisted of illusions involving nerve stimulation. The trials within each block were randomized and the participants removed their limb from the experimental setup to complete the questionnaire between illusion trials. This was done to reduce any confounding effect of the illusion over time.

Stimulation details

The technique for evoking a tapping sensation from the nerves was similar to what has been described previously.^{10,11} Participants were instructed to wash the area where the electrodes would be applied (cubital fossa or lateral knee) with soap and water and were seated in an upright chair. Rubbing alcohol was used to clean the skin before applying the electrodes. Electrodes were placed over the median, ulnar and/or peroneal nerve as described previously.¹¹

Stimulation was supplied via voltage-controlled, charge-balanced, biphasic, non-symmetric square pulses. Pulses were non-symmetric in that the anodic phase was set to a maximum value of 4 V with a width as needed to balance the charge.¹⁶ Voltage-controlled stimulation was used to decrease the risk of high current density in the case of reduced adhesion from the surface electrodes. The stimulation waveforms were created in MATLAB (2013a) and delivered using a National Instruments USB DAQ (NI USB-6229, Austin, TX) and an isolated biostimulator (Coulbourn Instruments model A13-75, Pittsburg, PA). Adhesive electrodes were cut to 30 mm by 17 mm (ValuTrode, Axelgaard Manufacturing, Fallbrook, CA).

Stimulation parameters were chosen as described previously.¹¹ Briefly, voltage amplitude was slowly increased at a frequency of 50 Hz to determine an approximate threshold and set a maximum comfort level (pulse durations used were 100 μ s and 500 μ s). A more complete threshold was determined using Parameter Estimation by Sequential Testing (PEST)^{17,18} with four threshold points.¹⁰ Stimulation between 1 and 4 Hz had been found to produce a tapping sensation in a majority of participants¹¹ so the frequency was initially set to 2 Hz and voltages at 75% and 90% of the range between threshold and maximum were

tested. The participant identified the parameter combination that felt the most like a tap and then this voltage-pulse width combination was tested at 1, 2 and 3 Hz to choose the final frequency.

A four degree of freedom robotic arm (Lynxmotion AL5D) was used to automate the tapping and allow synchronization with the stimulation. The robot was positioned over the rubber extremity to match where the participant reported the sensation (Figure 1). Attachments of different sizes and shapes were available to allow a better match between a participant's reported sensation area and what they saw happening on the rubber extremity. The timing between when the stimulation was sent and when the robot moved could be adjusted for each participant to provide simultaneous visual and somatosensory information (default delay for the stimulation was 0.1345 s).

Measurement details

Proprioceptive Drift was measured by having the participant drag their right index finger along the ruler placed over both the rubber and hidden limb, starting on the left. They were instructed to stop when they reached their middle finger or their big toe. For the baseline measurement, prior to performing any trials, the participant completed five trials of pointing. Following each illusion trial, the participants performed the drift measurement 3 times prior to removing their hand from the cover to complete the questionnaire. For each measurement, the drift was defined as the distance between where they pointed and where their limb was actually located. Average baseline drift values were subtracted from the average drift at each condition and used to compare trials.

After each illusion trial, participants answered nine questions for the physical tapping illusions and 10 for the nerve stimulation illusion (Table 1). Questions were on a scale from -3 to 3 labeled "Doesn't apply" to "Completely applies". The order of the questions was varied between trials and participants (4 total versions).

Data analysis

Questionnaire results were analyzed by comparing the average responses from the illusion questions (1-3 and 10) and the control questions (4-9). It has been reported that some people do not respond to the illusion.¹⁹ Participants who had an average value of -1 or less on the three illusion questions for the multi-location illusion were removed from all future analysis. Proprioceptive drift was quantified by subtracting the average of the trials of pointing at baseline from the average of after each illusion.

To compare illusions strengths, a repeated measures ANOVA was used with 4 or 5 factors (one for each illusion condition) and two measures (average of illusion questions

Table 1. Questions used to quantify the success of the rubber hand illusion. Questions 1–3 (and 10) were illusion questions and a positive answer indicated a successful illusion. Questions 4–9 were control questions, not related to the illusion and used to test for suggestibility. For the rubber foot illusion, hand was replaced by foot in each question.

1	I felt the touch of the investigator on the rubber hand.
2	It seemed as if the touch I felt was caused by the investigator touching the rubber hand
3	I felt as if the rubber hand was my hand
4	It felt as if my real hand was drifting towards the rubber hand
5	It seemed as if I had three hands
6	It seemed as if the touch I was feeling came from somewhere between my own hand and the rubber hand
7	It felt as if my real hand was turning rubbery
8	It appeared as if the rubber hand was drifting towards my real hand
9	The rubber hand began to resemble my own real hand in terms of shape, skin tone, freckles, or some other visual feature.
10	(only for stimulation condition) It felt as if the stimulation in my hand changed to match the visual stimulation of the robot

and proprioceptive drift). A pairwise comparison between each illusion was performed using a Bonferroni correction.

Results

Twenty-five able-bodied participants (13 female, 12 male, 2 left handed, 19.6 mean age) volunteered to take part in the rubber hand illusion trials. In three participants, referred hand sensation could not be obtained from one of the nerves without going over our self-imposed stimulation limits leaving a total of 24 median nerve illusion trials and 23 ulnar nerve illusion trials. In 33 of the 47 stimulation trials, participants reported a tapping-like sensation (i.e., tapping, pulsing, heartbeat), and in eight they reported paresthesias (i.e., tingling, buzzing). Responses from the remaining trials varied but included pulling, plucking and poking.

Sensations were evoked in the expected area of the hand innervated by the median or ulnar nerve. Of the 47 trials, sensation was reported in the phalanges for 19 and in the first metacarpal for 8. The remaining locations varied throughout the palm. The average pulse amplitude used to evoke these sensations was 36.4 ± 10.6 V for the median nerve and 39.7 ± 7.2 for the ulnar nerve. The pulse width used was 500 μ s in all but 5 trials on each nerve (average of 415 μ s).

Twenty able-bodied participants (11 female, 9 male, 19.5 mean age) took part in the rubber foot illusion trials. One participant only participated in the physical touch illusions due to a robot malfunction. Reported sensations varied, but a tapping sensation was reported from 12 participants and a pulsing sensation from an additional 3. Sensations were evoked on the dorsal surface of the foot with a mean pulse amplitude of 49.9 ± 16.3 V and pulse width of 500 μ s.

Two participants with amputations took part in a sub-set of this study; one for the rubber hand illusion and one for the rubber foot illusion. The upper limb participant had received a transradial amputation following an accident 1.5 years

prior to testing. This participant was experiencing phantom limb pain that manifested as a constant, gripping discomfort, occasionally accompanied by shooting pains that radiated from the phantom hand. During electrical stimulation, the part of the phantom hand innervated by the stimulated nerve relaxed. The second participant had received a transtibial amputation due to congenital arteriovenous malformation almost 2 years prior to testing. This participant was not experiencing phantom limb pain at the time of testing and reported a bending and cramping in the phantom toes during nerve stimulation. This was a noteworthy result since cramping of the toes was a common response to touch for this participant immediately prior to amputation. Both participants reported paresthesia as well.

Questionnaire responses

Not all participants experienced the illusion, even during the synchronous, multi-location trial. These non-responders were defined as participants who had an average score of less than -1 for the three illusion questions during the multi-location illusion condition. Since these participants never experienced the illusion during the experimental session, their data was removed from the analysis for all trials. There were six non-responders in the upper limb trials and 2 in the lower limb trials. There were also three participants (1 upper limb and 2 lower limb) that answered all questions strongly positive (average of 1.5 or greater for control questions), even during the asynchronous condition. These participants were also removed from the analysis.

Upper limb. Out of the 18 participants included in the analysis, 12 had positive average responses to the illusion questions during the one-location condition while 8 out of 17 and 13 out of 16 had positive responses for the median and ulnar nerve illusion conditions respectively. The multi-location and one-location conditions had strong positive average responses to the three illusion questions and

negative responses to most control questions, indicative of a successful illusion (Figure 2). The asynchronous condition had strong negative responses across all questions. The responses to the illusion questions for nerve stimulation were near zero but the ulnar nerve condition had a strong positive response to question 10, which was an indication that the stimulation was evoking an illusion. On average, participants answered positively to one control question, Q7: “It felt as if my real hand was turning rubbery”.

The responses to all three illusion questions averaged together for each illusion condition are shown in Figure 3 (solid bars). All conditions that were intended to produce an illusion were statistically different from the asynchronous condition ($p < .05$). There was no statistical difference between the two conditions with synchronous physical touch (multi-location and one-location, $p = .4$) nor between the two nerve stimulation conditions ($p = 1$). The two stimulation conditions were significantly different than the multi-location ($p = .01$) but not the one-location condition which consisted of synchronous tapping on the index finger ($p = .1$ for median and 0.4 for ulnar). This suggests that the weaker illusion seen from stimulation may be partially due to the fact that all sensations were evoked in the same hand location.

Lower limb. There were 15 lower extremity participants included in the analysis after removing two non-responders, two that answered control question positively and one where the robot was not functioning. Of these 15, 13 had positive responses to the one-location condition while 11 had positive responses to the peroneal nerve condition. Question-by-question results followed a similar pattern to the rubber hand illusion, with positive average responses to

the three illusion questions for the conditions that were intended to evoke an illusion and strong negative responses to the control questions. Similar to the upper limb trials, slight positive responses were seen for question 7 for the multi-location and peroneal nerve stimulation condition.

When looking at the responses to just the three illusion questions (Figure 3 - hatched bars) all illusion conditions were significantly different from the control condition which used asynchronous tapping. There were no significant differences for the average questionnaire responses between the nerve stimulation condition and the one-location condition ($p > .2$).

Proprioceptive drift. On average there was a drift towards the rubber hand or foot for all illusion conditions including the asynchronous control condition (Figure 4). In the upper limb (solid bars), the only significant difference was found between the ulnar nerve stimulation and asynchronous conditions ($p < .05$). For the lower limb (hatched bars), the peroneal nerve stimulation condition was trending significantly different than the asynchronous condition ($p = .056$). No other significant relationships were found.

Amputated limb. The participants with amputated limbs only took part in the illusion conditions using nerve stimulation since they did not have an intact limb to perform tapping on. Because of this there was no way to evaluate if they would experience a more traditional illusion or to compare illusion strengths across conditions.

The participant with a transradial amputation had strong negative responses (an average of -3) to all illusion questions suggesting that they did not experience an illusion. For the ulnar nerve illusion, their perception of where

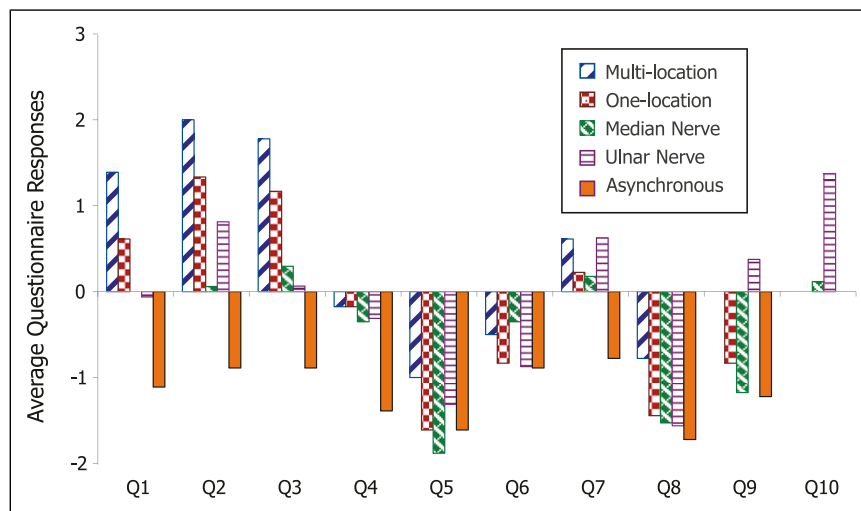


Figure 2. Average response for each question for each illusion condition. The multi-location illusion responses to questions 1–3 (blue hatches) were the highest suggesting a stronger illusion. The asynchronous (control-solid orange) illusion responses for all questions were negative.

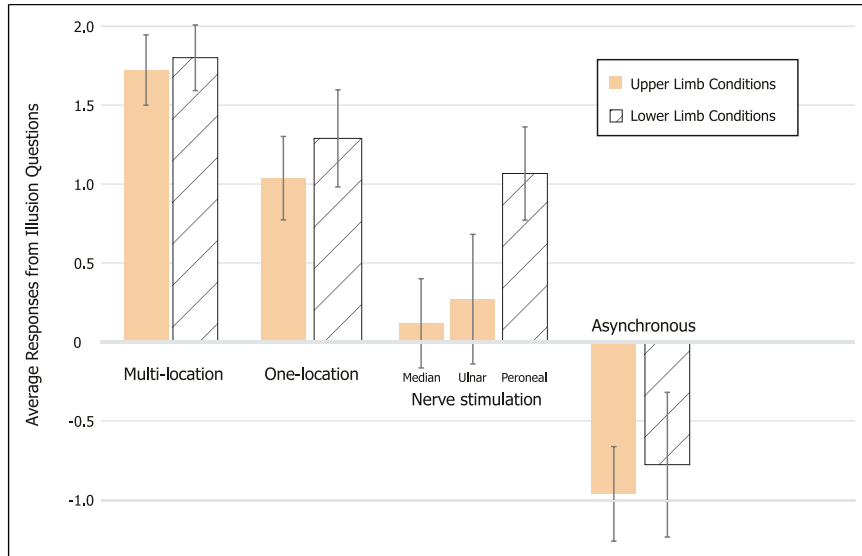


Figure 3. Average response of questions 1–3 (illusion questions) across the different conditions for upper extremity (solid bars) and lower extremity (hatched bars). Error bars are one standard error. All trials intended to evoke an illusion were statistically different than the asynchronous (control) trial.

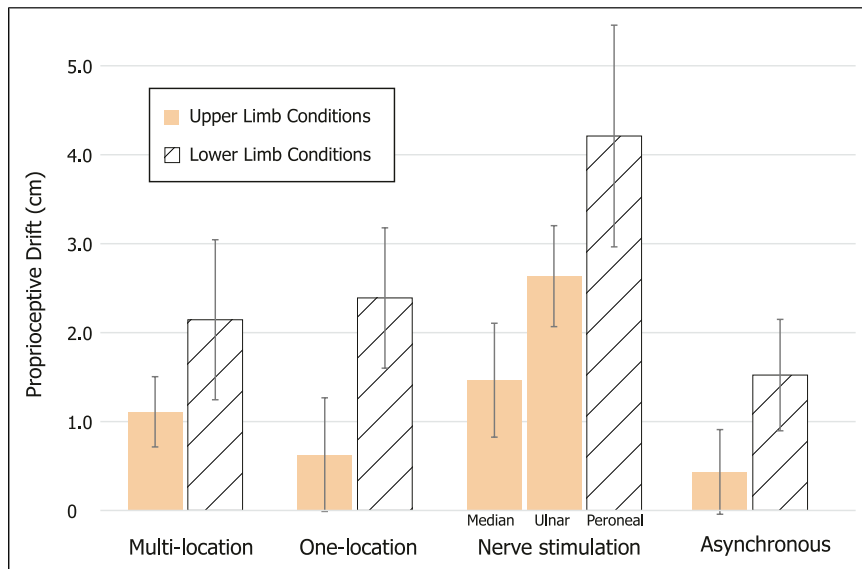


Figure 4. Average drift for each condition for both upper and lower limb illusions, error bars denote one standard error. In general, there was a drift toward the rubber hand in all illusion types.

their hand was (proprioceptive drift) shifted towards the rubber hand but for the median nerve it shifted away. Anecdotally, the participant did not report experiencing the illusion.

The participant with the trans-tibial amputation took part in in two stimulation conditions, one synchronous and one asynchronous. They had an average response of

1.3 for the illusion questions during the synchronous peroneal nerve stimulation condition and an average response of -1.3 for the asynchronous (control) condition suggesting an illusion was experienced. Proprioceptive drift was negative in both conditions. The reported sensations for this participant were bending and cramping in the phantom toes so a robot tapping on the

rubber foot did not authentically represent this sensation. This could have led to a weaker illusion.

Comparison between upper and lower limb. There were no significant differences in the multi-location, one location, or asynchronous illusion conditions between the upper and lower limb experiments ($p > .05$ for questionnaire and proprioceptive drift measures). Comparing the three illusions produced by nerve stimulation found a difference between the peroneal nerve and both the median and ulnar nerves for the questionnaire data ($p < .05$ Games-Howell test). When question 10 was included in the average for the illusion questions, there was only a difference between peroneal and median nerve conditions ($p = .016$, Games-Howell test). There were no significant differences in the data from the proprioceptive drift. This is consistent with prior work that found no difference between the rubber hand and foot illusions.²⁰

Discussion

The rubber hand and foot illusions were used to evaluate the authenticity of surface electrical nerve stimulation used to produce a referred sensation. Overall, the illusion evoked by nerve stimulation was not as strong as illusions evoked by physically tapping on the limb but stronger than the control condition. This suggests that, while the referred sensations did not feel identical to a physical touch, they were close enough in many people to induce embodiment of the rubber limb.

Traditionally the rubber hand illusion has been performed using stroking on the dorsal surface of the hand. Since innervation of the median and ulnar nerve are primarily on the palmar surface, all illusions in this study were performed on the palm. The other main difference between the illusion in the present study and prior studies was that, during nerve stimulation, the sensation was evoked in a single location. This was the reason to include the one-location condition and it was seen that the one location illusion was slightly weaker (though not statistically different) than the multi-location illusion. It is likely that some of the loss of strength in the nerve stimulation trials is due to the fact that sensations were evoked in a single location, not only the quality of the sensation.

The stimulation timing was adjusted to feel synchronous with the touch of the robot but the evoked somatosensations were not always congruent with the visual information. The participant-reported-sensations due to nerve stimulation varied from tapping, to pulsing, to tingling but the robot always performed the same motion (tapping). Others have successfully evoked the rubber limb illusion using incongruent sensations. Crea et al. compared illusions evoked using congruent stroking of a real and rubber foot to illusions evoked from vibrotactile stimulation of the real foot

(hidden from view) and stroking on the rubber foot.¹³ They found that strength of the illusion was weaker in the incongruent conditions and incongruency could be used to explain the lower illusion strengths found here in the stimulation conditions. It could be hypothesized that evoked sensations that felt more like tapping would produce a stronger illusion than a pulsing or tingling sensation. However, in this study the sample size was not sufficient to detect differences in the means between these three levels of sensation quality (tapping, pulsing and tingling).

Overall, the questionnaire responses to the control questions (questions 4–9) were strongly negative. This was true for all questions except question 7, which had positive response to all but one synchronous condition. In the original description of the rubber hand illusion,¹² the only question with a positive average response was similar to question 9 in the current work “The rubber hand began to resemble my own hand...”. The next highest control question, with an average slightly below zero, was similar to question 7 in the current work. In more recent work, questions similar to question 7 also had a higher average than the other control question (positive or near zero).^{21,22} This suggests that these questions are sometimes interpreted in a positive manner during a successful illusion.

It has been reported that humans are more accurate in pointing to their hand when the palm is up, rather than down.²¹ This may be due to humans spending a lot of time looking at the palmar side of their hands. This difference in pointing accuracy could help to explain the relatively higher drift associated with pointing at the big toe compared to the middle finger since humans spend less time looking at their feet. It has also been suggested that proprioceptive drift is not a valid measure of body ownership²³ since it can be induced by simply looking at a rubber hand (visuoproprioceptive integration).²⁴ Most studies that report proprioceptive drift when using a rubber hand illusion find differences between active illusion trials and asynchronous control trials that may be due to asynchronous stroking inhibiting this process of visuoproprioceptive integration.

Somatosensory information pertaining to touch on the hand reaches the cortex faster than information about touch on the foot. Hence the reaction time for touch to the hand is shorter than touch to the foot.²⁵ Visual information about touch on the hand and foot does not have this difference in conduction time. It has been found that the reaction time for visual information is similar to the reaction time of a somatosensory input from the foot, and slower than the reaction time to a somatosensory input from the hand.²⁵ This study of perceived simultaneity suggested that the nervous system compensates for the conduction difference by delaying the somatosensory information coming from the hand, to allow for correct detection of simultaneity between visual and somatosensory inputs when touch on the hand occurs. In the present study, the same default delay value

was used to trigger the robot tap for both upper and lower extremity illusion trials, meaning that the difference between electrical stimulation of sensation and the robot tapping was the same for both upper and lower extremity. This is consistent with the suggestion that upper extremity somatosensory information is delayed by the nervous system. Otherwise, a shorter delay of the stimulation would have been necessary to create a touch on the rubber foot simultaneous with the electrically evoked sensation, which had further to travel from the lower extremity.

Another difference between the rubber hand and foot illusions performed here is that the hand illusions were performed on the palmar surface, which consisted of glabrous skin, and the foot illusions were performed on the dorsal surface, which consisted of hairy skin. The density of sensory receptors is much higher on glabrous skin compared to hairy skin.²⁶ The lower density of sensory receptors on the dorsal foot may have caused the sensations evoked through peroneal nerve stimulation to be less distinct than those evoked through stimulation of the median and ulnar nerves. This may have led to an easier acceptance that the evoked sensation was similar to the robotic tapping and hence a stronger illusion when using peroneal nerve stimulation. This difference in density of skin receptors may explain the differences seen between rubber hand and foot illusion stimulation trials, but not during the trials based on physical touch.

Electrical stimulation has previously been used as part of the rubber hand illusion. Mulvey et al. used electrical stimulation to increase an illusion performed using synchronous stroking.²⁷ They were also able to evoke an illusion by applying transcutaneous electrical stimulation (TENS) on the real hand while participants observed the rubber hand.²⁸ In these studies, they were not attempting to electrically evoke a congruent sensation to what was seen on the rubber limb. Similar to the present study, Ehrsson et al. used referred sensation to evoke a rubber hand illusion in participants with amputations. Participants were recruited who reported sensations on their phantom hand due to touch on their residual limb. Mapping was done to identify which locations were referred to the hand and these locations were stroked in synchrony to the rubber hand. As in the present study, illusions evoked using referred sensation were not as strong as the traditional illusion, but significantly different than control trials.²⁹ Similarly, Marasco et al. used tactors to evoke referred sensations in the hand from reinnervated skin on the chest. These referred sensations as part of the rubber hand illusion were found to shift perception towards incorporation of the artificial limb into their body image.

The rubber limbs used had a light skin tone. Of the 45 participants in this study, most were White and non-Latinx. Of the remaining participants, three were Asian, two were Biracial (White and Black) and two were White and Latinx. Given the large number of people with lighter skin

tones in this study, it was not possible to look at potential differences due to skin tone. However, others have shown that the synchrony of the visual and tactile information matters more than what object is being touched. When testing with all White participants using both a light and dark-toned hand, the illusion could be produced in both cases but wasn't as strong with the non-matching skin tone hand.^{30,31} In addition, people have been reported to incorporate other objects into their body image, such as a table¹⁹ or a robotic hand,³² although these illusions were weaker than traditional illusions.

This study has found that the rubber hand and foot illusion can be performed without touching the distal limb of the participant. Electrical stimulation that produced referred sensation in the distal extremity was realistic enough to partially incorporate the rubber limb into a person's body image. This suggests that this stimulation method may be a valid technique to supply somatosensory feedback as a treatment for phantom limb pain.

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