Vibrotactile stimulation promotes embodiment of an alien hand in amputees with phantom sensations

Marco D'Alonzo, Francesco Clemente, *Student Member, IEEE*, Christian Cipriani, *Senior Member, IEEE*

The DOI of the final edited version of this paper is: 10.1109/TNSRE.2014.2337952.

Submitted for publication to IEEE Transactions on Neural Systems and Rehabilitation Engineering

Vibrotactile stimulation promotes embodiment of an alien hand in amputees with phantom sensations

Marco D'Alonzo, Francesco Clemente and Christian Cipriani

Correspondance to:
Dr Christian Cipriani, the BioRobotics Institute | Scuola Superiore Sant'Anna,
V.le R. Piaggio, 34, 56025 Pontedera (PI), Italy
Telephone: +39050883133
Fax: +39050883101
E-mail: ch.cipriani@sssup.it

Summary —Tactile feedback is essential to intuitive control and to promote the sense of self-attribution of a prosthetic limb. Recent findings showed that amputees can be tricked to experience this embodiment, when synchronous and modality-matched stimuli are delivered to biological afferent structures and to an alien rubber hand. Hence it was suggested to exploit this effect by coupling touch sensors in a prosthesis to an array of haptic tactile stimulators in the prosthetic socket. However, this approach is not clinically viable due to physical limits of current haptic devices. To address this issue we have proposed modality-mismatched stimulation and demonstrated that this promotes self-attribution of an alien hand on normally-limbed subjects. In this work we investigated whether similar effects could be induced in transradial amputees with referred phantom sensations in a series of experiments fashioned after the Rubber Hand Illusion using vibrotactile stimulators. Results from three independent measures of embodiment demonstrated that vibrotactile sensory substitution elicits body-ownership of a rubber hand in transradial amputees. These results open up promising possibilities in this field; indeed miniature, safe and inexpensive vibrators could be fitted into commercially available prostheses and sockets to induce the illusion every time the prosthesis manipulates an object.

Keywords— tactile perception, sensory substitution, rehabilitation engineering, cognitive neuroscience, sensory feedback.

I. INTRODUCTION

A key goal in rehabilitation engineering is to restore motor and sensory function of a lost arm with an artificial substitute that feels and acts like the biological limb. Since the sensorimotor control of grasping and manipulation largely relies on tactile feedback [1], a complete restoration of the upper limb is only possible when the individual can sense the touch and the movement of his/her prosthesis, thus feeling it as a part of the body. The lack of this sensory feedback is cited as one of the reasons for rejection of myoelectric prostheses; amputees often opt for body-powered limbs, which besides being lighter, provide position and force information to the body, directly through the harness and the Bowden-cable transmission [2].

The sense of body ownership refers to the particular perceptual status that identifies a part of the own body as self. The self-attribution is mediated by multi-sensory perceptual correlations [3]- [5]; for example, the attribution of a visible hand to the self depends on a match between the afferent somatic signals and visual feedback from the hand. The Rubber Hand Illusion (RHI) is a perceptual illusion which elicits a feeling of ownership of an alien rubber hand [3]; this effect can be induced in an individual when a fake but realistic hand, placed in full view, is stroked while synchronously stroking the person’s own hand, which is hidden from view. Specifically it was shown that after synchronous visuo-tactile stimulations, the perceived location of participant’s hand shifted towards the rubber hand. This illusion does not occur when the rubber hand and the participant’s own hand are stroked asynchronously, i.e. when temporal delays are longer than 300 ms [6].

Amputation causes sensory reorganizations that are thought to be attributable to functional changes in cerebral cortical maps of the body [7]. The result of these reorganizations is that neighbouring areas in the central body-map expand over the former hand area [8]. Therefore, it is frequent to find in the amputation stump a mapping of the phantom hand and points corresponding to the phantom digits can be identified [8]. Ramachandran has called this remapping of referred sensations (also known as referred phantom sensations) [9]. A recent study by Ehrsson and colleagues demonstrated the possibility of eliciting the

RHI on upper limb amputees by simultaneously stroking an alien hand and such specific points on their residual limbs [10]. The study suggested that similar effects can be achieved by replacing the rubber hand with a prosthesis with artificial sensors providing synchronous and physiologically relevant cutaneous touch feedback through an array of tactile stimulators on the stump (as in the study by Antfolk and colleagues [11]). The envisioned prosthesis, besides providing tactile feedback that could enhance closed-loop volitional control, holds the potential to be easily incorporated within one's body scheme because it would reproduce the perceptual illusion every time the prosthesis touches something.

The approach is exceptionally promising: even though it relies on non-invasive technology and stimulation techniques (as opposed to direct neural stimulation), it would allow for rudimentary recovery of reorganized physiological channels because a pressure on the prosthetic thumb would be felt as a pressure on the thumb of the phantom hand [10].

In order to deliver physiologically relevant touch feedback, tactile stimulators that display stimuli in the same modality of the sensory events on the artificial fingers, i.e. modality-matched (e.g. pressure to pressure) are necessary. For this reason Marasco and colleagues used a robotic touch/pressure interface coupled with a prosthetic limb and tested it with two targeted reinnervation amputees in a series of experiments fashioned after the RHI [12]. They were able to induce in their participants a vivid illusion of body ownership of the prosthesis, thus demonstrating the viability of the non-invasive, perceptual-tricking approach proposed by Ehrsson and colleagues [10].

However, the translation to the clinical practice of this method is tied to non-trivial technological issues. Current haptic devices cannot be exploited in portable systems because they are heavy, bulky and energy-inefficient [11]- [14]. Indeed, it is worth to note that, in order to provide self attribution of the whole hand (i.e. of all individuated digits), an array of devices capable to stimulate different locations on the skin should be applied on the residual limb of the amputee. Such a device would require enough space on the residual limb in order to host the actuators, and a large/heavy battery pack because of the large power consumption. In fact, even the state of art multifunction haptic stimulator for upper limb prosthetics [13] used by Marasco and colleagues, in their lab experiments [12], would be excessively large in size to be applied to the forearm of transradial amputees in an array fashion and in general inappropriate for clinical application. Hence, in our previous study we proposed to use sensory substitution, i.e. modality-mismatched feedback, in order to translate Ehrsson's original idea from the lab to the clinic [15]. Indeed miniature, inexpensive and safe arrays of **vibrators** (e.g. mobile-phone vibrators) can be easily and permanently fitted into a prosthesis equipped with tactile sensors [11], [16]. These can create an artificial sense of touch by mechanically stimulating reorganized afferent channels like referred phantom digits in transradial amputees [9], [10], or redirected cutaneous sensory nerves following targeted reinnervation in transhumeral amputees [12]. In our previous study we demonstrated that vibrotactile sensory substitution can promote self-attribution of an alien hand on normally limbed subjects when synchronous but modality-mismatched stimulations were delivered to the fingers of a rubber hand and of their own hand [15].

In the present work we have investigated whether similar effects could be induced in transradial amputees with referred phantom sensations. We employed the RHI experiment by Botvinick and Cohen [3] and manipulated visuo-tactile stimulations combining modality-matched and modality-mismatched feedback with synchronous or asynchronous stimulations on referred phantom digits on the residual limb or on the contralateral healthy hand. One could argue that the spreading of mechanical vibrations across the skin could partly inhibit the illusion in amputees, with respect to a mechanical stimulation precisely confined on the skin site (e.g. a pressure). This could not be the case, because in our previous study with transradial amputees we showed that similar multi-site tactile discrimination between pressure and vibrotactile stimulation can be achieved when the stimulus is applied onto the phantom hand map [11]. Therefore, in this work we expected to achieve similar illusion levels when stimulating the residual limb using modality-mismatched and modality-matched paradigms. As described in previous literature [10], [12], [15], we employed three independent measures of embodiment (questionnaires, pointing tests and skin conductance response test) to determine the extent of the illusion. Our results provided evidence that vibrotactile sensory substitution can promote the embodiment of a rubber hand in transradial amputees.

II. METHODS

A. Participants

Nine transradial amputees (amputation level between the elbow and wrist) participated in the study (seven males; aged between 24 and 76 years old). All participants gave their written consent and the study was approved by the local ethical committee. The experiments were conducted in accordance with the declaration of Helsinki. All subjects had their amputation after a traumatic accident (six had their right arm amputated). The participants were recruited by phone, practically at random, from a list of upper-limb amputees who were 20–80 years old at the time of the experiment, registered at the Italian national association of injured workers (ANMIL, http://www.anmil.it) and that lived in Tuscany. The only inclusion criterion were: experiencing referred phantom sensations of the missing hand and not taking any medication. The time after amputation and referred phantom sensations were factors that varied greatly across subjects, due to the minimal inclusion criterions (clinical data in Table I).

B. Evaluation conducted prior to the experiments

Before the RHI experiments commenced, all participants were interviewed to establish: (i) the existence of phantom limb pain and (ii) the existence and type/significance of referred phantom sensations. None of the participants reported phantom limb pain at the time of the experiment. Referred phantom sensations on the residual limb were experimentally verified and the corresponding skin sites were identified [10]. The subjects were asked if they felt that their phantom digits or another part of their phantom hand was being touched when different parts of the residual limb were touched. Each subject was then asked to indicate which part of the phantom hand (divided into digits I–V, palmar or dorsal side of the digits) corresponded to each part of the residual limb. Thus the sites on the stump were marked with a pen. Finally, the experimenter re-assessed the mapping while the participant had his/her eyes closed. A subset of these sites were selected as stimulation sites (Table I, last column), favoring those ones that could be easily reached by the experimenter using a paintbrush and that allowed the subject to maintain a comfortable posture throughout the experiment. When possible two sites were selected (this happened for seven subjects) and frequently (in seven subjects) one of these points corresponded to the phantom index (digit II).

C. Vibrotactile matrix stimulator

Vibrotactile stimulation was provided by means of a custom-built system [17] comprising two distinct miniature vibrators (310-101 series, Precision Microdrives UK). Each vibrator could be independently activated to vibrate at a pre-defined vibration frequency (160 Hz) and force amplitude (0.86 N, i.e. largely supra-threshold). These parameters were selected because they allowed for a correct perception of the stimulus, as shown in our previous works [11], [15]. Vibrators were triggered off through a keypad: as soon as a key was pressed the corresponding unit would start vibrating. Vibration was maintained as long as the key was kept pressed and switched-off simultaneously with key release. The time delay between the pressure of a key and the beginning of perceivable vibration was negligible (i.e. <10 ms). When used, vibrators were attached with tape on the selected referred phantom digits (Table 1, last column). Using this setup the experimenter was allowed to stimulate the rubber hand in full view with one hand and to press keys to produce vibrations on the hidden residual limb with the other hand (Fig. 1). When two stimulation sites were selected the experimenter could stimulate the rubber digits and the corresponding referred phantom digits in an alternative fashion (e.g. I-II-I-II).

D. Skin conductance sensor

Humans usually display a strong skin conductance response (SCR) to a threat stimulus on the rubber hand when the RHI occurs [18]. As in our previous work we recorded SCR (sampling rate 32 Hz) using a device worn by participants on the palm of their healthy hand (Q sensor palm system by Affectiva Inc.). The sensor was worn five minutes before the experiments began in order to achieve stable hand-electrode contact impedance.

E. Experimental session: general procedure

In this study we evaluated three **stimulation conditions**: *Phantom Hand Incongruent* (PHI), *Phantom Hand Congruent* (PHC) and *Intact Hand Congruent* (IHC).

***PHI**: Phantom hand incongruent*. The vibrotactile stimulators were carefully placed on the referred phantom digits on the amputation stump (Table I, last column). The experimenter hold a small soft paintbrush and used it to stroke the digits of a rubber, life-size cosmetic prosthesis (hereafter called rubber hand) in full view and activated the vibrotactile units to stimulate the referred phantom digits on the hidden stump (Fig. 1 and Fig. 2 A). The brushstrokes were delivered manually at a frequency of about 1 Hz (earphones playing a metronome aided a well trained experimenter). Each brushstroke was about 1 to 2 cm long and its duration was around 0.6-0.7 s. The duration of the vibration on the referred phantom digit matched the duration of the brushstroke on the equivalent digit of the rubber hand.

***PHC**: Phantom Hand Congruent*. The experimenter used two identical paintbrushes to stroke the fingers of the rubber hand (in full view) and the corresponding referred phantom digits on the hidden stump (Fig 2 B). Brushstrokes frequency, length and duration were identical to the PHI condition.

***IHC**: Intact Hand Congruent*. The experimenter used two identical paintbrushes to stroke the fingers of the rubber hand (in full view) and the corresponding fingers on the hidden real hand (Fig 2 C), exactly like in the original rubber hand experiment by Botvinick and Cohen [3]. Brushstrokes frequency, length and duration were identical to the PHI and PHC conditions.

It is known that when the visuo-tactile stimulation is asynchronous there is no illusion [3]. Hence we investigated the PHI, PHC, and IHC conditions both with **synchronous** and **asynchronous stimulation timing** in order to compare the outcomes and to assess whether such conditions (in particular the PHI) were able to elicit the illusion. In the synchronous case the stimulations on the rubber hand and on the body part were delivered synchronously. In the asynchronous case a small temporal delay (about 0.5 s) between stimulations was added. PHC and IHC conditions were included to verify that the participants could experience the RHI when either the stump or the intact hand where stimulated and to compare the strength of the RHI in the different experimental conditions. All combinations of stimulation and timing conditions (six in total) were tested twice, making a total of 12 trials for each subject. Between each trial participants had a 1-2 min long break to relax (in addition to the time needed to perform the tests or to change the experimental set-up). Each trial lasted 90 seconds. The order of trials was randomized across the participants and the overall experimental session lasted around 1 hour.

During the experiments, the participants sat with the residual limb and their contralateral arm resting on a table (Fig. 1). The rubber hand was placed on the table where it could be seen throughout the stimulation trial. The rubber hand was oriented in an anatomically correct posture (i.e. parallel to the hidden arm/stump) and with a pronation angle matching the hidden arm/stump. The rubber hand was right-handed or left-handed depending on the stimulation condition. During phantom hand stimulation conditions (PHC and PHI) the rubber hand had the same laterality of the residual limb (Fig. 2 A-B). In the case of the intact hand stimulation condition (IHC) the laterality was the same of the intact hand (Fig. 2 A). In all cases the residual limb (or intact hand) was hidden by a screen from the participant's view. The distance between the rubber hand and the participants' residual limb (or intact hand) was 10-20 cm. The participant was instructed to relax and fix his/her sight on the rubber hand for all the duration of the stimulation trial, while he/she was wearing the SCR sensor on the intact hand and earplugs to block out any sound arising from the vibrators (in fact no audible sound was produced).

Before each PHI and PHC stimulation trial the participants were asked to close their eyes and to indicate with their intact hand the felt position of their finger by means of a pre-stimulation pointing task [3]. A ruler mounted on the screen (and not apparent to the participant) was used to measure the end point of the movement. Immediately after each trial either one or two of the following tests of embodiment were carried out: (i) subjective data collection in the form of a questionnaire; (ii) proprioceptive drift by means of a post-stimulation pointing task; and (iii) SCR test. If two tests were presented then the priority order was the following: SCR, pointing task, questionnaire (following the protocol described in [15]). This order was chosen as the SCR test was brief (~12 s) and required the participant to simply keep visual contact of the rubber hand, hence preserving the illusion for the following test. The three tests were presented/performed in a pseudo-randomized order (also across subjects) in order to collect at the end of the session one measure from each test and each experimental condition, from each individual subject. Pre-stimulation and post-stimulation pointing tasks were not performed before/after the IHC stimulation trials, considering the difficulty to point on the ruler by the stump (in some cases the residual limb was so short that it would have forced the subject to stand up the chair, in order to touch the ruler).

F. Post-stimulation questionnaire

Each participant filled-in the questionnaire (one for each stimulation condition after the trial) which comprised of the nine statements designed by Botvinick and Cohen [3] in the original experiment and translated into Italian. Different versions of the questionnaire were delivered after the different trials in order to take into account the differences of the stimulation conditions (i.e. intact hand versus stump). The questionnaires required the participants to rate the strength of their agreement or disagreement with nine perceptual effects. Three statements (i.e. illusion statements) referred to the extent of sensory transfer into the rubber hand and the self-attribution of it during the trial. The other six statements (i.e. control statements) served as controls for compliance, suggestibility, and “placebo effect” [3]. The order in which the nine statements were presented was randomized across trials and participants. Participants were asked to rate the extent to which these statements did or did not apply, using a seven-point scale. On this scale, -3 meant “absolutely certain that it did not apply,” 0 meant “uncertain whether it applied or not,” and +3 meant “absolutely certain that it applied”.

G. Post-stimulation skin conductance response test

Before the experiments started the participants were informed that they would never be stabbed with a needle and that they would not experience any painful sensation; then, the experimenter informed and showed the participants how he would stab the rubber hand with a needle (threat stimulus) attached to a syringe (100 ml), later on.

This test was performed once for each stimulation condition, by each participant. After the stimulation the rubber hand was suddenly stabbed with the needle following the procedure adopted in our previous study [15]. Notably, the participant could not guess/predict if he/she would have been stabbed or not, given the randomized order of the tests. For each trial we identified a peak value in the SCR within 1–10 s of the onset of the threat stimuli. As a baseline we used the value registered 1 s before the threat stimulus was presented. The magnitude of the SCR was used to measure the extent of the illusion [18].

H. Post-stimulation point task and proprioceptive drift

After PHI or PHC stimulation trials new pointing tests were performed and the measures of where the stimulation was felt were noted. The proprioceptive drift was calculated as the difference between the pre-stimulation and post-stimulation pointing task measurements and provided behavioural evidence of the occurrence of the RHI [19]. A positive proprioceptive drift represented a mislocalization of the participant's stump toward the rubber hand, whereas a negative drift represented a mislocalization of the participant's stump away from the rubber hand.

I. Data Analysis

All measures from the tests of embodiment were collected and arranged based on the stimulation condition. The Kolgomorov-Smirnov test ($p > 0.05$) was used to verify that the data were normally distributed. If so, for each test a two-way repeated measures ANOVA [factors: stimulation condition (IHC, PHC, PHI), timing of stimulation (synchronous and asynchronous)] was performed in order to highlight differences among conditions and timing of stimulation and possible significant interactions. If the ANOVA suggested that there was a difference in stimulation condition, the groups were compared pair-wise using Bonferroni adjustment. If the ANOVA showed a difference in stimulation timing, the data from synchronous and asynchronous conditions were compared using the one-tailed, paired t-test, for each condition in order to assess if the illusion was promoted [20] - [21]. If the ANOVA did not show significant difference the groups were compared pair-wise using Bonferroni adjustment as in Tsakiris *et al.* [20]. A p-value less than 0.05 was considered statistically significant.

For the questionnaire only, prior to the two-way ANOVA we compared the mean score of the illusion statements against the mean score of the control statements using a two tailed paired t-test; this was necessary in order to verify that the subjects were not suggestible. The a priori hypothesis was that the illusion statements would be rated higher than the control statements.

Finally, the data from the three measurements were combined for analysis using a three-way repeated measures ANOVA [factors: stimulation condition (PHC, PHI), timing of stimulation (synchronous and asynchronous), measure (questionnaire, SCR, proprioceptive drift)], as suggested by the work by Ehrsson and colleagues (2008) [10]. The mean rating from the three illusion statements was employed as the measure from the questionnaires. From the pointing task and the SCR tests we used the proprioceptive drift and the SCR value from each condition and individual subject, respectively.

III. RESULTS

The Kolgomorov-Smirnov test demonstrated that all the data were normally distributed.

A. Questionnaire

The graph in Fig. 3 presents the mean ratings (± standard error) to the illusion and control statements for the three stimulation conditions: phantom hand incongruent (PHI), phantom hand congruent (PHC) and intact hand incongruent (IHC). The illusion statements were rated higher than the control statements in all stimulation conditions ($p<0.05$), in agreement with previous studies [3], [18], thus indicating that the subjects were not suggestible. Because of this, we focused our analysis on illusion statements, as suggested in previous studies [10], [15]. Larger ratings were given when the stimulations were synchronous, in each modality (Fig. 3). The two-way ANOVA showed that the effect of synchronicity produced significant differences [$F(1,8)= 5.9$ $p<0.05$], whereas different stimulation conditions did not produce significant differences. The interaction between the synchronicity and stimulation conditions was not significant. The post hoc analysis demonstrated statistical differences between synchronous and asynchronous stimulations for all conditions ($p<0.01$, $p<0.05$ and $p<0.05$ for IHC, PHC and PHI, respectively), whereas multiple comparisons with Bonferroni correction (three comparison tests: IHC vs. PHC, PHC vs. PHI, IHC vs. PHI) showed a significant difference only between the PHC and PHI conditions ($p<0.05$) (Fig. 3). Taken collectively the outcomes from the questionnaires (self-evaluation of the illusion) showed that vibrotactile sensory substitution on referred phantom digits (PHI) was able to promote embodiment of the alien hand, however this illusion was weaker when compared to the one elicited with the congruent paradigm (PHC).

B. *Skin conductance response test*

The SCR was greater in the synchronous cases (than in the asynchronous ones) for all the tested modalities (Fig. 4). The two-way ANOVA showed that the effect of synchronicity was significant [$F(1,8) = 10.0$, $p<0.05$] and that the effect of stimulation condition was not. The interaction between the synchronicity and stimulation conditions was not significant. The post hoc analysis showed significant differences between synchronous and asynchronous stimulations for all conditions ($p<0.05$). Multiple comparisons with Bonferroni correction (three comparison tests: IHC vs. PHC, PHC vs. PHI, IHC vs. PHI) did not demonstrate statistical differences across conditions (statistical power of the analysis < 40%).

C. *Proprioceptive drift*

In agreement with previous studies and as expected the mean proprioceptive drift was greater in the synchronous case than in asynchronous one for the two tested modalities (PHI and PHC) (Fig. 5). The two-way ANOVA showed a statistical difference between the synchronous and asynchronous trials [$F(1,8)=12.8$, $p<0.01$] and non-significant differences between the two stimulation conditions. The interaction between the synchronicity and stimulation conditions was not significant. Post hoc paired t-tests demonstrated statistical differences between synchronous and asynchronous stimulations for both the PHI ($p<0.01$) and PHC ($p<0.05$) conditions. The proprioceptive drift provided behavioral evidence that incongruent vibrotactile stimulation (PHI) promoted embodiment of the alien hand at levels similar to the congruent paradigm (PHC).

D. *Results across the three measures*

The three-way repeated measured ANOVA demonstrated statistically significant differences only between stimulations timing [synchronous vs. asynchronous, $F(1,8)=16.8$, $p<0.01$] and not between the other factors. The only significant interaction [$F(2,58)=5.0$, $p<0.05$] was the one between type of measure and timing of stimulation. Post hoc paired t-tests demonstrated statistical differences between synchronous and asynchronous stimulations for both the PHI ($p<0.01$) and PHC ($p<0.05$) conditions.

Taken across the three measures our results provide evidence that: i) vibrotactile sensory substitution (PHI condition) elicits feeling of body ownership of an alien hand in transradial amputees, when the vibration is applied onto referred phantom digits, and ii) that this illusion is similar to that achieved with a congruent paradigm (i.e. PHC) (80 % statistical power). In particular we demonstrated that after just a short exposure (90 seconds) to modality-mismatched stimulation using seen brushstrokes and felt vibrations, participants felt a vivid RHI.

IV. DISCUSSION

The illusion was assessed by means of three independent measures of embodiment. Through the questionnaires participants self-evaluated the illusion by rating perceptual statements and control statements which allowed to confirm they were not suggestible. The behavioural mislocalization of the proper hand towards the rubber hand was evaluated through the pointing task. Finally, the SCR provided an objective physiological evidence of autonomic system arousal. As the three measures converged in closely matched results we can consider them as robust. Another methodological asset of this study is that the subjects performed the twelve stimulation trials and the measurements in a randomized order so that our results are virtually free from any “learning” effect or bias due to eventual carry-over effects (these effects were limited by the long breaks between trials).

In this work a statistical difference in the measurement of embodiment, between synchronous and asynchronous stimulation was considered as the proof of the illusion in that condition. This difference was statistically relevant for the PHI condition (as well as PHC) both across and within tests; the analysis across the three measures also showed that there was no significant difference between PHI and PHC and the congruent and incongruent conditions elicited similar levels of illusion. However, the results from the questionnaire and SCR (Fig.3-4) suggest that the strength of the illusion in the congruent conditions (IHC, PHC) seemed larger than in the experimental condition. In other words it was possible to promote body-ownership in transradial amputees using vibrotactile substitution but this illusion could not match the one elicited with congruent stimulation. This is in agreement with our previous study [15] and supports the hypothesis that the vividness of the illusion seem to be modulated by the specificity of visuo-tactile conflict and on how the matching of the concurrent inputs is perceived as realistic based on a pre-existing representation of one's own body (cf. discussion in [15]). One should also consider that in the phantom hand conditions tactile stimulations reach the deafferented primary sensorimotor cortex through reorganized pathways and not through the physiological ones. Hence it seems obvious to elicit a weaker illusion on the amputated side. Nevertheless, the illusion seemed to be vivid in our group of participants. It is worth mentioning that the participants had a relatively old amputation: eight (out of nine) had their hand amputated more than 10 years before the experiments took place. Thus, since the time after amputation seems to influence the strength of illusion [10], we can expect to achieve a more pervasive RHI with people with a more recent amputation.

In this first exploratory study with amputees we used vibration stimuli which were known to elicit RHI in normally limbed individuals [15] and to be correctly perceived on referred phantom fingers [11], based on our previous experience. However, it is still unknown how the vibration parameters (amplitude and frequency) can affect the extent of the illusion; a vibration stimulus that better matches the visual input in terms of tactile encoding and pre-existing body representation could enhance the illusion. Conversely, a reduced matching could inhibit the illusion as previously observed in normally limbed individuals when using a modified RHI paradigm (i.e. tapping with the tip of a chopstick on the finger pads rather than brushstroking them) [15]. This work invites further studies in which this issue is explored.

In general we achieved results -in absolute values- in agreement with previous studies. This was true for the traditional RHI condition (i.e. IHC) [18] and for the PHC, which provided results similar to the equivalent condition investigated by Ehrsson and colleagues [10] in their first work on amputees (which they referred to as stump condition). To our knowledge, the latter, is the only study about the RHI involving transradial amputees (Marasco and colleagues investigated the RHI with transhumeral amputees that underwent targeted muscular reinnervation [12]). Ehrsson and colleagues found a large difference between PHC and IHC (which they referred to stump and finger conditions, respectively) [10]. In our case the general trend was that PHC and IHC elicited similar levels of illusion (Fig.3-4). The difference between the two studies might be explained by the fact that when our participants exhibited indistinguishable phantom digits (i.e. two or more digits felt on the same skin site) we targeted (for stimulation) the other digits that instead could be clearly distinguished. Ehrsson and colleagues, always targeted the index finger regardless its perception was fused with other fingers or not.

The vividness of the illusion greatly varied across participants as verbally reported after the experiments. For example FF reported stronger levels of illusion in the phantom hand conditions (especially PHC) than in the traditional RHI condition (i.e. IHC). Subject PD did not experience vivid referred phantom sensations and thus did not experience strong embodiment of the alien hand. Overall, the different levels of body ownership verbally claimed by the participants could be verified by analyzing the data on a subject basis. The variability across subjects could be explained by the fact that we used a group of amputees, which were heterogeneous with respect to many factors such as referred phantom sensations, time since amputation, age and level of amputation. It remains to be shown how much these factors affect the RHI when the stimuli (congruent or incongruent) are applied on the phantom map.

Many transradial amputees experience tactile phantom sensations when their residual limb is touched. Recent imaging studies have shown that amputees activate fronto-parietal multisensory areas when they embody a prosthetic limb [22], just as fully limbed individuals do when they experience the rubber hand illusion [23]. It is likely that the present ‘sensory –substitution’ version of the RHI also involves integration of visual and tactile signals in these areas. In particular, the tactile stimulation of phantom digits in the residual limb is capable to activate the missing hand area of the primary somatosensory cortex [24]. In this way, tactile signals from the residual limb can reach the hand section of the primary somatosensory cortex, and from there be conveyed to the multisensory association cortex where integration with visual signals takes place.

This study shows that it is possible to promote embodiment of a prosthetic alien hand in such clinical population, by using a sensory substitution paradigm. The achieved results, if exploited in the clinical practice, could produce a great impact in the field of prosthetic systems; indeed arrays of low-cost, miniaturized and low power consumption tactile sensors and vibrators could be easily incorporated into prosthetic hands and sockets, so to induce the illusion every time the prosthesis touches something. In addition to transradial amputees with referred phantom sensations, our results could have an important impact on transhumeral or shoulder disarticulation patients that underwent targeted muscular reinnervation [25], [26]. It is known that after this surgery, distinct hand sensations can be restored in the cutaneous area overlying the reinnervated muscles because sensory afferents from the transposed nerves reinnervate the denervated skin [27]. Hence, specific sites on this area could be used as stimulation points for the miniaturized vibrators in order to provide somatotopic, thus physiologically relevant stimulation. This feature could improve the controllability of the prosthesis by providing intuitive feedback to individual [12] but could also be an important asset in itself; in fact if the prosthesis could induce a feeling of ownership it is predictable that the ratio of unsatisfied patients will reduce, as hypothesized by Murray [28]. This alone could pay off the research efforts spent in the past decades for developing hand prosthetics with sensory feedback.

V. Funding

This work was supported by the European Commission under the WAY project (FP7-ICT-288551) and by the Italian Ministry of Education University and Research under the FIRB-2010 MY-HAND Project [RBFR10VCLD].

VI. References

[1] G. Westling, R. S. Johansson “Factors influencing the force control during precision grip.” *Exp Brain Res,* vol. 53 (2), pp. 277-284, 1984.

[2] E. Biddiss, D. Beaton, T. Chau “Consumer design priorities for upper limb prosthetics.” *Disabil Rehab Assist Technol* vol. 2 (6), pp. 346-357, 2007.

[3] M. Botvinick, J. Cohen “Rubber hands “feel” touch that eyes see.” *Nature*; vol. 391, pp. 756, 1998.

[4] P. Rochat “Self-perception and action in infancy.” *Exp Brain Res*, vol. 123, pp. 102–109.

[5] E. van den Bos, M. Jeannerod “Sense of body and sense of action both contribute to self-recognition.” *Cognition*, vol. 85, pp. 177–187, 2002.

[6] S Shimada, K Fukuda, K. Hiraki “Rubber hand illusion under delayed visual feedback.” *PLoS ONE*; vol. 4 (7), e6185, 2009.

[7] J. T. Wall, J. Xu, X. Wang "Human brain plasticity: an emerging view of the multiple substrates and mechanisms that cause cortical changes and related sensory dysfunctions after injuries of sensory inputs from the body." *Brain Res Rev*, vol. 39, pp. 181-215, 2002.

[8] V. S. Ramachandran, W. Hirstein "The perception of phantom limbs." The DO Hebb lecture, *Brain* 1998; vol. 121 (9), pp. 1603-1630.

[9] V. S. Ramachandran, M. Stewart, D. C. Rogers-Ramachandran "Perceptual correlates of massive cortical reorganization." *Neuroreport*; vol. 3, pp. 583-586, 1992.

[10] H. H. Ehrsson, B. Rosén, A Stockselius, C Ragnö, P. Köhler, G. Lundborg "Upper limb amputees can be induced to experience a rubber hand as their own." *Brain*; vol. 131 (12), pp. 3443–3452, 2008.

[11] C. Antfolk, M. D'Alonzo, M. Controzzi, B. Rosén, G. Lundborg, F. Sebelius, C. Cipriani, "Artificial redirection of sensation from prosthetics finger to phantom hand map on trans-radial amputees: vibrotactile versus mechanotactile sensory feedback." *IEEE Trans Neural Syst Rehab Eng*; 21(1), pp. 112-120, 2013.

[12] P. D. Marasco, K Kim, J. E. Colgate, M. A. Peshkin, T. A. Kuiken "Robotic touch shifts perception of embodiment to prosthesis on targeted reinnervation amputees." *Brain*; vol. 134: pp. 747-58, 2011.

[13] K. Kim, J. E. Colgate, J. J. Santos-Munne, A. Makhlin, M. A. Peshkin "On the Design of Miniature Haptic Devices for Upper Extremity Prosthetics." *IEEE-ASME Trans Mechatron*, vol. 15, pp. 27–39, 2010.

[14] C. Antfolk, M D'Alonzo, G Lundborg, B Rosen, F Sebelius, C Cipriani, "Sensory feedback in upper limb prosthetics" *Exp Rev Medical Dev*. vol. 10(1), pp. 45–54, 2013.

[15] M. D'Alonzo, C. Cipriani "Vibrotactile sensory substitution elicits feeling of ownership of an alien hand." *PLoS ONE*, vol. 7 (11), pp. 1-9, 2012.

[16] H. Sears, E. Iversen, S Archer, J. Linder, K. Hays "Grip force feedback in an electric hand – preliminary results." In: Proc. Myoelectric Controls/Powered Prosthetics Symposium 2008, Fredericton, NB, Canada, pp. 175-178.

[17] C. Cipriani, M. D'Alonzo, M. C. Carrozza "A Miniature Vibrotactile Sensory Substitution Device for Multi-fingered Hand Prosthetics." *IEEE Trans Biomed Eng*; vol. 59 (2), pp. 400-408, 2012.

[18] K. C. Armel, V. S. Ramachandran "Projecting sensations to external objects: evidence from skin conductance response." *Proc Biol Sci*; vol. 270, pp. 1499–1506, 2003.

[19] M. Tsakiris, P. Haggard "The rubber hand illusion revisited: visuotactile integration and self-attribution." *J. Exp. Psychol Hum Percept Perform*; vol. 3, pp. 80–91, 2005.

[20] M. Tsakiris, L. Carpenter, D. James, A. Fotopoulou "Hands only illusion: multi sensory integration elicits sense of ownership for body parts but not for non corporeal objects." *Exp Brain Res*; vol. 204: pp. 343-352, 2010.

[21] D. C.Howell "Statistical methods for psychology." 4th edn. Duxbury, Belmont, 1997.

[22] L. Schmalzl, A. Kalckert, C. Ragnö, H. H. Ehrsson "Neural correlates of the rubber hand illusion in amputees: A report of two cases." Neurocase (2013).

[23] H. H. Ehrsson, C. Spence, R. E. Passingham 'That's my hand!' Activity in the premotor cortex reflects feeling of ownership of a limb." *Science*, vol. 305, pp. 875-877, 2004.

[24] A. Björkman, A. Weibull, J Olsrud, H. H. Ehrsson, B. Rosén, I. M. Björkman-Burtscher . "Phantom digit somatotopy: a functional magnetic resonance imaging study in forearm amputees." 2012 Jul;36(1):2098-106.

[25] T. A. Kuiken, G. A. Dumanian, R. D. Lipschutz, L. A. Miller, K. A. Stubblefield "The use of targeted muscle reinnervation for improved myoelectric prosthesis control in a bilateral shoulder disarticulation amputee." *Prosthet Orthot Int;* vol. 28, pp. 245–253, 2004.

[26] T. A. Kuiken, G. Li, B. A. Lock, et al. Targeted Muscle Reinnervation for Real-time Myoelectric Control of Multifunction Artificial Arms. *JAMA*.; 301(6): 619-628, 2009.

[27] T. A. Kuiken, P. D. Marasco, B. A. Lock, R. N. Harden, J. P. Dewald "Redirection of cutaneous sensation from the hand to the chest skin of human amputees with targeted reinnervation." *Proc Natl Acad Sci USA*.; vol. 104(50), pp. 20061-6, 2007.

[28] C. Murray Embodiment and Prosthetics. In: Gallagher P, Desmond D, MacLachlan M, editors. Psychoproshetics. London: Springer;. pp. 119-29.

Figure 1

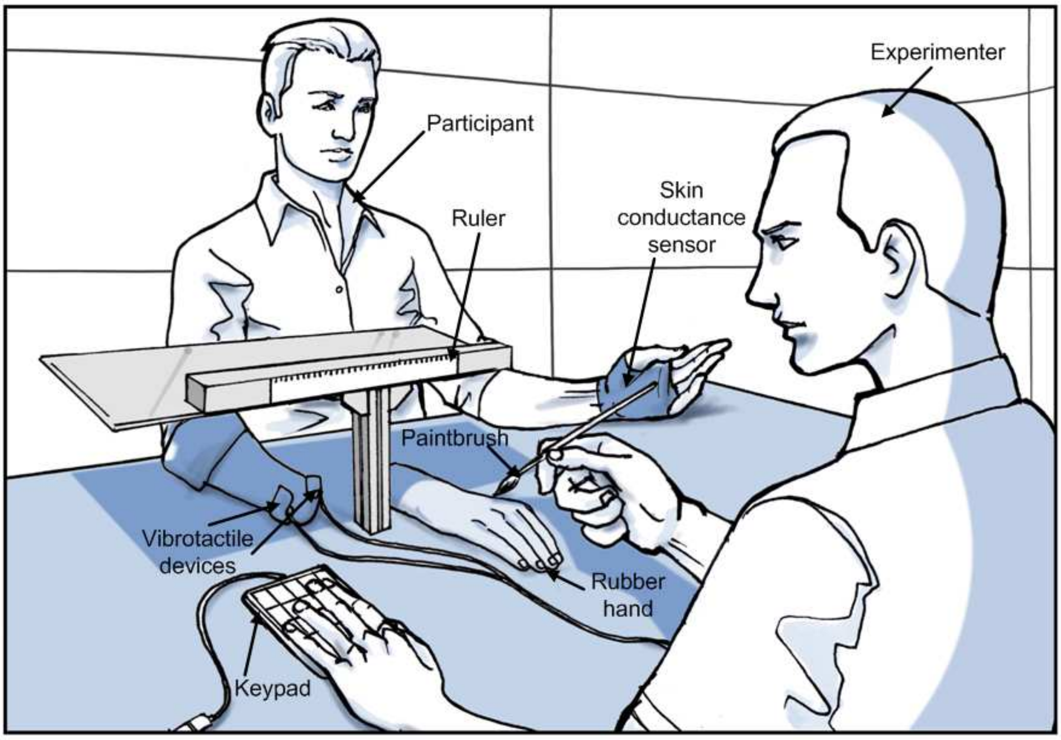

Experimenter
Participant
Ruler
Skin
conductance
sensor
Paintbrush
Vibrotactile
devices
Rubber
hand
Keypad

Figure 2

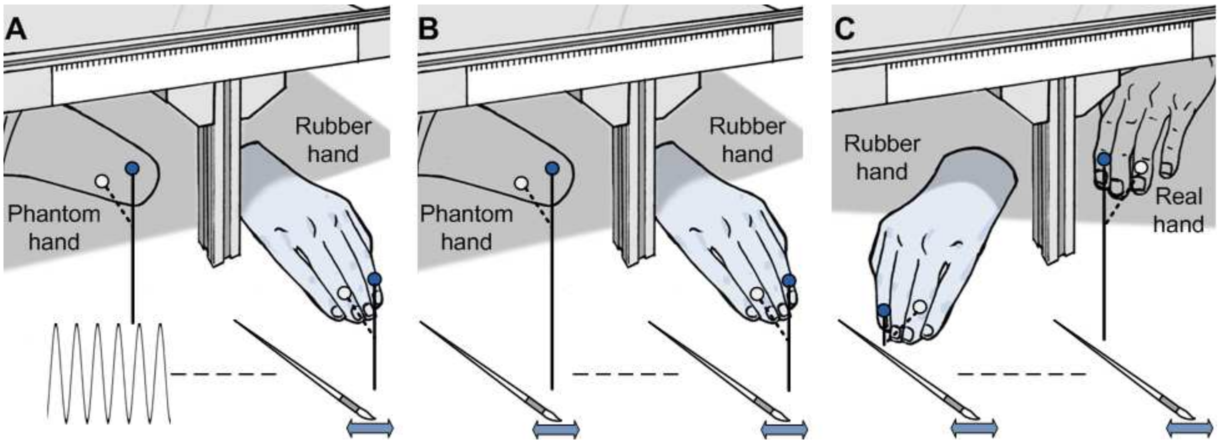
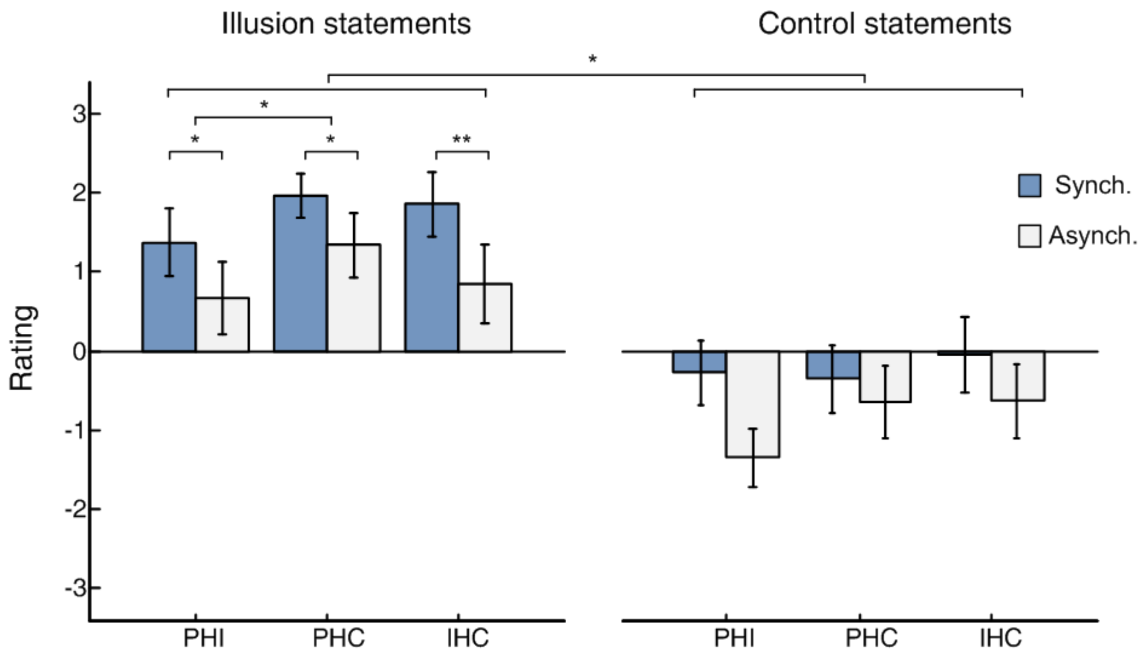
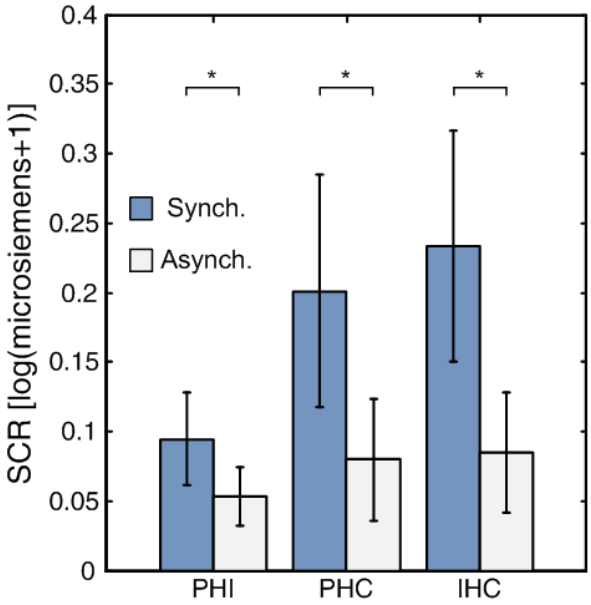

A
Rubber hand
Phantom hand
B
Rubber hand
Phantom hand
C
Rubber hand
Real hand

Figure 3



Illusion statements
Control statements
*
*
*
*
**
Synch.
Asynch.
Rating
3
2
1
0
-1
-2
-3
PHI
PHC
IHC
PHI
PHC
IHC

Figure 4



SCR [log(microsiemens+1)]
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
*
*
*
Synch.
Asynch.
PHI
PHC
IHC

Figure 5

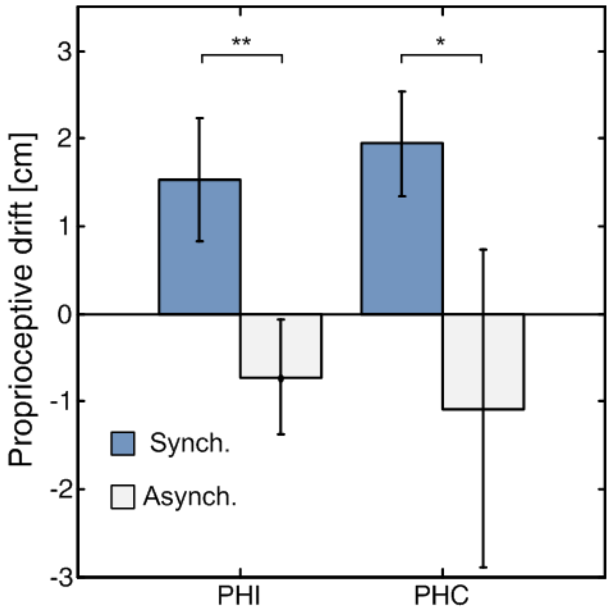


Table 1

Subject (gender, age)	Original dominant hand	Stump length (laterality)	Type of prosthesis[a]	Years since amputation	Phantom digits[b]	Stimulated referred phantom digits[b]
FF (m, 48)	R	Mid third (R)	Myo	28	I-V	II, III (Dorsal part)
PG (m, 50)	R	Upper third (R)	Myo	17	I-V	I (Dorsal part)
IP (f, 43)	R	Lower third (R)	Myo	18	I-V	II,IV (Palmar part)
FM (m, 43)	R	Lower third (R)	Cosm	18	I,(II-IV),V	I, V (Dorsal part)
CM (m, 54)	R	Upper third (R)	Myo	13	I-III,V	I, II (Dorsal part)
SP (m, 76)	R	Mid third (L)	Myo	32	I-V	I, II (Dorsal part)
PD (f, 24)	L	Mid third (L)	Myo	3	I-II	II (Dorsal part)
DV (m, 73)	R	Mid third (R)	Cosm	50	I,II,V	I,II (Dorsal part)
LA (m, 73)	R	Mid third (L)	Myo	63	I,II,V	II (Dorsal part)

[a] Myoelectric or cosmetic,. [b] I: thumb, II: index, III: middle, IV: ring, V: little. Digits that were perceived *fused* together are grouped within brackets.

Figure and table captions

Fig. 1. Experimental set-up. Experimental set-up during the incongruent stimulation of the residual limb (PHI condition). Participants wore earplugs to block out any noise arising from the vibration and a skin conductance sensor on the palm of their intact hand. Participants were instructed to fix their sight on the rubber hand, throughout the experiment. The experimenter provided incongruent visuo-tactile stimuli by brush stroking the rubber hand digits and activating vibrations on the correspondent referred phantom digits. Vibrotactile stimuli were triggered off by the experimenter using a keypad. Throughout the experiment the rubber hand was in full view, whereas the stump was hidden by a screen.

Fig. 2. Experimental conditions. Schematic diagrams showing the three stimulation conditions used to induce the Rubber Hand Illusion (RHI). A) Phantom Hand Incongruent stimulation (PHI) was our experimental (modality-mismatched) condition: brushstrokes and vibrations were delivered on the rubber hand and on the phantom hand, respectively. B) Phantom Hand Congruent stimulation (PHC): brushstroke stimulation was delivered on rubber hand and on the phantom hand map on the stump. C) Intact Hand Congruent stimulation (IHC) was the classic RHI experiment as designed by Botvinick and Cohen (1998). We investigated the PHI, PHC, and IHC conditions both with synchronous and asynchronous stimulation timing. In the latter a small temporal delay (about 0.5 s) between stimulations was added.

Fig. 3. Results of questionnaire for different conditions. Illusion statements: 1) It seemed as if I was feeling the stimulation in the location where I saw the rubber hand touched; 2) It seemed as though the sensation I felt was caused by the paintbrush touching the rubber hand; 3) I felt as if the rubber hand was my hand). Control statements: 4) It felt as if my phantom hand (or intact hand) was drifting towards the rubber hand; 5) It seemed as if I might have more than two arms; 6) It seemed as if the touch I was feeling came from somewhere between my own stump (or intact hand) and the rubber hand; 7) It felt as if my stump (or intact hand) was turning 'rubbery'; 8) It appeared (visually) as if the rubber hand was drifting towards my stump (or intact hand); 9) The rubber hand began to resemble my stump (or intact hand), in terms of shape,

skin tone, freckles or some other visual feature. * indicates a p-value < 0.05. ** indicates a p-value < 0.01.

Fig. 4. Physiological induced sweating. Mean psychologically induced sweating, as measured by the skin conductance response (SCR) after the threat stimuli on the rubber hand recorded in the Phantom Hand Incongruent (PHI), Phantom Hand Congruent (PHC) and the Intact Hand Congruent (IHC) conditions. * indicates a p-value < 0.05.

Fig. 5. Results of proprioceptive drift. Mean proprioceptive drift (in cm) measured as a difference between pre-stimulation and post-stimulation pointing task for the Phantom Hand Congruent (PHC) and Phantom Hand Incongruent (PHI) conditions. * indicates a p-value <0.05, ** indicates a p-value < 0.01.

Table 1. Details of participants