doi:10.1093/brain/awq361 Brain 2011: 134; 747–758 | 747

BRAIN
A JOURNAL OF NEUROLOGY

Robotic touch shifts perception of embodiment to a prosthesis in targeted reinnervation amputees

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Existing prosthetic limbs do not provide amputees with cutaneous feedback. Tactile feedback is essential to intuitive control of a prosthetic limb and it is now clear that the sense of body self-identification is also linked to cutaneous touch. Here we have created an artificial sense of touch for a prosthetic limb by coupling a pressure sensor on the hand through a robotic stimulator to surgically redirected cutaneous sensory nerves (targeted reinnervation) that once served the lost limb. We hypothesize that providing physiologically relevant cutaneous touch feedback may help an amputee incorporate an artificial limb into his or her self image. To investigate this we used a robotic touch interface coupled with a prosthetic limb and tested it with two targeted reinnervation amputees in a series of experiments fashioned after the Rubber Hand Illusion. Results from both subjective (self-reported) and objective (physiological) measures of embodiment (questionnaires, psychophysical temporal order judgements and residual limb temperature measurements) indicate that returning physiologically appropriate cutaneous feedback from a prosthetic limb drives a perceptual shift towards embodiment of the device for these amputees. Measurements provide evidence that the illusion created is vivid. We suggest that this may help amputees to more effectively incorporate an artificial limb into their self image, providing the possibility that a prosthesis becomes not only a tool, but also an integrated body part.

Keywords: neural-machine-interface; tactile; haptic; sensation; rubber-hand-illusion

Introduction

Advanced prosthetic limbs share many attributes with the limbs they replace including multiple joint actuators and tactile sensors. Providing sensory feedback from prosthetics is difficult because there is no connection from the artificial hand to the neural channels that served the missing limb (Scott, 1990; Lebedev and Nicolelis, 2006; Patil and Turner, 2008). Functional difficulties

Received May 22, 2010. Revised October 27, 2010. Accepted October 28, 2010. Advance Access publication January 20, 2011

arise because the amputee must rely on vision instead of touch to direct the manipulation of objects. Lack of sensory feedback is often cited as a reason that amputees reject motorized (myoelectric) devices (Wright *et al*., 1995; Lundborg and Rosen, 2001) and cable-driven, body-powered prosthetic limbs are preferred by some amputees because the actuator cables of the limb provide some sensory feedback (Stark and LeBlanc, 2004). Earlier efforts to displace feedback from the prosthesis to alternate body surfaces by either electrical or mechanical means have met with limited success (Beeker *et al*., 1967; Prior and Lyman, 1975; Shannon, 1979; Scott *et al*., 1980; Patterson and Katz, 1992). This is likely because the amputee must learn to translate and utilize input that is not physiologically relevant (Anani *et al*., 1977; Scott, 1990).

Functional advantages may be afforded by integrating physiologically relevant sensory feedback with prosthetics, such as goal confirmation vibration detection, pressure discrimination and limb positioning (Dhillon and Horch, 2005; Schultz *et al*., 2009; Sensinger *et al*., 2009). There also appear to be functional cognitive benefits associated with returning cutaneous sensation. Limb loss disrupts an amputee's body image (Rybarczyk and Behel, 2008), which is probably linked to the loss of afferent input from the amputated limb. Evidence suggests that the sense of body self-identification is intrinsically linked with cutaneous touch (Botvinick and Cohen, 1998; Armel and Ramachandran, 2003; Ehrsson *et al*., 2004; Tsakiris and Haggard, 2005; Longo *et al*., 2008; Moseley *et al*., 2008). These studies used the Rubber Hand Illusion to explore the inter-relation of touch, vision and body self-identification.

The Rubber Hand Illusion is a perceptual illusion where touch and vision are used to make a subject feel that a rubber model of a hand belongs to their body. The illusion is generated by stroking the hidden hand of a subject while synchronously stroking a rubber hand positioned in place of their hidden hand. When the subject feels and sees this correlated activity it induces an involuntary (Welch, 1972) embodiment of the rubber hand (Armel and Ramachandran, 2003). We find the idea of incorporating a rubber hand into the self-image of a subject compelling because it suggests that a similar effect could be achieved with a prosthesis that provided physiologically relevant sensory feedback. To investigate this idea we have created an artificial sense of touch for a prosthesis using a robotic tactile interface (G10 tactor) that is linked to the sensory nervous system through surgically redirected nerves that once served the missing hand (targeted reinnervation) (Kuiken *et al*., 2004, 2007*a*; Kim *et al*., 2010).

In this study we employed a variation of the Rubber Hand Illusion to measure limb embodiment in two targeted reinnervation amputees, using changes in tactile and visual input from a sensate prosthesis. We used three independent measures of embodiment (questionnaires, psychophysical temporal order judgements and physiological temperature measurements) to determine if a prosthetic device that provided a physiologically appropriate sense of cutaneous touch could drive a shift in perception towards incorporation of the device into the self-image of the amputees. We hypothesize that if the prosthesis is incorporated into the self-image under visual-tactile conditions where the Rubber Hand Illusion is generated, then we should see measurable changes in outcome that differ from visual-tactile conditions that do not generate the Rubber Hand Illusion.

Materials and methods

Amputee subjects

A 23-year-old male right traumatic transhumeral amputee (S-1) and a 41-year-old female left traumatic transhumeral amputee (S-2) participated in this study. Both had the targeted reinnervation surgery $\geqslant$1.7 years prior to these experiments. Detailed information on this surgical procedure and outcomes has been described (Kuiken *et al*., 2004, 2007*a*, *b*; Hijjawi *et al*., 2006; O'Shaughnessy *et al*., 2008; Dumanian *et al*., 2009). These transhumeral amputees were chosen because they both underwent the sensory reinnervation component of the surgical procedure and showed clear sensory percepts to touch projected to the missing limb. Neither amputee was coupled to the neural control of their prosthetic device for these experiments. All of the experiments were conducted at the Rehabilitation Institute of Chicago with Northwestern University with institutional review board approval and the written informed consent of the subjects.

Targeted reinnervation

Targeted reinnervation was developed to provide intuitive sensory feedback and motor control for upper-limb prosthetics (Kuiken *et al*., 2004, 2007*a*, *b*; Zhou *et al*., 2007). In targeted reinnervation, the limb nerves remaining after amputation are surgically redirected to new skin and muscle sites (Hijjawi *et al*., 2006; Dumanian *et al*., 2009). A sensory neural-machine-interface is created by denervating a patch of target skin near the nerve redirection site to provide a receptive environment for sensory reinnervation. When the reinnervated target skin is touched it causes the amputees to experience the sensation that their missing limb is being touched (Kuiken *et al*., 2007*a*, *b*). The redirected sensation is clear and strongly projected to different parts of the missing limb. These amputees typically report either a sense of pressure or a tingling sensation when their reinnervated skin is pressed with a blunt probe (Kuiken *et al*., 2007*a*). They can sense gradations in pressure, i.e. the harder the target skin is pushed the stronger the projected sensation (Sensinger *et al*., 2009). The targeted reinnervation amputees can also feel hot, cold and pain (Kuiken *et al*., 2007*a*), they can differentiate vibration (Schultz *et al*., 2009) and the target skin gains a degree of tactile functionality approaching that normally found in the hand (Marasco *et al*., 2009). The sensation arising from targeted reinnervation is different than phantom sensation, which is a phenomenon likely arising from the reorganization of functional connections in the central nervous system (Ramachandran *et al*., 1992*a*, *b*; Borsook *et al*., 1998; Flor *et al*., 1998, 2000).

G10 tactor

The G10 tactor (Kinea Design LLC, Evanston, IL, USA) is a miniature haptic robot designed to provide touch information to amputees (Kim *et al*., 2010). It displays touch input from a subminiature industrial load cell (Omega Engineering Inc., Stamford, CT, USA) as proportional pressure and transients along one degree of freedom through the tactor head to the skin of the amputee with up to 12 mm of travel. The G10 tactor was attached to a thermoplastic cuff and positioned over the reinnervated skin of the amputees where they felt sensations

projected to their hand and fingertips (Fig. 1A). Pressure input to the load cell (affixed to the prosthesis with adhesive-backed hook-and-loop pads) signalled the G10 tactor to push on the redirected cutaneous nerves in the residual limb skin, which evoked sensations projected to the missing hand. When the G10 tactor pressed into the target skin of Subject S-1 he felt a mild tingling or shocking sensation. This sensation was graded; the harder the tactor pushed, the stronger the sensation was felt. When the G10 tactor pressed into the target skin of Subject S-2 she felt a graded sensation of pressure.

The Rubber Hand Illusion and questionnaires

The Rubber Hand Illusion was generated on the amputated side of the subjects by having them watch the investigator touch the prosthetic hand and load cell while the G10 tactor pressed into the reinnervated target skin of the residual limb (Kuiken *et al*. 2007) (Fig. 1A–C). The targeted reinnervation amputees were seated in a quiet room with a prosthetic arm fastened to a table in an anatomically appropriate position within their viewing frame. The load cell was positioned on the prosthesis to match the projected sensation. The investigator randomly touched the load cell signalling the tactor to elicit a projected sensation (Fig. 1C). The proximal end of the prosthesis and the shoulder of the amputee were covered with a cloth. The Rubber Hand Illusion was also generated on the contralateral intact limb of the amputees as a control. In this case the Rubber Hand Illusion was created in the typical fashion by obscuring the real limb behind a screen and positioning the prosthetic limb, in full view, in place of the hidden hand. To elicit the illusion, the investigator repeatedly touched the amputee's intact hand while simultaneously touching the corresponding locations on the prosthetic hand as the amputee watched quietly (Fig. 1D).

The Rubber Hand Illusion, generated by the G10 tactor, was assessed under five different conditions (Fig. 2A): (i) 'Synchronous condition': the load cell was positioned on the prosthetic hand where the tactor elicited hand sensation (spatially and temporally correlated touch); (ii) 'spatial mismatch condition': the load cell was placed on the forearm of the prosthesis but the tactor elicited hand sensation (spatial difference with temporal correlation); (iii) 'temporally asynchronous condition': a 'dummy' load cell was positioned on the prosthesis where the tactor elicited hand sensation and the G10 tactor was activated at random intervals following each touch of the 'dummy' load cell (spatial correlation with temporal difference); (iv) 'visual only condition': the amputee watched the hand of the prosthesis and the load cell being touched but the G10 tactor did not apply touch input (spatial correlation with no tactile input); and (v) 'fixation condition': the prosthesis was covered, the tactor was turned off, and the amputee visually fixated on a mark on the table just beyond the hand of the prosthesis. The five stimulus conditions were randomly presented to the amputee three times for 5 min, with a 1 min period of quiet inactivity fixating on a mark, before and after the trial with the prosthesis covered. After each trial the amputee filled out a two-part questionnaire (adapted from Ehrsson *et al*. 2008). Each questionnaire consisted of nine statements that the amputees were instructed to assign a value on a seven point visual analogue scale from 'disagree strongly' (− − −) to 'agree strongly' (+ + +). They also supplied an open-ended self-report of their impressions each time. Of the nine statements on the questionnaire, three were related to the predicted phenomena and six were included to control for task compliance and suggestibility (Table 1). The nine statements were arranged randomly on five different versions of the questionnaire and the five different versions were given in random order. The numerical values of the answers for each question were averaged across the three presentations of each stimulus configuration. The 95% confidence intervals (CI) were computed using a multiple comparisons procedure and Tukey's honestly significant difference criterion; implemented in the Matlab (MathWorks Inc., Natick, MA, USA) multicompare function (pooling errors across all five conditions and nine questions to yield conservative CI). Any two questions were considered significantly different if their CI did not overlap (Hochberg and Tamhane, 1987). For the self-reports, the amputees provided descriptions of what they felt during each trial. Their subjective reports were examined for statements referring to ownership or embodiment of the prosthesis.

The Rubber Hand Illusion was also generated, in the typical fashion, on the contralateral intact limb and assessed under the synchronous condition—the investigator touched the intact hand and prosthetic hand in the same places simultaneously (spatially and temporally correlated touch) (Fig. 1D). The stimulus condition and questionnaires were delivered and the analysis was performed as described above.

Temporal order judgements: vibratory units

A psychophysical temporal order judgement task was used to assess the amputee's response to vibratory input to each limb under three Rubber Hand Illusion conditions elicited on the amputated side. In this experiment we assessed the responses of the amputees to vibratory input that was applied to their intact hand and their projected-sensation-hand on their reinnervated skin. Subject S-2 could feel the vibration from a commercially available vibratory unit (C2 tactor, Engineering Acoustics Inc., Casselberry, FL, USA) projected to the tips of her thumb, index and middle fingers. Subject S-1 could feel the vibration projected to his thenar eminence and thumb. For this test one vibratory unit was taped to reinnervated skin and the other vibratory unit was taped in a position on the intact hand matching the redirected sensation. The vibratory unit on the reinnervated skin applied the stimulus for the test and also generated the illusion. During stimulus presentation, the active vibratory unit remained in the same location on the reinnervated skin while the physical position of a visually observed 'dummy' unit affixed to the prosthesis was changed for each of the following three stimulus conditions (Fig. 2B): (i) synchronous condition: the vibration was felt at the same place where the inactive 'dummy' unit was placed on the prosthesis; (ii) spatial mismatch: the inactive 'dummy' unit was placed on the forearm of the prosthesis, 20 cm proximal to the fingertips, but the vibration was projected to the missing hand; and (iii) fixation condition: the vibration was projected to the missing hand but the prosthesis and inactive 'dummy' unit were covered with a cloth while the amputees fixated on a mark on the table. The subjects wore headphones playing grey noise (Bose, Framingham, MA, USA). Vibration bursts (12 ms at 250 Hz and ~0.7–1 mm displacement) were delivered at timing offsets of 10, 20, 30, 60, 90 and 120 ms. Offsets were randomly presented 12 times (totalling 240 offsets) for each condition with 50% firing right-first and 50% left-first (Spence *et al*., 2001). The amputees decided (forced choice) which side received tactile stimulus first and indicated their answer by pressing a right or left foot pedal. An auditory cue signalled the presentation of a stimulus. Stimuli were delivered and the data were collected by a computer running Matlab (MathWorks Inc.). Both subjects completed 20 practice trials prior to testing, to familiarize themselves with the task. A psychometric curve fit to the percentage 'right-first' response data was used to estimate the 'point of subjective simultaneity' and the 'just noticeable

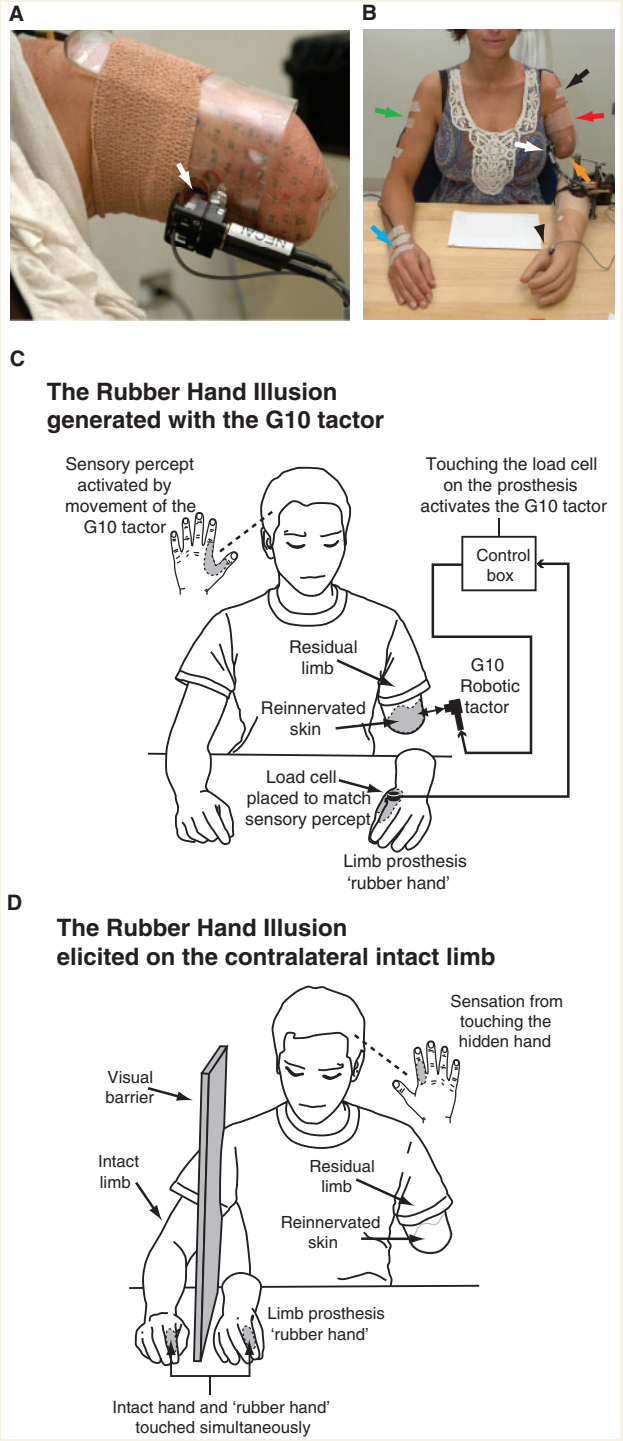

Figure 1 Photographs of the experimental arrangement. (**A**) The placement of the G10 tactor on the reinnervated skin of Subject S-2. The plunger (white arrow) pushes into a region of skin where she feels sensation projected to the dorsal skin between digits 1 and 2 of her missing hand. (**B**) The placement of the prosthetic limb on the table in front of Subject S-2. The amputee fine-positioned the arm where it felt most natural. The G10 tactor can be seen on the inner aspect of her residual limb (white arrow) and the load cell that provides touch input to the G10 tactor can be seen placed in the centre of the projected field of sensation (black arrowhead). Coloured arrows mark the location of each thermistor: proximal residual limb (black arrow), mid residual limb (red arrow), distal residual limb (orange arrow), proximal intact limb (green arrow), intact hand (blue arrow). The colours of the arrows correspond to the colours for each thermistor location for graphs in Fig. 6 and Supplementary Figs 1 and 2. (**C**) Schematic diagram of the experimental setup for the Rubber Hand Illusion where the G10 tactor was used to provide a physiologically relevant artificial sense of touch for a prosthesis. The illusion was generated on the amputated side of the subjects by having them watch the investigator touch the prosthetic hand and load cell while the G10 tactor pressed into the reinnervated target skin of the residual limb. (**D**) Schematic diagram of the experimental setup for the typically induced Rubber Hand Illusion using the contralateral intact hand of the amputee. To generate the illusion the amputee watched quietly as the investigator repeatedly touched the amputee's hidden intact hand at different locations while simultaneously touching the corresponding locations on the visible prosthetic hand.

difference' by computing a least-squares fit to the function: $f(x) = \frac{1}{1+e^{-\ln(3)(x-PSS)/IND}}$ using the Matlab 'fit' routine which provided 95% CI for each variable.

Temporal order judgements: G10 tactor

For these experiments we used a different configuration of the temporal order judgement task. Here the Rubber Hand Illusion was generated using the G10 tactor on the amputated limb in the same fashion as the questionnaire trials while the amputee also performed the temporal order judgement task by responding to vibratory input that was applied to each shoulder (Fig. 2C). We presented the three following Rubber Hand Illusion conditions: (i) synchronous condition: the load cell was positioned on the prosthetic hand similar to where the tactor elicited sensation projected to the missing hand (spatially and temporally correlated touch); (ii) temporally asynchronous condition: a 'dummy' load cell was positioned on the prosthetic similar to where the tactor elicited sensation projected to the missing hand and the G10 tactor plunger was activated at random intervals following each touch of the 'dummy' load cell by the investigator (spatial correlation with temporal difference); and (iii) fixation condition: during the trial the prosthesis was covered with a cloth, the tactor was turned off, and the amputee fixated on a mark on the table just beyond the hand of the prosthesis. The Rubber Hand Illusion condition was run for 5 min alone and then continued while the amputees completed the temporal order judgement trials by responding to input from vibration units affixed over the deltoid muscle of each shoulder. The timing offsets were applied and data were collected as described above.

Temperature

We measured the temperature of the residual limb while the amputee observed the experimenter creating the Rubber Hand Illusion with the G10 tactor on the amputated limb in the same fashion as the questionnaire trials (Figs 1B and 2A). Skin temperature was measured at proximal, middle and distal points on the residual limb, on the intact upper limb and hand, and ambient room temperature using thermistors (Omega Engineering Inc., Stamford, CT, USA). The thermistors were jacketed in conductive film, taped to the skin and then covered with cloth to minimize air currents. The thermistor circuitry was developed in-house (resolution to 0.02°C) and consisted of a

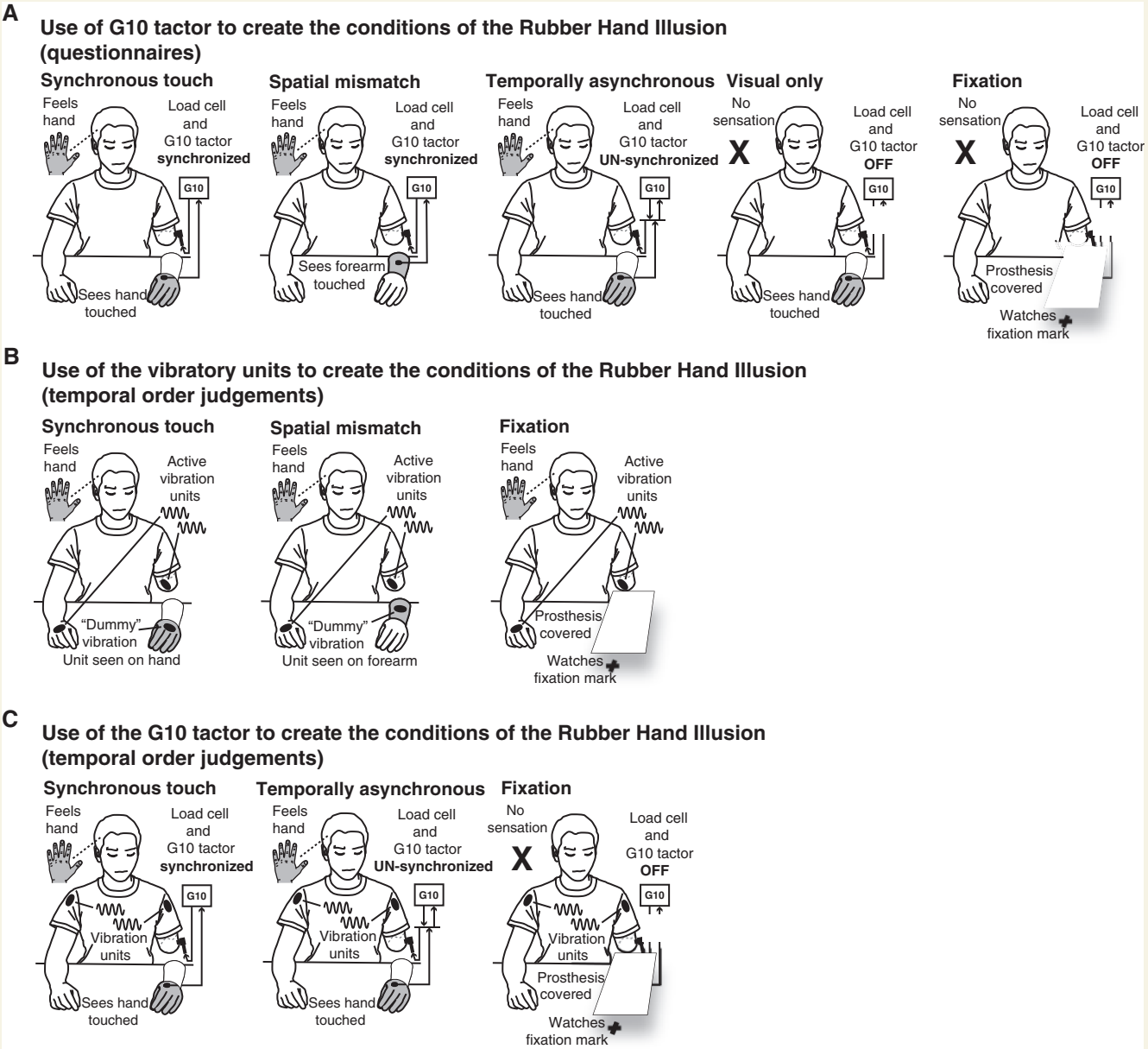

Figure 2 Schematic diagrams showing how the Rubber Hand Illusion was elicited during each condition of the different experimental approaches. (**A**) Rubber Hand Illusion and questionnaires. The state of the amputee and the placement of the G10 tactor and during the testing condition (synchronous touch) and the four control conditions (spatial mismatch, temporally asynchronous, visual only and fixation). During the temperature trials the experiment was run using the testing condition (synchronous touch) and two control conditions (temporally asynchronous and fixation) described in this figure. Refer to Fig. 1B for the placement of the thermistor units. (**B**) Rubber Hand Illusion and temporal order judgements: vibratory units. The state of the amputee and the placement of the two active and one 'dummy' vibratory units during the testing condition (synchronous touch) and the two control conditions (spatial mismatch and fixation). (**C**) Rubber Hand Illusion and temporal order judgements: G10 tactor. The state of the amputee and the placement of the two active vibratory units and the G10 tactor during the testing condition (synchronous touch) and the two control conditions (temporally asynchronous and fixation).

Wheatstone bridge, an instrumentation amplifier (Texas Instruments, Dallas, TX, USA), and a 5 V power regulator (STMicroelectronics, Geneva, Switzerland). Temperature data were collected with a computer running Matlab (MathWorks Inc.) and a PC104 computer (Advantech Co., Ltd, Milpitas, CA, USA) running Matlab xPC (MathWorks Inc.). Three different illusion conditions were randomly presented twice to the amputees: (i) a synchronous condition (spatially and temporally correlated touch); (ii) a temporally asynchronous condition (spatial correlation with temporal difference); and (iii) a fixation condition (the prosthesis was covered, the tactor was turned off and the amputee fixated on a mark on the table). The amputees sat quietly before each condition to stabilize body temperature. The test was run with an initial 1 min baseline period of quiet inactivity followed by 11 min of presentation of the condition, followed by 5 min of inactivity. During periods of inactivity the prosthesis was obscured with a cloth and the amputee fixated on the point on the table.

Table 1 Statements listed on subject questionnaire

Subject questionnaire
Statements of predicted phenomena
(1) I felt the touch of the investigator on the prosthetic hand
(2) It seemed as if the investigator caused the touch sensations that I was experiencing
(3) It felt as if the prosthetic hand was my hand
Control statements
(4) It felt as if my residual limb was moving towards the prosthetic hand
(5) It felt as if I had three arms.
(6) I could sense the touch of the investigator somewhere between my residual limb and the prosthetic hand
(7) My residual limb began to feel rubbery
(8) It was almost as if I could see the prosthesis moving towards my residual limb
(9) The prosthesis started to change shape, colour and appearance so that it started to (visually) resemble the residual limb.

Results

Responses to questionnaires

The questionnaire responses were used to assess the amputees' experience during the five conditions of the Rubber Hand Illusion applied to the amputated limb. When Subject S-1 was presented with the synchronous condition he agreed more with statements related to ownership of the limb (statements 1–3) than he did for the control statements (4–9) for all of the other conditions (Fig. 3A, Table 1). Subject S-1 scored significantly higher on ownership statements 1 and 2 than for any of the control statements during the synchronous condition, judged by non-overlap of 95% CI (CI = 1.95 centred on the mean of the three responses). Subject S-1 did however, show elevated responses to control statement 7 'My residual limb began to feel rubbery' across all conditions. Subject S-1 scored significantly higher on ownership statements 1 and 2 under the synchronous condition than he did for all statements under the spatial mismatch, temporally asynchronous, visual only and fixation conditions. Although Subject S-1 did show overlap of the 95% CI between the synchronous and spatial mismatch conditions for ownership statement 3.

Subject S-2 agreed more strongly with ownership statements 1 and 2 under the synchronous condition than she did for the rest of the statements and conditions (Fig. 3B). Furthermore, for these two ownership statements she scored significantly higher, as judged by non-overlap of 95% CI (CI = 3.73 centred on the mean of the three responses), under the synchronous condition than for the temporally asynchronous, visual only and fixation conditions. While elevated, Subject S-2's agreement with ownership statements 1 and 2 under the synchronous condition were only significantly different than control statements 5, 7 and 8. There was overlap of the 95% CI between ownership statements 1 and 2 and control statements 4, 6, 8 and 9 under the synchronous condition. Although Subject S-2's responses were higher for ownership statements 1 and 2 for the synchronous condition there was not a significant difference in her responses between the synchronous and spatial mismatch conditions for any of the statements. Subject S-2 agreed significantly more with ownership statement 3 under the synchronous condition than all the other statements under the temporally asynchronous, visual only and fixation conditions. However, her level of agreement to this ownership statement under the synchronous condition was lower than both ownership statements 1 and 2 and similar in magnitude to responses to the control statements 4, 6 and 9 in both the synchronous and spatial mismatch conditions.

The open-ended self reports for both Subjects S-1 and S-2 under the synchronous condition included spontaneous statements of ownership. Subject S-1 reported that 'During the more intense drawn out sensations I felt the urge to grab back at the experimenter's hand. [I] also felt more like [my] entire arm was intact.' He also declared, 'After a few minutes I moved my phantom hand and expected the prosthetic to move and was surprised it did not'. Subject S-2 provided similar reports such as 'Many times throughout the process it was like my real hand' and 'Seemed real at times'. Under the spatial mismatch condition there appeared to be confounding sensations for Subject S-1. For example, he reported: 'Confusing due to sensation in phantom fingertips but does not match' and 'Touch did not match feeling in the phantom limb'. Conversely, Subject S-2 felt some engagement with the limb under the spatial mismatch condition, reporting 'The arm felt connected'. For the temporal asynchrony condition Subject S-1 stated 'What I was seeing did not match what I felt (delay in sensation)' and Subject S-2 reported 'Nothing-no connection'. During the visual only condition Subject S-1's reports suggested some form of discomfort. He imagined a scar on one trial and mentioned a spasm in his phantom on another. He also reported 'Phantom hand numbness'. Subject S-2 reported 'No connection' for this condition. During the fixation condition both S-1 and S-2 reported 'Nothing'.

The questionnaire responses were also used to assess both amputees experience during the synchronous condition of the Rubber Hand Illusion applied to their contralateral intact limbs (Fig. 4). Subject S-1 showed high scores for questions 1–3 with significantly lower scores for questions 4–9 (CI = 1.99 centred on the mean of the three responses). Interactions between his residual and intact limbs were not significantly different ($P = 0.496$). Subject S-2 showed high scores for questions 1–3 with lower responses for questions 4–9 (CI = 3.77 centred on the mean of the three responses). Interactions between her residual and intact limbs were just outside of statistical significance ($P = 0.055$).

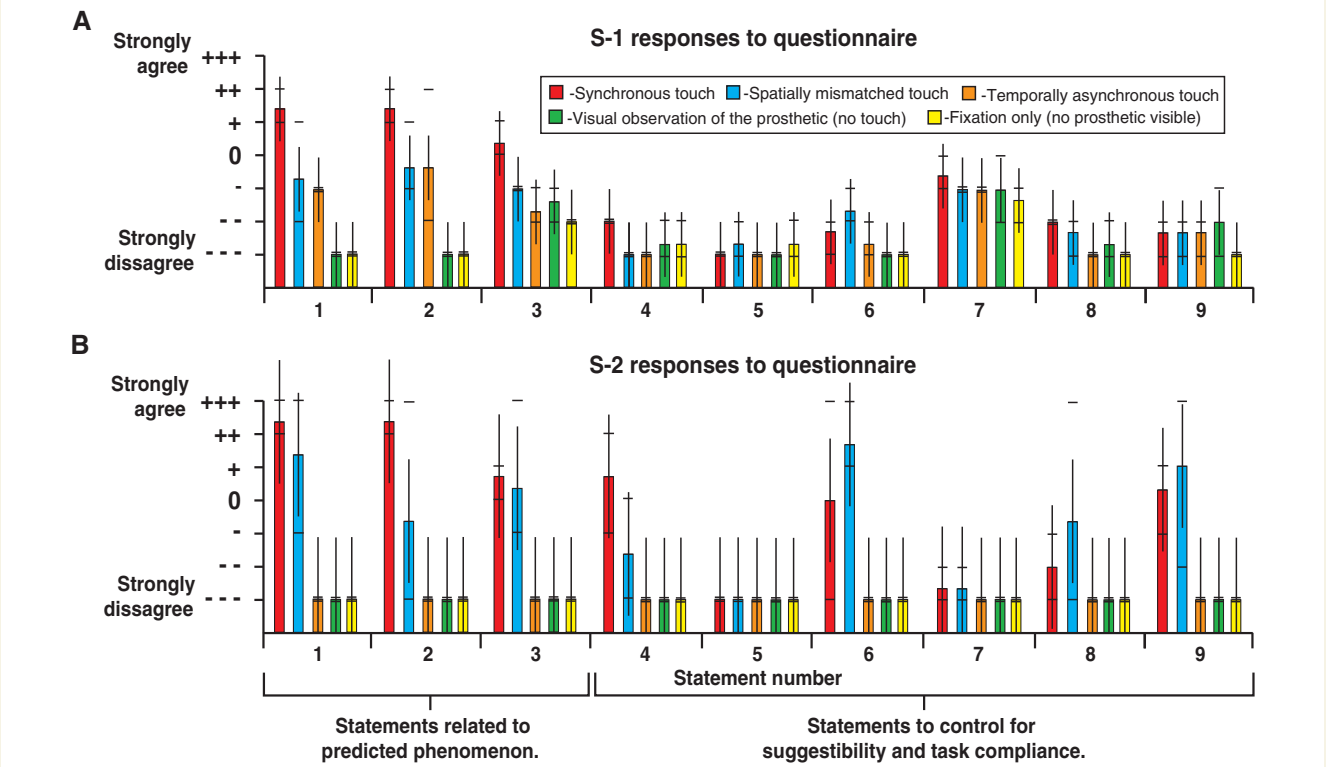

Figure 3 Questionnaire results for Subject S-2 (**A**) and Subject S-1 (**B**) for five different stimulus conditions. Vertical error bars indicate 95% CI (S-1 = ± 0.975, S-2 = ± 1.865) from a multiple comparisons procedure; horizontal lines indicate range, $n = 3$. Significance judged by non-overlap of CI. Statements 1–3 = predicted phenomena (1, 'I felt the touch of the investigator on the prosthetic hand'; 2, 'It seemed as if the investigator caused the touch sensations that I was experiencing'; 3, 'It felt as if the prosthetic hand was my hand'). Statements 4–9 = controls [4, 'It felt as if as if my residual limb was moving towards the prosthetic hand'; 5, 'It felt as if I had three arms'; 6, 'I could sense the touch of the investigator somewhere between my residual limb and the prosthetic hand'; 7, 'My residual limb began to feel rubbery'; 8, 'It was almost as if I could see the prosthesis moving towards my residual limb'; 9, 'The prosthesis started to change shape, colour and appearance so that it started to (visually) resemble the residual limb']. For Subject S-1 CI for scores related to ownership of the limb did not overlap with control scores. There was some overlap between the ownership and control scores for Subject S-2.

However, a multiple comparison shows that only the answers to question 7 were significantly different from each other. All others were statistically the same. Both amputees gave free report statements implying ownership of the rubber limb.

Temporal order judgements

Temporal order judgement tasks were used to calculate the 'Point of Subjective Simultaneity' and 'Just Noticeable Difference' for two different configurations of the Rubber Hand Illusion. In the first configuration, the vibratory input was applied to equivalent positions on the reinnervated target skin and intact hand while the observed location of an inactive 'dummy' vibratory unit was changed for each stimulus condition (Figs 2B and 5A). Subject S-2 had point of subjective simultaneity values of −29.9 ms (95% CI = 10.9 ms) for the synchronous condition, −17.8 ms (95% CI = 14.0 ms) for the spatially mismatched condition, and −7.1 ms (95% CI = 6.9 ms) for the fixation condition with slight overlap of the 95% CI (Fig. 5B). The just noticeable difference for Subject S-2 was 19.9 ms (95% CI = 11.4 ms) for the synchronous condition, 28.6 ms (95% CI = 15.9 ms) for the spatial mismatch condition and 20.5 ms (95% CI = 7.4 ms) for the fixation condition (Fig. 5C). These values were not significantly different from each other. Subject S-1 showed point of subjective simultaneity values of −3.4 ms (95% CI = 28.1 ms) for the synchronous condition, −9.0 ms (95% CI = 29.0 ms) for the spatially mismatched condition and −1.4 ms (95% CI = 24.7 ms) for the fixation condition (Fig. 5B). The just noticeable difference for Subject S-1 was 40.5 ms (95% CI = 34.7 ms) for the synchronous condition, 46.1 ms (95% CI = 36.2 ms) for the spatial mismatch condition and 45.8 ms (95% CI = 31.1 ms) for the fixation condition (Fig. 5C). No values for Subject S-1 were significantly different from each other.

In the second experimental configuration the conditions of the Rubber Hand Illusion were generated by pressing the reinnervated skin of the residual limb with the robotic touch interface at the same time that the vibratory stimuli for the temporal order judgement task were applied to each shoulder (Figs 2C and 5D). We found that the point of subjective simultaneity and just noticeable difference values were not significantly different between conditions (Fig. 5E, F). Subject S-2's point of subjective simultaneity was −10.4 ms (95% CI = 31.6 ms) for the synchronous condition,

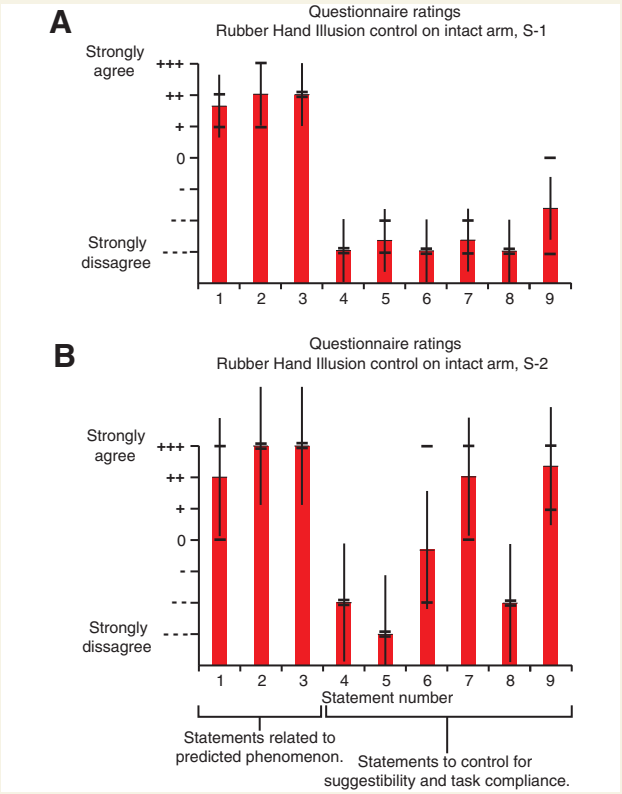

Figure 4 Questionnaire results for application of the Rubber Hand Illusion on the intact limbs of both amputees (vertical error bars indicate 95% CI from a multiple comparisons procedure; horizontal lines indicate range, $n = 3$). (**A**) Results for Subject S-1 showing high scores in questions 1–3 with significantly lower scores for questions 4–9 (95% confidence interval = $\pm$ 0.993) (Table 1). (**B**) Results for Subject S-2 showing high scores in questions 1–3 with lower responses for questions 4–9 (95% confidence interval = $\pm$ 1.887) (Table 1). Subject S-2 scored highly on question 4 during the Rubber Hand Illusion on her amputated limb (Fig. 3). During the synchronous conditions Subject S-2 was often observed pushing her residual limb towards the prosthesis as though she was attempting to make them align. She did not score highly on question 4 with her intact side (above). The movement of Subject S-2's residual limb correlates with the wording of question 4 and suggests that she may have actually felt like her 'residual limb was moving towards the prosthetic hand'.

−6.1 ms (95% CI = 15.6 ms) for the temporally asynchronous condition, and −7.3 ms (95% CI = 6.4 ms) for the fixation condition (Fig. 5E). The just noticeable difference for Subject S-2 was 34.6 ms (95% CI = 37.7 ms) for the synchronous condition, 41.5 ms (95% CI = 19.2 ms) for the temporally asynchronous condition and 28.9 ms (95% CI = 7.4 ms) for the fixation condition (Fig. 5F). Subject S-1's point of subjective simultaneity was 7.0 ms (95% CI = 32.4 ms) for the synchronous condition, −11.1 ms (95% CI = 60.0 ms) for the temporally asynchronous condition and −3.0 ms (95% CI = 70.0 ms) for the fixation condition (Fig. 5E). The just noticeable difference for Subject S-1 was 46.8 ms (95% CI = 40.8 ms) for the synchronous condition, 106.8 ms (95% CI = 108.9 ms) for the temporally asynchronous condition and 109.6 ms (95% CI = 129.4 ms) for the fixation condition (Fig. 5F).

Temperature measurements

The residual limb skin temperature was measured during three conditions of the Rubber Hand Illusion presented with the robotic touch interface (Fig. 2A). During the synchronous condition trials the average absolute change in temperature (measured from the start of the application of the Rubber Hand Illusion to the termination of the trial) for Subject S-2's proximal residual limb was 0.65°C (SD = 0.14°C) compared with 0.45°C (SD = 0°C) and 0.3°C (SD = 0.11°C) for the temporal asynchrony and fixation conditions, respectively (Fig. 6). There was also a small average absolute change in temperature during the synchronous condition for her mid residual limb; 0.27°C (SD = 0.01°C) compared with 0.19°C (SD = 0.04°C) and 0.16°C (SD = 0.02°C) for the temporal asynchrony and fixation conditions, respectively (Fig. 6). We used the absolute average change in temperature because in Trial 2 of the synchronous condition the temperature of S-2's proximal residual limb first dropped rapidly then reversed and climbed over the course of the stimulus presentation (Supplementary Fig. 1). During Trial 2 of the temporal asynchrony condition we observed an elevation of temperature for Subject S-2's proximal residual limb. This temperature fluctuation was associated with a strong agreement with ownership statement 1 on a questionnaire (questionnaires were administered at the termination of all temperature and temporal order judgement tasks, Supplementary Fig. 1). No condition-specific modulation of temperature was observed for Subject S-2's distal residual limb, proximal intact limb or intact hand. We also saw no condition specific modulation of temperature for Subject S-1 during this experiment (Supplementary Fig. 2).

Discussion

The results of this study provide evidence that a robotic touch interface, linking a prosthetic arm to the previously amputated cutaneous sensory nerves of a missing limb, can be used to elicit a shift in perception towards incorporation of the artificial limb into the self-image of two targeted reinnervation amputees. Taken collectively, these results suggest that providing physiologically and anatomically appropriate direct sensory feedback for a prosthetic limb creates a vivid sense of ownership of the device.

Responses to questionnaires

In the questionnaire experiments we hypothesized that, when stimulated in the synchronous condition versus the control conditions, the subjects would agree more strongly with the three embodiment-related statements than the other five control statements. We found that both amputees agreed more strongly with statements 1–3, which reflected ownership of the limb and scored significantly higher in the synchronous condition than in the

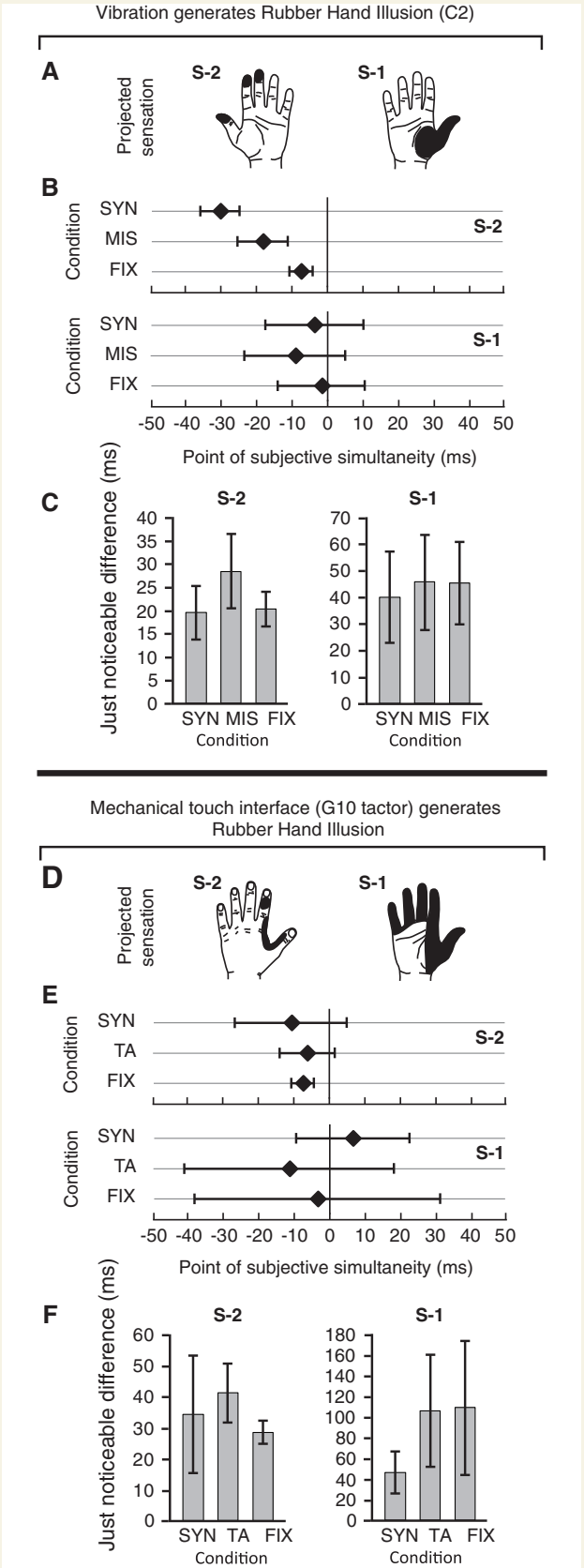

Figure 5 Results of temporal order judgement tasks for the two different experimental configurations each with three different stimulus conditions (error bars = 95% confidence interval). (**A–C**) Use of the vibratory units to generate the Rubber Hand Illusion; (**D–F**) use of the touch interface to generate the Rubber Hand Illusion while vibratory input for the temporal order judgement task was applied to the shoulders. (**A**) Diagrams of projected sensation elicited by the vibratory input applied to the reinnervated skin. (**B**) The point of subjective simultaneity. (**C**) The just noticeable difference. (**D**) Diagrams of projected sensation elicited by the G10 tactor pushing into the reinnervated skin. (**E**) The point of subjective simultaneity. (**F**) The just noticeable difference. FIX = fixation; MIS = spatial mismatch; SYN = synchronous; TA = temporal asynchrony.

temporally asynchronous, visual only, and fixation conditions (Fig. 3). The magnitudes of Subject S-1's responses were lower overall but he demonstrated a separation between ownership and control statements. In contrast, Subject S-2 showed less distinction between the ownership and control statements although her responses indicated a stronger reaction than Subject S-1 to the synchronous condition. Subject S-2 agreed with control questions mentioning movement or transformation. Rather than indicating suggestibility, this may reflect an unanticipated perceptual phenomenon because both amputees reported they felt like they wanted to 'reach out to' or 'grab at' the experimenters hand during the illusion. Self reports also suggested a perceptual shift towards ownership of the prosthetic limb. Subject S-1's declaration 'After a few minutes I moved my phantom hand and expected the prosthetic to move and was surprised it did not' may relate most clearly to the utility of integrating a prosthesis into the self-image of an amputee.

The responses indicated that the illusion was not completely abolished by the spatially mismatched condition. The effect was evident for Subject S-1 and pronounced for Subject S-2 (Fig. 3). It is not surprising that moving the touch sensor from the hand to the forearm did not completely disrupt the illusion considering the robustness of the illusionary effect to changes in anatomical position of the rubber hand (Armel and Ramachandran, 2003) and evidence of cortical remapping following similarly incongruous visual/tactile input (Schaefer *et al*., 2006).

The vividness of the Rubber Hand Illusion appears to relate to the magnitude of the agreement with the ownership statements (Botvinick and Cohen, 1998; Ehrsson *et al*., 2008). We hypothesized that if the robotic touch interface created a vivid sense of embodiment then we should see similar magnitudes of questionnaire responses between the amputated and intact limbs. The robotic touch interface appeared to provide strong sense of embodiment because the magnitude of the agreement with ownership statements was similar for both amputees between both sides (Fig. 4, also see Fig. 1D). Others have demonstrated success utilizing amputee's phantom sensation to induce embodiment of an artificial arm. However, their approach probably activates sensory pathways not directly connected to the afferent channels of the missing limb, which may be reflected in lower response magnitudes (Ehrsson *et al*., 2008). We also found that presentation of the Rubber Hand Illusion did not appear to alter perception of the illusion administered to the amputated side (Supplementary Fig. 3).

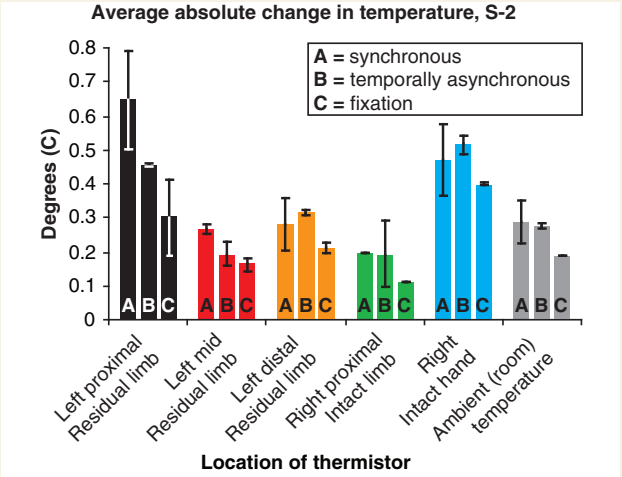

Figure 6 Average absolute changes in skin temperature calculated from the onset of the stimulus condition (time = 1 min) to the termination of the experiment (time = 17 min) for Subject S-2 at three points on her residual limb, two points on her intact limb and for the ambient room temperature measured during the three different stimulus conditions (error bars = ±1SD, $n = 2$). Colours correspond to individual temperature traces in Supplementary Fig. 1.

Temporal order judgements

We used psychophysical temporal order judgement tasks to probe the amputee's response to the Rubber Hand Illusion under two different, but related, experimental configurations. Shifts in the output measurements of the temporal order judgement task reflect modulations of central tactile processing mechanisms related to incorporation of a rubber hand into the self-image of able bodied individuals (Moseley *et al*., 2008).

In the first configuration of the experiment we compared input from both fingertips (intact and projected sensation) by using similar testing points for application of the vibratory input (Fig. 5A). During these tests only the location of the inactive 'dummy' vibratory unit was changed. We hypothesized that when performing the temporal order judgement task under the synchronous condition, the point of subjective simultaneity would show a greater shift than in comparison with the fixation and spatially mismatched conditions. Subject S-1 did not respond robustly to this experiment. However, for Subject S-2 the synchronous condition triggered the strongest shift of the point of subjective simultaneity (Fig. 5B). The point of subjective simultaneity is a reflection of the relative weighting given to processing input from each limb (Moseley *et al*., 2008). This suggests that for Subject S-2 observing the correct tactile input to the prosthesis modulated the weighting of central temporal processing relative to tactile input from each limb. Furthermore, the magnitude of change for Subject S-2's point of subjective simultaneity was similar to reports for able bodied subjects (Moseley *et al*., 2008).

In the second configuration of the experiment we generated the conditions of the Rubber Hand Illusion by pressing the reinnervated skin with the robotic touch interface while applying the vibratory stimuli for the psychophysical task to each shoulder. We hypothesized that when performing the temporal order judgement task under the synchronous condition, the point of subjective simultaneity would show a greater shift than in comparison with the fixation and temporally asynchronous conditions. Neither amputee appeared to respond robustly to this experiment, probably because they had to simultaneously attend to two different tasks (Fig. 5E). We did find however, that Subject S-1's CI for both the point of subjective simultaneity and just noticeable difference were smaller for the synchronous conditions than for the temporal asynchrony and fixation conditions (Fig. 5E and F). When his perception of the prosthesis shifted towards embodiment under the synchronous condition, his performance on the task improved markedly as opposed to operating at near chance with either incongruous or non-existent input (Fig. 5E and F).

We calculated the just noticeable difference, a measure of the time difference between stimulus onsets that is needed for the subject to determine which one came first (Schicke and Roder, 2006), for both configurations of the temporal order judgement task. This measure indicates how well the subject performed; the smaller the difference the better the performance. We hypothesized that when performing the temporal order judgement task under the synchronous condition the just noticeable difference would show a greater decrease than in comparison with the control conditions. While there was overlap of the CI across the two configurations of the tests for both amputees, in all but one instance the just noticeable difference was lower for the synchronous conditions than for the asynchronous and mismatched conditions. It appears that presenting the amputees with synchronous visual and tactile input helped them process tactile information more effectively than incongruous presentation. This suggests that a prosthesis returning direct physiologically appropriate 'synchronous' feedback may provide an advantage over 'mismatched' feedback through the physical contact between the prosthetic socket and the residual limb or feedback through sensory substitution (Lundborg and Rosen, 2001).

Temperature measurements

Skin temperature regulation reflects Rubber Hand Illusion mediated limb ownership and disownership in able-bodied subjects. When individuals take ownership of the rubber hand the temperature of the disowned real hand drops (Moseley *et al*., 2008). We hypothesized that if the robotic touch interface provided a vivid sense of embodiment then we should observe a measurable change in the physiological skin temperature of the residual limb during the synchronous condition versus the fixation and temporal asynchrony conditions. We found that during the synchronous condition of the illusion Subject S-2 showed a modulation of temperature of her residual limb (Fig. 6 and Supplementary Fig. 1). This result suggests that the ownership illusion generated by the robotic touch interface was vivid enough to elicit a physiological change in temperature regulation. Subject S-1 did not show a similar physiological temperature response to the Rubber Hand Illusion in these experiments (Supplementary Fig. 2). However, in preliminary experiments

where touch input was supplied to the prosthesis that visually matched Subject S-1's 'mild electrical' percepts of sensation, we saw an increase of temperature for his residual limb (refer to Supplementary Fig. 4 for additional details). Typically, the average temperature for the amputee's residual limbs was ~1.5°C cooler than their intact limbs. When Subject S-2 experienced the illusion we saw a net increase in temperature for her proximal residual limb (Supplementary Fig. 1). It is possible that the observed temperature differential was associated with amputation related peripheral nerve damage and complex regional pain syndrome (Uematsu, 1985; Bruehl *et al*., 1996; Wasner *et al*., 2002). However, it is conceivable that the changes in temperature regulation of the residual limb when the amputee received synchronous visual and tactile feedback may reflect a restoration of the limb within her self-image (Moseley *et al*., 2008).

Important considerations

Here we found evidence of systematic changes in the testing results of both amputees related to the synchronous condition, however, both amputees responded somewhat differently to testing. The differences in responses may reflect physiological variations in post-reinnervation sensation characteristics. For instance, in other studies with targeted reinnervation amputees we have observed variations in interpretation of sensation projected to the missing limb, tactile acuity, vibratory frequency discrimination and pressure discrimination (Kuiken *et al*., 2007*a*; Marasco *et al*., 2009; Schultz *et al*., 2009; Sensinger *et al*., 2009).

We chose to use the Rubber Hand Illusion because we could uncouple the motor control of the limb from the test of sensory functionality. For example, a lag in command and control speeds during typical functional testing would likely mask any observable changes in sensory outcomes relying on the speed of the user. In addition, there is not currently an appropriately sensorized multifunctional prosthetic hand that could be used to conduct functional tests.

Since we had a limited subject population we were aware that providing clearly consistent data for individual testing approaches would be difficult so we chose to assess the amputees' responses to the Rubber Hand Illusion with three independent measures. The questionnaires and temporal order judgement tasks have been used by others to examine the Rubber Hand Illusion (Botvinick and Cohen, 1998; Ehrsson *et al*., 2008) and temperature has also been implicated in being related to the Rubber Hand Illusion and limb ownership (Moseley *et al*., 2008). The Rubber Hand Illusion is a robust phenomenon (Armel and Ramachandran, 2003) and appears to be sensitive to the relative strength of the tactile input (Ehrsson *et al*., 2008). The Rubber Hand Illusion has also provided a new understanding of how multisensory integration contributes to body-ownership (Makin *et al*., 2008; Longo *et al*., 2010; Tsakiris, 2010). While we were able to readily generate the Rubber Hand Illusion with these two amputees, future studies will be required in more individuals to determine if the use of a robotic touch interface can routinely be used to establish a sense of embodiment for a prosthetic limb.

Conclusion

Here we have described how using a neural-machine-interface that provides a physiologically appropriate artificial sense of cutaneous touch appears to elicit a shift in perception towards incorporation of a prosthetic limb into the self-image of two targeted reinnervation amputees. Long-term use of a physiologically relevant cutaneous touch interface of this type may help to augment mechanisms of prosthetic motor control and function (Dhillon and Horch, 2005; Wang *et al*., 2010). The results presented here also suggest that this approach may help amputees regain more intact self-images (Van Dorsten, 2004; Murray, 2008; Rybarczyk and Behel, 2008) seeing prosthetic devices less as tools that they simply wear and more as parts of their own bodies.

Acknowledgements

The authors thank Greg Dumanian, Aimee Schultz, Levi Hargrove, Steven Manuel, Blair Lock, Sue Marasco, Tom Idstein, Laura Miller, Alex Makhlin, Julio Santos-Munne, Robert Lipschutz, Jon Sensinger and Mary Wu for their help with this project.

Funding

National Institutes of Health (grant numbers R01-HD-4-3137, R01-HD-4-4798, N01-HD-5-3402 to T.A.K.); the Searle Funds at The Chicago Community Trust; the Defense Advanced Research Projects Agency (number 908090 under Prime Contract number N66001-06-C-80060 to T.A.K. and number 908087 under Prime Contract number N66001-06-C-8005 to J.E.C.).

Conflict of interest: J.E.C. and M.A.P. are equity-holders in Kinea Design, LLC which developed an apparatus for this study. Conflicts are managed by committee in the McCormick School of Engineering and Applied Science at Northwestern University.

Supplementary material

Supplementary material is available at *Brain* online.

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