

The effect of tactile and visual sensory inputs on phantom limb awareness

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Summary

Multiple sensory stimuli contribute to the conscious awareness of the body. It is well known that limb amputation can result in abnormal body awareness, but the manner in which the CNS constructs and updates a body schema after injury is largely unknown. The purpose of the present study was to systematically evaluate the effects of sensory inputs on phantom limb awareness (PLA) shortly after unilateral upper extremity amputation. The location, quality and intensity of spontaneous and tactile-evoked phantom sensations and awareness were assessed in 13 amputees who were referred sequentially for their initial post-operative rehabilitation. Subjects were tested in three visual conditions: (i) with their eyes open; (ii) with their eyes closed; and (iii) while they viewed their intact hand in a mirror, which created an illusion of their amputated hand (i.e. mirror visual illusion). The mirror illusion was also used to test the effect of combined visual and movement-related stimuli during active voluntary movement. Spontaneous PLA was reported by 12 of the 13 amputees and was not affected by normal visual inputs. Tactile stimulation of the residual limb or face evoked dual percepts in six

amputees; i.e. these amputees perceived these touch stimuli as if they were being applied both to the stimulus site and also to a location on the missing limb. This mislocalization phenomenon was most prevalent in the eyes-closed condition. Thus, normal vision can strongly override the phantom component of touch-evoked dual percepts. In eight cases, the visual illusion of the missing limb transiently enhanced the spontaneous conscious awareness of the phantom limb. However, the visual illusion did not change the capacity of a tactile stimulus to induce dual percepts. These findings demonstrate that (i) phantom awareness of an amputated body part is common within the 14 months after traumatic upper extremity amputation, (ii) evoked dual percepts are less common than spontaneous PLA, (iii) visual, tactile and sensorimotor systems contribute to PLA, (iv) subtle changes in congruence of sensory information affects both evoked dual percepts and spontaneous PLA, however, (v) sensorimotor information pertaining to the state of the motor system can strongly influence spontaneous PLA, whereas the visual system can predominantly influence evoked PLA.

Keywords: amputation; plasticity; illusion; perception; multisensory

Abbreviations: PLA = phantom limb awareness; PLP = phantom limb pain; PLS = phantom limb sensations

Introduction

More than 80% of individuals who have undergone amputation report phantom limb sensation (PLS), defined as a sensory experience that is perceived to originate from the missing body part (Sherman *et al.*, 1984; Jensen *et al.*, 1985; Kooijman *et al.*, 2000). Phantom sensations are not a unitary phenomenon (Sherman *et al.*, 1989; Katz, 1992a; Fraser *et al.*, 2001). Current clinical and experimental observations

suggest that different types of phantom phenomena may arise from both unique and common mechanisms (Sherman *et al.*, 1989; Katz, 1992b). Therefore, a better understanding of different phantom phenomena could provide insight into the potential underlying causes. Some amputees (13–24%) describe PLS as exteroceptive and/or proprioceptive sensations, such as tingling, itching, pressure, movement, warmth

or cold. However, a larger number of patients (47–71%) describe their phantom experience as a general awareness of the presence of the limb rather than a specific somatic sensation (Jensen *et al.*, 1984; Ramachandran and Hirstein, 1998; Halligan, 2002). For example, amputees may experience conscious awareness of a particular position, shape and size of their missing limb (Halligan *et al.*, 1993; Knecht *et al.*, 1995; Aglioti *et al.*, 1997; Sherman, 1997). Thus, we wish to distinguish between the concepts of somatic sensation and corporeal awareness. For our purposes, we define a somatic sensation as a specific feeling, such as warmth, pressure, cold, joint position or pain, that is normally evoked when stimuli are applied to the body. But it is also possible to have a general conscious awareness of a body part, including the size and position of the part, without actually feeling any specific sensation. Berlucchi and Aglioti acknowledged the terms ‘body schema’ and ‘corporeal awareness’ to represent ‘the mental construct that comprises the sense impressions, perceptions and ideas about a dynamic organization of one’s own body and its relation to that of other bodies’ (Berlucchi and Aglioti, 1997). Applying these concepts to the situation of phantom phenomena, a ‘phantom sensation’ would refer to specific feelings of sensory stimulation of the missing limb. For example, amputees may experience that something is actually touching the phantom limb or that cold water is passing over the missing limb. On the other hand, ‘phantom limb awareness’ (PLA) would refer to the general knowledge of the presence/existence of the missing limb as one’s own. The universal characteristic of phantom phenomena is that they are experienced as integral parts of the body (Melzack, 1992; Halligan, 2002). Thus, PLS is always accompanied by PLA, but PLA can occur without any specific PLS (Halligan *et al.*, 1993; Knecht *et al.*, 1995; Aglioti *et al.*, 1997; Sherman, 1997; Fraser *et al.*, 2001).

Both PLS and PLA can be spontaneous or elicited by a tactile sensory stimulus, such as a light touch (Ramachandran *et al.*, 1992, 1995; Halligan *et al.*, 1993; Knecht *et al.*, 1995; Aglioti *et al.*, 1997; Flor *et al.*, 2000). The latter phenomenon includes dual percepts (Katz, 1992b), which occur when a tactile stimulus applied to the residual limb is perceived both locally at the stimulus site and concurrently in the missing limb. The referred sensation can be topographically precise and modality-specific (PLS) or just a vague general awareness of the missing limb (PLA) (Doetsch, 1998). Thus, tactile inputs can induce or change phantom sensations and/or awareness. Dual percepts may also arise from tactile stimulation of more remote body sites, including the face (Ramachandran *et al.*, 1995; Aglioti *et al.*, 1997) or bilateral upper trunk (Knecht *et al.*, 1996). There is evidence that the distant referred somatic phantom sensations represent a perceptual correlate of remapping of additional new receptive fields on neurons in primary somatosensory cortical networks that concurrently preserve their original function (see review by Doetsch, 1998).

Although there is a great deal of information on the pathways and neural events related to the perception of

somatic sensations, relatively little is known about how the different senses interact to construct or update a body schema. As suggested by Botvinick and colleagues, one way to examine how different sensory inputs are integrated to affect body awareness is to alter sensory input from one modality and/or compare the effect of conflicting versus congruent inputs from different modalities that signal body schema (Botvinick *et al.*, 1999). For instance, altering proprioceptive input in normal subjects distorted perceived body shape, size and orientation (Lackner, 1988). Furthermore, an experimental manipulation that combined visual and touch stimuli evoked false attribution of a rubber hand (Botvinick and Cohen, 1998). Ramachandran and Hirstein described an interaction between sensory inputs from different modalities in amputees who described a painful clenched phantom hand. This interaction was invoked when amputees viewed an image of their intact hand that created a visual illusion of their missing hand (i.e. the mirror-box illusion). When the amputees opened and closed their intact hand, the combined visual and sensorimotor inputs relieved the painful cramping of a clenched phantom hand (Ramachandran and Hirstein, 1998). These findings demonstrate the potential for the interaction of vision with sensorimotor inputs to change the perception of spontaneous PLS/PLA.

To the best of our knowledge, there are no systematic studies of how vision and sensorimotor inputs interact to change the perception of evoked versus spontaneous PLS and/or PLA, particularly in the early period after limb amputation. Existing data are based on case studies of patients who had longstanding phantom pain and/or who were selected on the basis of symptoms (Ramachandran *et al.*, 1992). However, the subjective perception of the PLS and PLA can change within the first year after amputation of an upper extremity (Jensen *et al.*, 1984; Pascual-Leone *et al.*, 1996). This probably contributes to the discrepancies amongst previous studies of phantom phenomena since the subjects in each study were evaluated in different post-amputation time frames. Therefore, we chose to study subjects during the early stages of rehabilitation after amputation. The aim of this study was twofold: first, to determine the prevalence of spontaneous and evoked PLS and PLA in a non-selected group of persons shortly after unilateral upper extremity amputation, and secondly to investigate the effects of altering tactile and visual (real and illusory) inputs on spontaneous and evoked PLS and/or PLA.

Material and methods

Subjects

Every patient who had undergone unilateral upper extremity amputation and was attending out-patient rehabilitation at either of two designated amputee regional rehabilitation centres (St John’s Rehabilitation Hospital and West Park Healthcare Centre) between June 2000 and February 2002 was asked to participate in this study, which was approved by

Table 1 Findings based on the structured interview

Patient	Age (yr), sex	Time since amputation (months)	Side and level of amputation	Prosthesis	Spontaneous phantom phenomena	
					Phantom position	Phantom pain
A	33, M	1.5	Right transradial	No	Neutral position but 'tight'	Transient throbbing, pulsing or cramping
B	31, M	2.5	Left midcarpal	No	Clenched thumb over index finger	Squeezing and transient cramping
C	49, F	2.5	Left shoulder disarticulation	No	Shoulder and elbow clenched in pre-op. position, fingers mobile	Transient throbbing and burning in the hand
D	37, M	3	Left shoulder disarticulation	No	Elbow and fist loosely flexed, Shoulder rotated internally	Deep, throbbing, gnawing, aching
E	25, M	3.5	Right carpal–metacarpal (thumb intact)	No	Fixed in flexed position; more aware of digits 4 and 5	None
F	20, M	3.5	Left transradial	No	None	None
G	43, M	5	Right transradial	No	Digits 1 and 2 pinching, transient	Burning in palm
H	21, F	5.5	Right carpal–metacarpal (thumb intact). <i>Traumatic</i>	No	Clenched fist	Transient, stabbing or burning
I	35, M	5.5	Left carpal–metacarpal	No	Finger thumb opposition	Cramping, burning
J	24, M	8	Right wrist	Yes, functional	Vague clenched fist	Transient, cramping
K	57, M	8.5	Left transradial	Yes, cosmetic	Clenched and stiff	Transient, shocking
L	45, M	12	Right transradial	Yes, functional	Clenched and stiff	Cramping, twitching, pins and needles
M	49, M	14	Right transradial	Yes, functional	Transient cramping	Transient cramping, shocking, pins and needles

the research ethics boards of each of the two rehabilitation centres. This method of sampling ensured that the subject cohort was representative of all upper extremity amputees at these institutions and not only those with unique sensory symptoms. Informed consent was obtained from all subjects at the time of recruitment, before participation in the study. Of the 15 patients who were approached, only two declined to participate in the study, one because of a pending court case and one because of reluctance to participate in the mirror-box component of the study.

Table 1 provides details of the 13 individuals. All subjects had undergone unilateral upper extremity amputation following a work-related traumatic injury, with the exception of two subjects, who had elective amputation secondary to osteosarcoma (Subject C) or polycythaemia (Subject K). Subject D experienced a 5-day delay between his traumatic injury and the amputation. This was the only subject with a history of pre-amputation paralysis. When possible, subjects were evaluated before they commenced prosthetic training. At the time of recruitment into the study, three subjects had recently commenced training with a functional prosthesis and one had a cosmetic prosthesis.

Experimental design

Each subject was interviewed using a semistructured format by one interviewer (J. P. H.). The interviews documented medical history, present residual-limb (stump) sensations and

pain, PLS, PLA, phantom pain, visual analogue scale ratings for pain intensity and for vividness of non-painful sensory experiences, and the McGill Pain Questionnaire (Melzack, 1975) for stump and phantom pains. Testing for evoked PLS/PLA and the mirror-box visual illusion (see below) followed the interview. The interview and examination were videotaped and later reviewed to ensure complete and accurate data collection.

Evaluation of spontaneous phantom sensations, awareness and/or pain

During the interview, each subject was asked to describe the location, quality, frequency, position and intensity of spontaneous (i.e. in the absence of known sensory stimulation) sensations and/or awareness in the residual limb or referred to the phantom limb.

Evaluation of evoked sensations and/or awareness

Light tactile stimuli were applied with a brush or cotton swab, in the manner described by Ramachandran and colleagues (Ramachandran *et al.*, 1995), to several locations on the ipsilateral and contralateral face (forehead, cheek, upper lip and chin) and several locations both proximally and distally on the intact limb and on the residual limb (stump). The

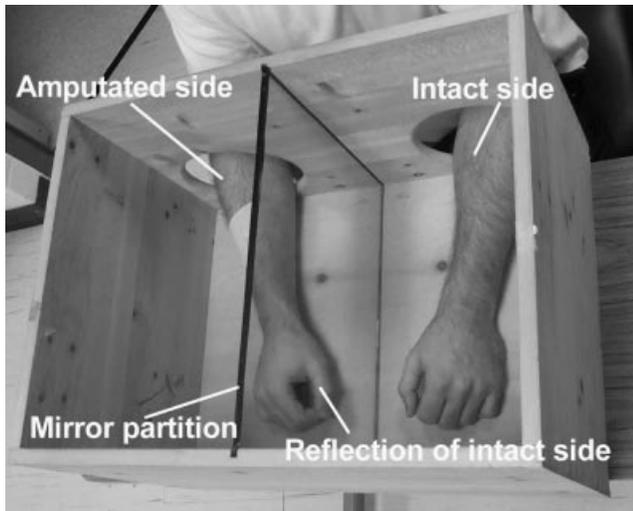


Fig. 1 Mirror-box illusion. The subject placed both upper extremities in an open box containing a mirror partition. The side of the box that contained the amputated limb was covered with a towel (not shown). The subject viewed the intact forearm/hand and its mirror image to create the illusion of an intact left and right forearm/hand extremity.

stimuli were applied in both a static manner and a dynamic manner to the skin under two conditions: first with the subject's eyes closed and then with subject's eyes open so that they watched the tactile stimulus touch the skin. The stimuli were presented two to five times at each location in a random manner, making sure each area was tested at least twice in each visual condition. Each subject was asked to describe the location, quality and intensity of any evoked sensation(s). Evoked sensations that were felt in both the missing limb and on the intact body were defined as 'dual percepts'.

Visual illusion

Testing for the mirror-box illusion (Fig. 1), described by Ramachandran and colleagues (Ramachandran *et al.*, 1995), was structured as follows. The subject placed both upper extremities in an open box containing a mirror partition and then viewed the intact hand and its mirror image to create the illusion of two intact hands. The side of the box that contained the amputated limb was uncovered with a towel. Testing consisted of three phases. In Phase 1, subjects viewed the intact limb and its reflection. They were then asked to move the intact hand (e.g. rotate it, make a fist, wiggle the fingers) and to imagine moving the phantom hand while continuing to view the intact hand and its reflection. Subjects were asked to describe the location, quality, position and intensity of any PLS or PLA that arose at rest and during movement.

In Phase 2, subjects viewed the intact limb and its reflection while the tactile stimulus was applied (i) to the intact hand, (ii) to the residual limb, and then (iii) simultaneously to various locations on the distal residual limb and identical locations on the intact limb. This created three conditions of

congruent and conflicting visual illusion and tactile input. In condition (i) the subject received tactile input from the intact hand and watched the stimulus touch the intact hand and its reflection in the mirror. In condition (ii) the subject received tactile stimulation of the residual limb, but did not see the stimulus touch it because the mirror blocked the view of the residual limb. In condition (iii) the subject received simultaneous tactile stimulation bilaterally (to the residual limb and the intact side) and the mirror box created an illusion of bilateral stimulation of two intact upper extremities.

Phase 3 of mirror-box testing involved only those subjects who previously reported dual percepts in response to tactile stimulation of the residual limb. Tactile stimuli were applied simultaneously to points on the residual limb that had previously evoked a dual percept and to the location on the intact hand that corresponded to the location of referred sensation in the phantom associated with the dual percept. Thus, the subject viewed an illusion of a touch that matched the timing and location of the referred component of the dual percept. On the basis of the observations of Pavani and colleagues (Pavani *et al.*, 2000), we predicted that the visual illusion of touch would be spatially and temporally congruent with the tactile-evoked PLS and would augment the ability to evoke a dual percept. We were also interested to see whether the visual illusion changed the evoked dual percept by inducing a more specific or localized sensation. During these procedures the subjects were asked to describe the location, quality, position and intensity of any new (or any changes in qualities of any existing) evoked PLS or PLA.

Results

Table 1 contains a subject-by-subject summary of the findings from the structured interview. Table 2 provides a summary of the findings of testing for dual percepts and the mirror-box illusion.

Spontaneous phantom sensations and awareness

Twelve of the 13 subjects reported non-painful spontaneous PLA. One subject denied experiencing any phantom phenomena at any time after amputation. All 12 subjects who reported PLA included a description of the phantoms as 'stiff', 'tight' and/or in a flexed position. Five of these subjects described a phantom limb with the phantom hand in a relatively immobile clenched position. Some included comments that the hand felt 'as if the fist is trying to open' or 'like it needs to stretch'. The two subjects with unilateral shoulder disarticulation reported that their shoulder and elbow were fixed in a slightly flexed position; one described a clenched fist and one reported that she was able to move the phantom hand 'as if I was typing'. Five of the 13 subjects reported a shortening (i.e. telescoping) of their phantom limb over time.

Table 2 Tactile and visual testing

Patient	Dual percepts		Visual illusion effects	
	From face	From stump	Observation and movement	Tactile stimulation
A	No	No	Phantom more vivid More certain of phantom position Easier to move phantom slightly	No new referred sensations
B	Forehead	Yes: increased desire to move thumb	Phantom more vivid Increased pressure, pulsing and burning when seeing reflection move Could move phantom slightly	More vivid referred sensations No new referred sensations
C	No	No	Phantom more vivid Could move phantom fingers but could not position entire phantom limb in mirror box Painful fatigue in phantom upper arm	No new referred sensations
D	No	No	Intense sensations began to focus in hand at first, then cramping pain was 'calmed'	No referred sensation
E	Cheek	No	Phantom more vivid, aware of all digits Some of the stiffness was relieved	No referred sensations
F	No	No	No change	No referred sensation
G	No	No	Remained clenched Pain in stump muscles from trying to move phantom	No new referred sensations
H	No	Yes	Phantom more vivid Could move fingers but they still felt 'stiff' Ability to move lasted several seconds after eyes closed	More vivid referred sensations No new referred sensations
I	Cheek	Yes	No change	More vivid referred sensations No new referred sensations
J	No	Yes	No change	No new referred sensations
K	No	Yes	Phantom more vivid More certain of phantom position Could move phantom slightly Could move fingers but they still felt 'stiff'	No new referred sensations No new referred sensations
L	No	No	No change	No new referred sensations
M	No	Yes	Hand remained flexed Could move phantom slightly Could move fingers but they still felt 'stiff' Pain in stump muscles from trying to move phantom	No new referred sensations

Eleven of 13 subjects reported phantom limb pain (PLP), described as arising from a deep location (i.e. beneath the skin). All subjects who experienced PLP also experienced non-painful PLA. Six of the eleven subjects with PLP described a chief complaint of painful cramping or squeezing. Four subjects complained of burning pain. Two subjects complained of transient shocking pain. The only two subjects who reported dysaesthesias (a painful pins-and-needles sensation) were the two subjects who had undergone amputation >12 months before the interview. Three subjects stated that their pain included a component of throbbing pain. Six of the 11 subjects with PLP completed the McGill Pain Questionnaire. The most common words chosen were 'aching' (4/6), 'sharp' (4/6), 'intense' (3/6), 'pulsing' (2/6), 'pricking' (2/6), 'tingling' (2/6), 'taut' (2/6), 'tight' (2/6) and 'agonizing' (2/6).

Tactile-evoked dual percepts

Dual percepts were evoked in seven out of 13 subjects. Light touch of the residual limb evoked non-painful sensations at both the stimulus site and in the phantom in six of the 13 subjects. The character of the evoked phantom component of the dual percept was not identical to that of the primary percept. That is, the light touch stimulus did not evoke a 'light-touch' sensation in the phantom limb, but rather evoked the general awareness of a particular area of the phantom, the character of which varied across subjects. Furthermore, there was no evidence of any topography of these percepts. In one case, the tactile stimulus evoked an increased desire to move the phantom thumb.

In three subjects, light tactile stimulation of the ipsilateral face evoked non-painful dual percepts at the stimulus site and

in the phantom. Two subjects reported dual percepts from stimulation of either the face or the stump (Table 2). Compared with the dual percepts evoked from the stump, the face-evoked sensations were poorly localized in the phantom limb and were not evoked consistently with repeated testing.

Visual effects

Effect of normal visual inputs on spontaneous phantom awareness

All subjects were asked to comment on any situation that altered the phantom experience. Four subjects (Subjects A, D, I and J) noted that their PLS and/or PLA were diminished when they were engaged in a distracting activity, such as when they were busy working at a task and increased when they were relaxed or resting at the end of the day. Four subjects (subjects B, D, K and L) found that the symptoms were aggravated when they were using the muscles of the residual limb intensively, especially during rehabilitation therapy. Four subjects (Subjects B, E, H and M) found that massage or rubbing of the residual limb relieved the phantom PLS, while three subjects (Subjects A, E and K) found that massage aggravated their symptoms. However, none of the subjects reported that their spontaneous PLS or PLA was suddenly altered when their eyes were closed, nor did the PLS or PLA change when the subject ($n = 4$) wore a prosthesis.

Effect of normal visual input on dual percepts

Dual percepts evoked by tactile stimulation of the face were reported only when the subject's eyes were closed. Dual percepts evoked from the residual limb occurred only with the subject's eyes closed in four of the six subjects. In these four subjects, dual percepts could not be evoked when the subject's eyes were open whether or not (s)he observed the stimulus as it was applied to the skin. The remaining two subjects reported dual percepts from stimulation of the residual limb with their eyes open or closed. However, in these two subjects the phantom percepts could only be evoked from skin areas within 15 cm of the stump tip; this may represent a mechanism of referral different from that operating with stimuli evoked from the face or more proximally in the stump.

Visual illusion effects

In the Phase 1 of mirror-box testing, seven of the 13 subjects immediately, and of their own accord, reported a more vivid awareness of their phantom when they viewed their mirrored intact hand, whether or not they were moving their intact hand. Five of the seven subjects experienced a new or enhanced ability to move the phantom when they viewed the mirrored intact hand moving; the remaining two subjects

reported that the phantom limb felt 'less stiff' and 'more relaxed'.

Viewing an illusion of the amputated hand during the tactile stimulation procedure (Phases 2 and 3 of mirror-box testing) did not evoke any new or additional referred sensations or dual percepts. Subjects in whom dual percepts could not be evoked with their eyes open did not experience dual percepts in the mirror box. Thus, of the different combinations of touch with conflicting or congruent visual illusion, no change was observed from the normal eyes-open condition.

Discussion

This is the first study to evaluate phantom sensory phenomena in a non-selected group of subjects early in the rehabilitation period following acquired upper extremity amputation. Furthermore, with the exception of the study of Jensen and colleagues (Jensen *et al.*, 1984), previous studies of groups of subjects have not reported the characteristics of PLA *per se*. In addition, although 11 of the 13 subjects experienced painful traumatic amputations (the other two had elective amputations), only one experienced long-standing pre-amputation pain and only one had a history of pre-amputation paralysis (5 days). None of the subjects had amputation aetiology of peripheral vascular disease or diabetes. Finally, this is the first study to evaluate the effects of multiple sensory stimuli on spontaneous and evoked phantom PLS and PLA in individuals with more recent upper extremity amputation.

Prevalence and character of evoked phantom sensations and awareness

Approximately half of the subjects reported dual percepts during light touch of the face or arm. Interestingly, the evoked phantom percept was not a specific sensation but rather a general awareness of a particular area of the phantom. This quality of sensation is similar to that described by Halligan and colleagues in a single case study of an amputee with dual percepts (Halligan *et al.*, 1994). Previous studies of groups of amputees who were tested many years after amputation reported a similar prevalence of 'mislocalization' of light touch stimuli to the face (Elbert *et al.*, 1994; Flor *et al.*, 2000) or the limbs (Flor *et al.*, 1998, 2000). However, in these studies the subject could localize the phantom sensation more specifically and half of the subjects with dual percepts reported that the distribution was topographic (Flor *et al.*, 2000). Thus in, the present cohort of subjects (each examined once and within 14 months of amputation) the prevalence of dual percepts to tactile stimulation was similar to that in previous reports, but the character of these percepts was different from that previously reported in studies of groups

of amputees many years after amputation (Knecht *et al.*, 1996).

Prevalence and character of spontaneous phantom awareness

We evaluated only current postamputation phenomena and did not rely on retrospective reporting based on patient memories of pre- or postoperative sensory complaints. Nikolajsen and colleagues showed that patient memory of the characteristics and intensity of earlier postamputation phantom sensations was poor (Nikolajsen *et al.*, 1997). We found that study participants commonly experienced phantom phenomena, including non-painful and/or painful PLS and PLA. Thus, evoked and spontaneous sensations did not necessarily occur together and spontaneous PLA was more common.

Our sample group was inclusive and our design was prospective, but the high percentage (92%) of subjects who experienced phantom sensations is similar to the prevalence reported by retrospective studies (Sherman *et al.*, 1984; Katz and Melzack, 1990; Kooijman *et al.*, 2000). However, we report new data about the quality of the phantom limb experience, particularly phantom awareness. All 12 subjects who reported phantom phenomena mentioned awareness of the missing limb that was described as a feeling of stiffness of the phantom limb in a clenched or a flexed position. Only one subject experienced kinetic sensation (ability to move the phantom hand), but her phantom shoulder and elbow were relatively immobile. Thus, in this group of subjects the relatively immobile position of part or the whole of the phantom limb was a consistent finding.

We prospectively studied a unique cohort of amputees with respect to age, aetiology of amputation and medical complications. In contrast, previous prospective studies included subjects who had lower extremity amputations as a result of complications from pre-existing diabetes and peripheral vascular disease and who had experienced longstanding pre-amputation pain (Jensen *et al.*, 1983, 1984, 1985; Nikolajsen *et al.*, 1997). This difference has two implications. First, Nikolajsen and colleagues showed that, during the early stages of recovery (up to 3 months), PLP shared some characteristics with longstanding pre-operative pain. With the exception of two subjects, our subjects did not experience longstanding pre-amputation pain, thus eliminating this factor. Secondly, Weiss and Lindell (1996) examined the relationship between the aetiologies of amputation (blood clot, non-clot diabetes, and miscellaneous) in 92 consecutive unilateral lower extremity amputees throughout rehabilitation. Those with diabetes and blood clot aetiology had the highest levels of phantom pain and the greatest number of medical conditions. Those with gangrene or infection had high levels of pain and a longer period before prosthetic training could begin. None of our subjects had diabetes-related amputation

and only one of our subjects had blood clot-related amputation. Thus, our group may have experienced less phantom pain and less postoperative complications. In summary, the characteristics and qualities of any non-painful phantom awareness may have been under-reported in previous prospective studies of patients with non-traumatic amputation because of a patient and/or examiner focus on pain.

Effect of sensory inputs on phantom sensations and awareness

Effect of visual input on dual percepts

In the present study, we found that vision had a powerful effect on tactile-evoked dual percepts. That is, seeing the actual stimulation typically served as a 'reality check', negating the percept that the stimulus had been applied to the missing body part. Previous studies of dual percepts have used the eyes-closed condition only (Elbert *et al.*, 1994; Flor *et al.*, 2000). Curiously, in two subjects the visual input was not powerful enough to override the phantom percept. Both of these subjects had distal amputations (mid-carpal and carpal–metacarpal). The lack of visual effects in these two amputees may simply be a curiosity (especially given the small number of subjects) or it may imply a different mechanism for tactile-evoked phantom sensations in distal versus proximal amputees (Roricht *et al.*, 1999).

The effect of normal visual input could also reflect the conflicting versus congruent nature of the tactile and visual sensory input. There is behavioural evidence of intermodal matching and intersensory bias within the different circuits that contribute to the final perception of body schema. In healthy volunteers, a combination of visual and touch stimuli, when synchronous (or temporally congruent), was sufficient to fool the nervous system into self-attribution of a rubber hand (Botvinick and Cohen, 1998). However, when the stimuli were temporally but not spatially congruent it appeared that intersensory bias occurred in which congruent sight and touch information overruled proprioception (Botvinick and Cohen, 1998). In our study, the subject was well aware of the location of the stimulus to the face or to the stump when tested in the eyes-open condition, i.e. the visual information conflicted with the referred phantom sensation. The dual percept was not perceived in the eyes-open condition, thus illustrating visual dominance over touch (Farne *et al.*, 2000). In contrast, eyes-open versus eyes-closed may not have provided such a dramatic contradiction of vision and touch in the two subjects with very distal amputation, since the location of the observed touch was closer to the site of the referred sensation. In this situation the two inputs may have had sufficient congruence to promote an interaction between vision and touch (Ladavas *et al.*, 2000). Therefore, vision may have determined the ultimate evoked percept

when the visual input clearly conflicted with the tactile evoked perception.

Effect of visual and or tactile sensory inputs on spontaneous PLA

A visual illusion that produced an image of the missing limb transiently enhanced the awareness and/or the ability to move a phantom limb in seven of the 13 subjects. The visual illusion also allowed these subjects to experience and describe more vividly the exact position of the phantom hand. Our findings extend those reported by Ramachandran and colleagues, who found that, when viewing the reflection of the intact hand in the mirror box, subjects reported proprioceptive and kinaesthetic sensations in the missing limb and relief of cramping pain (Ramachandran *et al.*, 1995).

The visual illusion effects were neither enhanced nor dampened by the addition of tactile stimuli (Phase 2 of mirror-box testing). Thus, vision moderately influenced PLA, perhaps in an interaction with ongoing proprioceptive and kinaesthetic sensory inputs, but tactile inputs did not change this effect. In comparison, Sathian (2000) evaluated the effects of a mirror illusion in six poststroke patients with anaesthetic hands. All six demonstrated evidence of contralateral referred sensations evoked by pressure stimuli (but not pinprick or cold stimuli). However these patients showed a different response to a mirror illusion. Three of the six patients reported that the mirror illusion augmented the referral effects (Sathian 2000). However, in our subjects contralateral referred sensations occurred in two subjects, but they were fleeting and not reliable and the mirror-box illusion did not induce, change or augment the contralateral/intermanual referral effects. This lack of effect of the mirror box could be related to congruence versus the conflicting nature of the combined inputs. The subjects described by Sathian and colleagues (Sathian *et al.*, 2000) had a pre-existing intermanual referral of tactile input, whereas our subjects essentially did not. Thus, the visual illusion may have augmented a more robust, *pre-existing* intermanual tactile referral in the poststroke patients but was not sufficient to elicit dual percepts or intermanual referral in our subjects. The visual illusion was congruent with the tactile referral in the poststroke patients but it was congruent with the tactile response in our subjects.

In contrast, we tested the effect of voluntary movement of the intact hand during Phase 1 of the mirror-box testing. In this situation, information related to the desired and actual states of the motor system could have influenced body awareness. There is evidence that congruence of information from the motor system with multimodal sensory information can affect conscious awareness of body schema (Andersen *et al.*, 1997; Slachevsky *et al.*, 2001). Sensorimotor integration of information concerning current limb position and intention and sensory feedback must be monitored to ensure that sensory feedback and motor outputs are congruent with

current awareness of the body (Andersen *et al.*, 1997). Wolpert and colleagues proposed the 'internal model' of sensorimotor integration to describe and predict the sensorimotor transformations that underlie motor learning, motor control and 'state estimation' (Wolpert *et al.*, 1995; Wolpert and Ghahramani, 2000). The sources of information for the internal model include not only sensory signals from the muscles, joints and skin but also 'efference copy' from motor commands (Wolpert *et al.*, 1995; Frith *et al.*, 2000). Our findings may be interpreted in the light of the forward model sensorimotor integration (Wolpert *et al.*, 1995) and recent electrophysiological and imaging studies that support a new model for the organization of the posterior parietal cortex (PPC) (Rizzolatti *et al.*, 1998). The forward model thus functions to anticipate sensory feedback and compensate for the sensory effects of movement in order to minimize performance error (Blakemore *et al.*, 1998a) and, in doing so, provides an estimate of true location of the body part.

There is evidence that humans are normally not consciously aware of normal sensory feedback from posture or movement (Fournieret and Jeannerod, 1998) or other components of the internal model (Kawato and Wolpert, 1998). Hypotheses concerning which components of the internal model of sensorimotor integration are normally available to conscious awareness are under investigation. It has been proposed that the comparison (within the forward model) of predicted versus intended sensory consequences of a movement is not normally available to conscious awareness since the accurate prediction, or congruence, between predicted and intended sensory consequences allows attenuation of the sensory feedback (Frith *et al.*, 2000; Blakemore *et al.*, 2002). Thus, the comparison becomes available to conscious awareness only when there is a sensory mismatch between predicted sensory consequences and intended or actual sensory feedback conflict (Blakemore *et al.*, 1998b; Fink *et al.*, 1999; Frith *et al.*, 2000). When our subjects viewed the mirror image, the visual illusion of the missing hand and the attempt to move the hand did not concur with the sensory feedback from the residual limb, and this sensory conflict presumably augmented a conscious awareness of the phantom limb. Brain imaging studies of healthy male volunteers during a bimanual activity in which a mirror visual feedback provided a mismatch between intention, proprioception and visual feedback revealed increased activity in the right lateral prefrontal cortex that could represent the central monitoring of the induced cognitive conflict (Fink *et al.*, 1999).

Interestingly, it has been noted by other investigators that dual percepts from the face cannot be evoked by self-stimulation (Jensen *et al.*, 1984; Ramachandran and Hirstein, 1998). We were not able to test this reliably as the face responses in our patients did not persist in repeated tests. Recently Blakemore and colleagues have argued that the well-known attenuation of self-produced tickle response is due a central mechanism and is based on a decreased discrepancy between predicted and actual sensory feedback

when the stimulus is generated internally (self-tickle) rather than externally (Blakemore *et al.*, 1998b, 2000). The dual percepts in our study were generated by a passive, externally applied stimulus. On the basis of our findings of the behaviour of the evoked versus spontaneous PLS/PLA, the reported lack of *self-produced* dual percepts may represent a similar mechanism. Further studies of this effect requires patients that have more reliable dual percepts.

The phantom limb experience cannot be attributed to a single explanatory mechanism (Jensen *et al.*, 1984; Sherman, 1997). Katz reviewed the existing literature and concluded that the phantom limb experience is 'determined by a complex interaction of inputs from the periphery and widespread regions of the brain subserving sensory, cognitive and emotional processes' (Katz, 1992a). Following amputation, there was reorganization of the monkey S1 somatosensory cortex such that neurons in the hand area contralateral to the amputated side responded to stimulation of the face (Merzenich *et al.*, 1984; Pons *et al.*, 1991). Ramachandran and Rogers-Ramachandran (2000) proposed that the topographic remapping of the ipsilateral face to the phantom limb was a perceptual correlate of S1 reorganization. However, we were unable to find topographic remapping in our group of (non-selected) subjects (examined within 14 months of amputation), which is consistent with the suggestion that functional sensory remapping is a relatively rare phenomenon (Knecht *et al.*, 1995; Flor *et al.*, 1998). Furthermore, previous studies have demonstrated that the amount of S1 reorganization correlated with PLP intensity (Flor *et al.*, 1995) and to the frequency of mislocalization of painful stimuli (Knecht *et al.*, 1996), but not to measures of non-painful PLA (Flor *et al.*, 2000). Instead, the presence of non-painful phantom sensations correlated with increased activity in PPC and S1 and decreased activity in S2. Kew and colleagues showed that regional cerebral blood flow was increased in contralateral M1, S1 and PPC in traumatic but not congenital amputees (Kew *et al.*, 1994). They suggested that PLS might be related to a change in activity in the PPC. Our findings further demonstrate that the reorganization of S1 in itself is not sufficient to explain each component of phantom phenomena.

Our findings demonstrate that spontaneous and evoked phantom sensations are two separate phantom phenomena. The evoked dual percepts were less common and behaved in a different manner from spontaneous phantom awareness. Vision, touch and sensorimotor information about the desired and actual states of the motor system contribute the phantom corporeal awareness that is commonly observed after traumatic upper extremity amputation. Our data indicate that the effect of conflict of sensory information on evoked dual percepts and spontaneous PLA is not identical. Specifically, the data indicate that spontaneous PLA is predominantly influenced by conflicting sensorimotor information pertaining to the state of the motor system, whereas evoked PLS and PLA are predominantly influenced by conflicting visual information.

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