Dissociation of phantom limb phenomena from stump tactile spatial acuity and sensory thresholds

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Summary

Most amputees experience phantom limb sensations and/or phantom limb pain as well as residual limb (stump) pain that are resistant to treatment. Phantom phenomena are not homogeneous; each patient presents with a unique combination of spontaneous or evoked sensations, pain, and/or awareness. In an effort to understand the underlying mechanisms, postamputation pain has been subclassified based on the perceived sensory qualities reported by the individual. However, little is known about the relationship between subjective phantom phenomena and sensory function of the residual stump. The aim of the present study was to determine if sensory processing, as measured psychophysically, reflected subjective reports of specific qualities of phantom and/or stump sensory phenomena. Twelve individuals who had recently (within 6 months) undergone traumatic unilateral upper extremity amputation participated in the study. Limb temperature, thermal thresholds, tactile sensory thresholds and tactile spatial acuity were compared between the residual limb and the intact limb, and related to patient reports of specific stump and phantom sensory phenomena. All but one subject reported phantom sensations and/or phantom pain. The remaining subject reported only stump pain. Mean skin temperature of the residual limb was significantly lower than that of the intact contralateral limb by approximately 0.9°C in the proximal portion of the stump and 1.7°C at the stump tip. However, the temperature of the stump (compared with the intact limb) did not reflect subjective reports of stump or phantom limb thermal characteristics. Thermal threshold abnormalities differed among patients, and did not suggest any pattern of small fibre loss of function or generalized hyperexcitability. Other than within grafted tissue or near the scar area, skin areas that the patient described as abnormally sensitive or tender to touch were not accompanied by corresponding abnormalities in static tactile thresholds or tactile spatial acuity. Tactile spatial acuity was heightened near the scar area only. The proportion of subjects who had decreased two-point discrimination thresholds at the stump did not differ significantly according to the reporting or non-reporting of dual percepts. Thus, despite a common injury, the sensory abnormalities varied within this cohort of subjects. In addition, psychophysical threshold measures of sensory function did not reflect, in any simple way, subjective phantom phenomena. Therefore, classification of phantom phenomena based on peripheral sensory function may be a misleading step in the search for specific mechanisms underlying postamputation sensory phenomena.

Keywords: amputation; perception; plasticity; psychophysics; QST

Abbreviations: CDT = cold detection threshold; CPT = cold pain threshold; HPT = heat pain threshold; WDT = warm detection threshold

Introduction

Most individuals who have undergone amputation continue to experience sensory phenomena that are perceived to originate from the missing body part (Jensen *et al.*, 1985; Sherman, 1997; Kooijman *et al.*, 2000). Phantom phenomena include painful and non-painful sensations with particular exteroceptive qualities and/or non-specific awareness of the existence or position of the missing limb (see definition in Hunter *et al.*, 2003). Each amputee presents with a unique combination of stimulus-independent (i.e. spontaneous; occurring in the absence of known sensory stimulus) and stimulus-dependent (i.e. evoked) phantom sensations, pain and/or awareness (Katz, 1992*a*). Spontaneous phantom phenomena can include those perceptions that are normally generated via activation of thermoreceptors (signalling warmth/coolness), deep or proprioceptive receptors (signalling limb position, size, volume or movement) and/or tingling sensations (Sherman *et al.*, 1989; Katz, 1992*b*; Fraser *et al.*, 2001). Evoked phantom sensations, such as sensory mislocalization (Cronholm, 1951) or dual percepts (Katz, 1992*b*), are transient and can occur in response to a variety of sensory stimuli (e.g. light touch) applied to intact body parts, such as the stump tip, the trunk, or the face (Ramachandran *et al.*, 1992*b*; Halligan *et al.*, 1993; Aglioti *et al.*, 1994, 1997; Flor *et al.*, 2000). The same individual may also report residual limb (stump) pain (Sherman, 1989), including spontaneous pain and/or evoked hyperalgesia, hypoalgesia, and/or allodynia (Kooijman *et al.*, 2000).

A large number of clinical interventions have been unsuccessful in producing permanent change in the reported stump and phantom perceptions (Sherman, 1989), thus underscoring the poor clinical utility of a diagnostic system that is based on the underlying aetiology or location of nerve injury. Woolf and Mannion (1999) proposed a classification system for neuropathic pain based on presumed underlying mechanisms. This approach is clinically appealing because treatment could then be directed at a specific mechanism. It was predicted that clinical identification of the underlying mechanism(s) would be based on qualitative assessment of the individual's signs and symptoms (Woolf and Decosterd, 1999) or response to specific pharmacological treatments (Jensen *et al.*, 2001).

Sherman (1997) proposed a subclassification system for phantom limb pain based on the sensory qualities of phantom pain and suggested causal mechanism(s) for each subclass based on observed physiological correlates of a pain of a specific quality. He reasoned that if the trigger for phantom pain was in the periphery, then peripheral changes in physiology (i.e. limb blood flow, nerve conduction and muscle tension) should correlate directly with specific characteristics of phantom pain (Sherman, 1997). Indeed, previous authors had reported that sensory characteristics such as perceived temperature of the phantom (Cronholm, 1951) correlated with skin temperature of the residual limb. In selected groups of amputees reporting phantom or stump pain, fluctuations in intensity of burning phantom pain (Sherman and Bruno, 1987) correlated negatively with changes in stump temperature. Similarly, in a group of subjects with cramping pain, the fluctuations in cramping pain intensity correlated with changes in electromyographic activity (Sherman *et al.*, 1989). However, these correlations between physical signs and phantom perceptions are based on subgroups of patients who were selected based on symptoms, and they fail to provide evidence of underlying causal mechanisms for phantom pain. To this end it is useful to compare individual signs and symptoms with the results of quantitative sensory tests.

There are no systematic studies that evaluate the relationship between psychophysical threshold measures of the function of large and small fibres and subjective reports of phantom phenomena, although Katz (1992*a*) reported a direct correlation between stump skin conductance and phantom limb paraesthesias. The aim of the present study was to determine if tactile thresholds, temperature thresholds and tactile spatial acuity are associated with subjective reports of post-amputation sensory perceptions. We chose to evaluate this relationship in a unique, unselected cohort of subjects with recent traumatic unilateral upper extremity amputation and no complicating medical problems. We hypothesized that, if phantom phenomena are directly related to peripheral sensory function, then the specific sensory qualities of the perceptions would be reflected by altered sensory function of the contributing pathways.

Methods

Subjects

Twelve subjects were recruited from two designated regional rehabilitation centres (St John's Rehabilitation Hospital or West Park Healthcare Centre) between June 2000 and December 2002. The local research ethics board at each centre approved the study. Every patient who had recently (within 6 months) undergone unilateral upper extremity amputation (below the shoulder joint) as a consequence of traumatic injury, and who was attending outpatient rehabilitation, was asked to participate in the study. This method of sampling ensured that the subject cohort was inclusive of upper extremity amputees at these institutions, and not limited to those with unique sensory symptoms. Subjects were excluded if the mechanism of injury may have included traction to the brachial plexus, or if they had a history of pre-amputation sensory dysfunction, or coexisting problems (diabetes or vascular or neurological disease) that would impede valid sensory testing. Informed consent was obtained from all subjects at the time of recruitment, prior to participation in the study. Of the 13 patients who were approached, one declined to participate in the study due to a pending court case.

Study design

One author (J. P. H.) conducted semistructured interviews to collect information on medical history, as well as descriptions of spontaneous stump and phantom sensations, awareness and/or pain. Psychophysical testing followed the interviews on the same day or within 1 week. Thermal threshold testing was conducted at a different hospital location within 10 days of the interview; thus, only those subjects willing to travel to the alternative location underwent thermal threshold testing.

During the interview and the psychophysical testing, subjects were seated in a quiet room, free from temperature fluctuations, drafts and noise. The forearm(s) rested on a rubber mat on a supportive table. The interview and psychophysical examination were videotaped and later reviewed to ensure complete and accurate data collection. During each psychophysical test the subject was asked to keep his or her eyes closed.

Evaluation of stump and phantom sensory phenomena

During the semistructured interview, each subject was asked to describe the current perceived size, shape, movement, and thermal qualities of the phantom limb as well as the location, quality, frequency and intensity of painless and painful stump and phantom awareness and sensations. Each of these qualities was assessed by open-ended questions followed by closed-ended questions for clarification (Bernstein and Bernstein, 1985). Subjects were asked to rate the intensity of their usual spontaneous phantom and stump pain on a 10 cm visual analogue scale, with text as anchors: 'no pain' and 'worst pain imaginable'. Since much of the psychophysical testing was done on a different day than the interview (see above), subjects were simply categorized as positive for phantom limb pain if they had reported that they currently (within the past week) experience phantom limb pain once a day or more frequently. Similarly, they were counted as positive for stump pain if they had reported that they currently experience spontaneous or evoked stump pain. Each subject was then asked to describe any previously experienced 'evoked' phantom limb painful or non-painful sensory phenomena such as those evoked by abrupt fluctuations in air or water temperature or by tactile stimuli.

Examination of evoked phantom sensations or awareness proceeded as follows. While subjects kept their eyes closed, light tactile stimuli were applied with a brush, in a manner described by Ramachandran and colleagues (Ramachandran and Hirstein, 1998), to 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 stump, circumferentially testing each limb segment (i.e. forearm, arm and hand) at two proximal–distal positions. The stimuli were applied two to five times at each location; stimuli were repeated up to five times at one location until the subject's response was decisive and consistent. Each subject was asked to describe the location, quality and intensity (weak or strong) of any sensation(s) evoked locally or in the phantom limb. Evoked sensations that were reportedly felt in both the phantom limb and at the stimulation site were defined as 'dual percepts' (Katz, 1992*a*).

Skin temperature

Skin temperature was measured with a 1 cm diameter surface probe (Model P-08440-00; Cole-Parmer, Chicago, IL, USA) connected to a digital thermistor thermometer (Model 8110-20; Cole-Parmer). Skin temperature was measured at two sites, the stump tip and the proximal site, as defined below. The procedure was repeated at homologous contralateral locations. Each measure was performed twice and the two measures were averaged. Skin temperatures from the amputated side were compared with measures from the homologous location on the intact side (paired t test). The effect of side (stump/intact) versus site (proximal/distal) was calculated with two-way repeated-measures analysis of variance (ANOVA). Significance was set at $P < 0.05$.

Psychophysical measures

Selection of test sites

Tactile detection thresholds and two-point discrimination thresholds were tested at sites on the upper limbs proximally and distally near the tip of the stump. Each person had a unique stump configuration, precluding exact standardized test locations. This issue was resolved by choosing two locations as follows: (i) the 'stump tip' measurement was within 5 cm of the tip of the stump; (ii) the 'proximal site' measurement was mid-forearm (except for patient 8, for whom it was mid-arm). At the distal site, if the scar tissue was present, additional sites were chosen so that both scar and non-scar tissue was tested. Homologous sites on the intact limb were then chosen. Regions that contained areas of postoperative healing (scars or grafts) were also tested. Areas with long hair were avoided when stimulus sites were chosen. Digital photographs were taken of each subject's stump and test results were documented on the printout of the photograph.

Tactile detection thresholds

Tactile detection thresholds were determined within each region with the Touch Test™ Sensory Evaluator (Stoelting, Wood Dale, IL, USA). This device consists of a set of 20 monofilaments (i.e. von Frey probes) of constant length but a stepwise progression of diameters. Each monofilament is labelled with a number that represents the $\log_{10}$ of the force (mg) required to cause the filament to bend when the tip of the fibre is applied at right angles to the skin. Thresholds were first approximated by the gross–medium staircase method (Yarnitsky, 1997). Then, five consecutively increasing (in force) monofilaments were selected. The monofilaments were chosen so that at least two were below the grossly determined threshold and at least two were above the grossly determined threshold. The final thresholds were then determined with a modification of Dixon's up-and-down method (Dixon, 1965), whereby the threshold was repeatedly crossed in both the ascending and descending direction until there were three consistent threshold values (Gottrup *et al.*, 1998). Null stimuli (approaching the subject with a probe but turning the probe slightly so that no contact with the skin was achieved) were applied once in every four to eight fibre applications. This was done to control for false positives that may have been caused if the subject detected the movement of the examiner or the warmth of the examiner's hand as it approached with the probe. Within each ascending or descending series at a stimulus site, each subsequent stimulus was moved slightly to a new location (but within 0.5 cm). The tactile detection threshold was defined as the monofilament with smallest force detected in three threshold crossings.

Two-point discrimination threshold

The two-point discrimination threshold was determined at each test area with a calliper probe (Model 16011 Two-Point Aesthesiometer; Layfayette Instrument Company, IN, USA). Testing was restricted to areas that could detect a minimum 0.166 g of force during previous tactile threshold testing. All trials were conducted with the subject's eyes closed. At each testing site the approximate threshold was determined with the gross–medium staircase method (Yarnitsky, 1997), and then a more precise measure of threshold was determined by the multiple random staircase method (Yarnitsky, 1997). Null stimuli were single stimuli, administered randomly every 10–15 applications. A modified version of Dixon's up-and-down method was used, and the threshold was crossed repeatedly in each direction until three consistent threshold values were reported (Dixon, 1965; Gottrup *et al.*, 1998). The stimulus was moved slightly to a new location (but within 0.5 cm) for each ascending or descending series. The two-point discrimination threshold was defined as the average minimum distance between the two calliper tips at which the subject reported feeling the two probe tips at each threshold crossing.

Thermal thresholds

Thermal stimuli were delivered to the test sites (excluding scar and grafted skin areas) by a Peltier-type stimulator (TSA 2001; Medoc, Israel) with a 9 cm^2 (3 × 3 cm) thermode. Thermal thresholds were established by the method of limits (Yarnitsky, 1997) in the following order: cold detection threshold (CDT), warm detection threshold (WDT), cold pain threshold (CPT) and heat pain threshold (HPT). Starting at a baseline temperature (32°C), the temperature was ramped at a rate of 0.5°C/s for CDT and WDT and 1.0°C/s for HPT and CPT. Each ramp was repeated for five consecutive trials. Intertrial intervals were 4 s for CDT and WDT trials and 10 s for CPT and HPT trials. Each subject was asked to depress a handheld button when he or she perceived the onset of the thermal sensation (for CDT and WDT) or pain (for CPT and HPT). Pressing the button caused the ramp to end, and the thermode returned to baseline temperature at a rate of 1°C/s for CDT and WDT and 10°C/s for HPT and CPT. Threshold was defined as the mean of the detected temperature for the five runs at each test site. For each subject, the four thresholds (CDT, WDT, CPT, HPT) were compared between the stump and the homologous site (t test). In addition, the group mean of each the four thresholds (CDT, WDT, CPT, HPT) at each stump site (proximal and distal) was compared with the group mean for the same threshold at the homologous contralateral site (paired t test). Significance values for a threshold difference were set at $P < 0.05$.

Results

Characteristics of subjects

Table 1 provides details of the 12 study subjects. All subjects (mean age 34.7 years, SD 11.8 years) were evaluated within 6 months (mean 3.9 months, SD 1.3 months) after undergoing a unilateral (right = 5; left = 7) upper extremity amputation as a consequence of a traumatic work-related injury. At the time of recruitment into the study, one subject (subject 8) had recently commenced training with a functional prosthesis.

At the time of the interview, 11 of the 12 subjects reported non-painful spontaneous phantom sensations, and nine subjects also reported experiencing spontaneous pain in the phantom limb (Table 1). One subject (subject 5) denied experiencing any phantom phenomena at any time after amputation. Phantom hands were described as being fixed in a flexed position (Table 1). Eight subjects reported the phantom was of normal length and three subjects (subjects 1, 8 and 11) reported intermittent shortening (telescoping) of the phantom.

Thermal testing

Skin temperature

In general, within each individual the stump sites were cooler than corresponding sites on the intact contralateral side, and distal stump sites were cooler than proximal stump sites (Fig. 1). Mean skin temperature was lower on the amputated side compared with homologous sites on the intact side, both at the proximal measurement site (32.8°C, SD 1.4°C versus 33.7°C, SD 1.0°C; $t(11) = -2.98$, $P = 0.01$) and at the stump tip (32.2°C, SD 2.61°C versus 33.9°C, SD 1.77°C; $t(11) = -4.262$, $P = 0.002$). The effect of side (stump/intact) versus site (proximal/distal) was calculated with a two-way repeated measures ANOVA. There was a statistically significant effect for side [$F(1,11) = 18.763$, $P < 0.001$] but not for site [$F(1,11) = 0.192$, $P = 0.67$]. The interaction between side and site was not statistically significant [$F(1,11) = 4.493$, $P = 0.058$], although it approached significance. With a larger n, this interaction may or may not have been statistically significant.

Subjective reports of perceived thermal state of the stump and phantom limb

When asked to compare the perceived thermal state of the stump with that of the intact limb two subjects (subjects 2 and 4) reported that the stump felt warmer and five (subjects 3, 6, 10, 11 and 12) reported that the stump felt cooler compared with the contralateral intact arm. The remaining five subjects reported that they did not notice a difference in perceived stump temperature compared with the intact limb (Fig. 2, left graph).

When the 11 subjects with awareness of the phantom limb were asked about the perceived thermal state of the phantom (Fig. 2, right graph), five subjects (subjects 1, 2, 7, 9 and 11) reported that the phantom felt warm, one subject (subject 10) reported that the phantom felt cool, and the remaining five reported that they were not aware of any thermal quality of the phantom limb experience. All subjects reported that these thermal perceptions were consistent and did not change from day to day.

In addition, three subjects reported that they had experienced a subjective increase in sensitivity of the stump to air temperature or water temperature compared with the contralateral intact side.

Relationship between subjective reports of perceived spontaneous thermal sensation and objective measures of stump skin temperature

Mean skin temperature differences between the two limbs (stump minus intact) were calculated for both the proximal and distal measurement sites for subjects grouped by

Table 1 *Characteristics of patients*

Patient	Age/sex	Time*	Level of amputation	S	Spontaneous phantom awareness and phantom limb sensations			Spontaneous phantom limb pain		Stump pain	
					Position	Vividness*	Characteristics	Intensity*	Characteristics	Intensity*	Characteristics
1	33/M	1.5	Trans-radial	R		10	Neutral 'tight' Tingling	$3.5^{\dagger}$	Throbbing, pulsing or cramping	$2^{\dagger}$	Evoked pain (tenderness to pressure at stump tip)
2	31/M	2.5	Mid-carpal	L		9	Clenched and 'thumb over index finger'	$7.2^{\dagger}$	Squeezing, cramping, pressure	2	Evoked pain (tenderness to pressure at stump tip) Spontaneous burning at tip
3	25/M	3	Radial-carpal	L		8.3	Neutral or clenched	7.6	'Thumb nail digs into palm Itching Stabbing	4	Evoked pain (tenderness to pressure at stump tip) Spontaneous ache
4	25/M	3.5	Carpal-metacarpal (thumb intact)	R		9.8	Flexed – 'stiff'	0	None	$2.5^{\dagger}$	Evoked pain (tenderness to pressure or tap to stump tip)
5	20/M	3.5	Transradial	L	No phantom	0	No phantom	0	No phantom	$1^{\dagger}$	Spontaneous ache Spontaneous stiffness
6	46/M	4	Proximal phalanges	L		1	Neutral	0	None	2	Evoked neuroma pain (shocking)

7	48/M	4	Transmetacarpal	L		8.5	Flexed slightly	4	Squeezing pain in digit 2 Shocking if tries to straighten phantom	1	Spontaneous to air, itchy, dry Evoked neuroma pain (shocking)
8	55/F	5	Mid-humerus	L		8	Elbow flexed 90° or feels fingers	1.5	Cramped fist position or aching throbbing, dull	2	Evoked pain (tenderness to pressure to scar)
9	43/M	5	Transradial	R		9	Digits 1 and 2 pinched with 2 and 3 crossed	9.5[†]	Burning in palm Sometimes cramped fist	2.9[†]	Evoked pain (tenderness to pressure at stump tip)
10	21/F	5.5	Carpal-metacarpal (thumb intact)	R		9	Clenched fist. Digits 2 and 3 squeezed together Tingling	3.5[†]	Stabbing Burning	3.2	Ache, tight, tingling Evoked pain (tenderness to pressure to palm)
11	35/M	5.5	Carpal-metacarpal	L		10[†]	Neutral or thumb opposed to digit 2	3	Cramping and burning Stabbing in tips of digits 2 and 3	2	Cramping and burning Evoked pain (pressure to tip) Tingling
12	30/M	3.5	Transradial	R		10	Flexed slightly Fingers crossed Tingling	8.5[†]	Cramping and squeezing	8	Cutting, shocking Evoked pain (tenderness to pressure at stump tip)

*Intensity measured on a visual analogue scale (cm) [†]intermittent pain. M = male; F = female; S = side; R = right; L = left; *time post amputation (months).

subjective thermal state of stump versus skin temperature difference (cooler, no difference, warmer) (Table 2A) or grouped by the perceived thermal state of the phantom (cool, neutral, warm) (Table 2B). Subjects' perceptions of the thermal state of the stump compared with the intact limb did not consistently reflect the actual side-to-side differences in skin temperature (Fig. 2, left graph; Table 2A). The effect of subjective thermal state of stump (cooler, no difference, warmer) versus skin temperature difference (proximal site, distal site) was calculated with a two-way repeated measures ANOVA. There was no significant effect for subjective thermal state of stump [$F(2,9) = 0.568$, $P = 0.585$] or site [$F(1,9) = 3.247$, $P = 0.105$], nor was there interaction between the subjective thermal state of the stump and the skin temperature difference [$F(2,9) = 0.101$, $P = 0.905$]. Similarly, subjects' perceptions of the thermal state of the phantom (cool, neutral, warm) did not reflect the actual skin temperature (Fig. 2, right graph; Table 2B) of the stump measured at either the proximal or the distal site. There was no significant effect for the perceived thermal state of the phantom [$F(2,9) = 0.623$, $P = 0.56$] or site [$F(1,9) = 1.667$, $P = 0.229$], nor was there interaction between the perceived thermal state of the phantom and the skin temperature difference [$F(2,9) = 0.0287$, $P = 0.972$]. Thus, we did not detect any skin temperature differences (stump minus intact) that reflected the subjects' grouping based on the perceived thermal state of the phantom or of the stump.

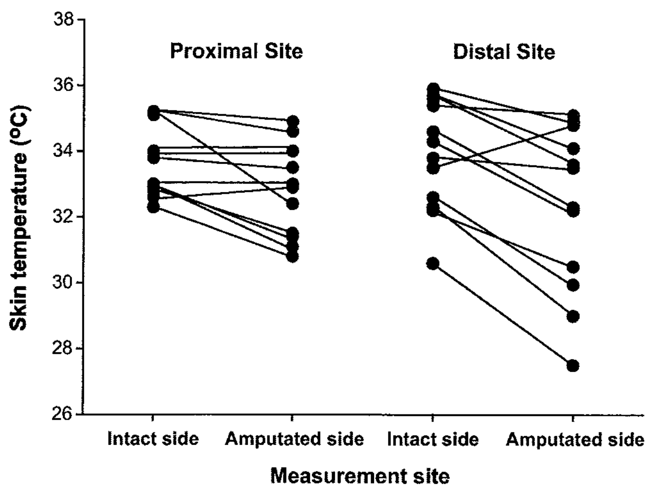

Fig. 1 Skin temperatures for individual subjects for the amputated side (stump) compared with contralateral homologous sites on the intact side. Skin temperature was measured at two sites, the 'stump tip' and the 'proximal site', as defined in Methods. The left side of the figure shows a comparison of proximal measures; the right side shows a comparison of distal measures.

Thermal thresholds

Thermal thresholds were measured in six subjects, including the one subject who denied experiencing any awareness of a phantom limb (subject 5). All thresholds measured at the intact limb were within normal limits as described by Harju (2002). Individual subjects showed a significant ($P < 0.05$; t test) difference in at least one of the four different types of thresholds measured from the stump when compared with the intact limb (Fig. 3). We did not detect any significant pattern in threshold change or consistent change in thermal thresholds; two subjects showed raised thresholds on the operated side compared with homologous areas on the intact side; two subjects showed decreased thresholds; two subjects showed both. Grouped data showed no significant difference in any of the four thresholds when stump was compared with the intact side (paired t test, $P > 0.05$) (Table 3).

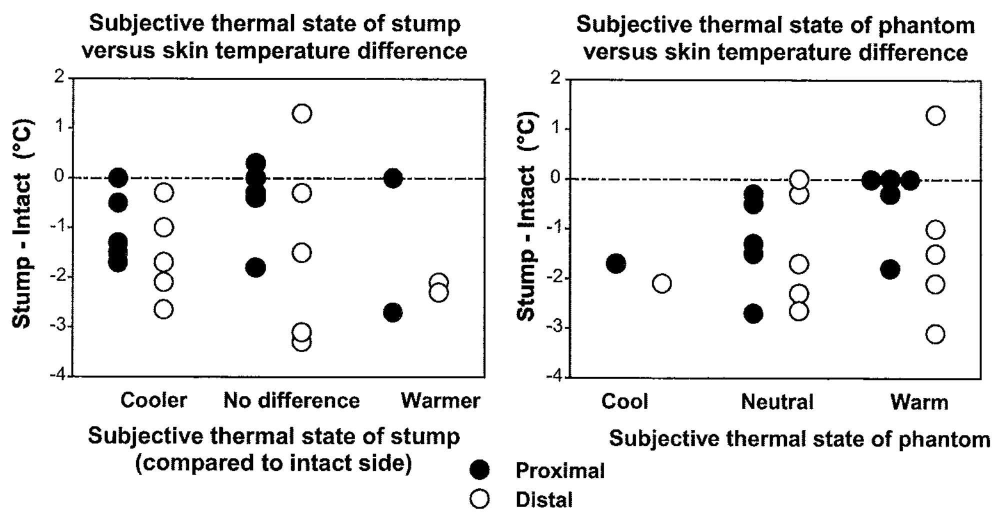

Fig. 2 The left graph ($n = 12$) shows the perceived thermal state of the stump (compared with the intact limb) versus actual skin temperature differences [stump – intact (°C)]. The right graph shows the perceived thermal state of the phantom ($n = 11$) versus actual skin temperature differences [stump – intact (°C)]. Skin temperature differences at proximal sites are represented by filled symbols and those at distal sites by open symbols.

Tactile testing

Subjective reports of perceived sensitivity of stump to tactile stimuli

Seven subjects (58%) reported that they were aware of specific stump areas that were 'less sensitive' to tactile stimuli, usually in small areas near the scar or grafted tissue. Eleven subjects (92%) reported stump areas where they perceived that the stump was 'more sensitive' to tactile (pressure) stimuli. These 'more sensitive' areas were restricted to the scar or graft area in all but four (33%) subjects, who also reported additional areas of sensitivity to light pressure in the forearm (subject 1) and over the tip of the medial carpal bones (subject 2), and unpleasant sensitivity (dysaesthesia) to light pressure of the palm (subjects 10 and 11). All subjects reported that these perceptions were consistent and did not change from day to day. None of the subjects reported areas in which very light tactile stimuli produced intense pain, as described in patients who were diagnosed with 'reflex sympathetic dystrophy' (Gracely *et al.*, 1992).

Table 2 *Skin temperature differences (°C; Stump-intact)*

(A)	Subjective thermal state of stump compared with intact limb		
	Cooler	No difference	Warmer
Proximal site	−1.0 ± 0.7	0.44 ± 0.8	−1.4 ± 1.9
Distal site	−1.6 ± 0.9	−1.38 ± 1.9	−2.2 ± 0.1
n	5	2	2
(B)	Subjective thermal state of phantom		
	Cool	Neutral	Warm
Proximal site	−1.6	−1.0 ± 1.06	−0.42 ± 0.78
Distal site	−2.1	−1.8 ± 1.24	−1.28 ± 1.64
n	1	5	5

All data are mean ± SD.

Tactile detection thresholds

Tactile detection thresholds were not significantly different ($Z = -1.34$, $P = 0.18$; Wilcoxon signed rank test) on the two limbs except for small areas near the scar or near grafted tissue (Fig. 4). The tactile detection threshold in the non-grafted areas of the stump and homologous sites on the contralateral side ranged from 0.07 to 0.69 g, (median = 0.17 g bilaterally; 25th and 75th percentiles, 0.17 g, 0.407 g). Two subjects had relatively low thresholds (0.07 g) to light touch in areas outside the immediate scar area (subjects 3 and 10). However, in eight subjects, skin areas at the operative sites on the distal

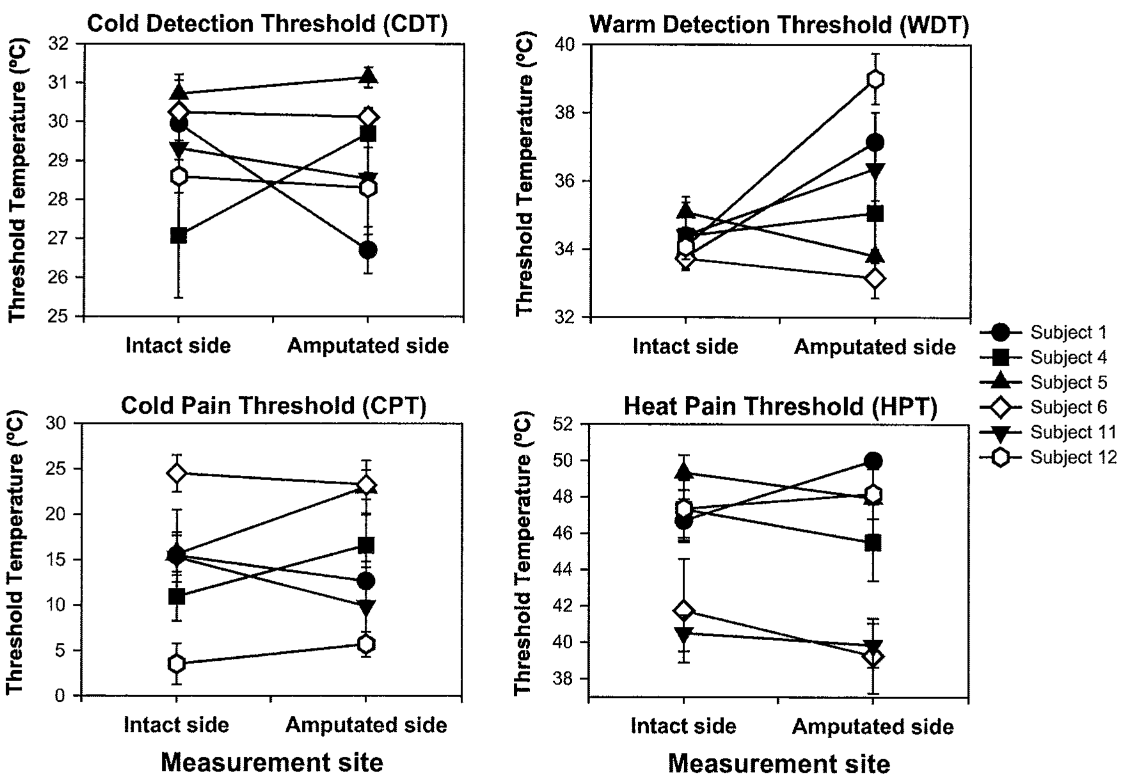

Fig. 3 Thermal detection thresholds for six subjects measured at the distal affected/amputated side and homologous sites on the intact limb. Symbols show the mean and standard deviation of five threshold measures.

Table 3 *Thermal threshold (°C): grouped data (n = 6)*

	CDT	WDT	CPT	HPT
Stump	29.1 ± 1.6	35.7 ± 2.2	15.1 ± 7.1	45.1 ± 4.5
Intact	29.3 ± 1.3	34.2 ± 0.5	14.2 ± 6.9	45.5 ± 3.5
Paired *t* test	*t*(5) = –0.306	*t*(5) = 1.567	*t*(5) = 0.467	*t*(5)= –0.428
	P = 0.77	*P* = 0.18	*P* = 0.660	*P* = 0.69

All data are mean ± SD. CDT = cooling detection threshold; WDT = warming detection threshold; CPT = cold pain threshold; HPT = heat pain threshold.

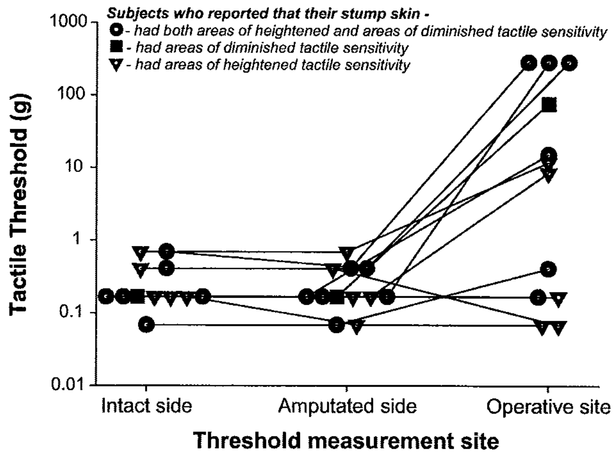

Fig. 4 Tactile detection thresholds for 12 subjects measured at the distal affected/amputated side and homologous sites on the intact limb compared with the tactile detection threshold for the distal stump but within an area of scar tissue (operative site). There was no significant difference in tactile detection thresholds between distal stump sites and homologous sites on the intact limb except for the scar or grafted skin. Symbols represent the individual subject's report of stump sensitivity to touch when questioned during the interview. Von Frey thresholds did not reflect the subjects' reports of heightened or diminished stump tactile sensitivity.

stump were less sensitive (subjects 1, 2, 5, 7, 8, 9, 11 and 12). In these eight subjects, the median threshold detection threshold at the operative site was 45.5 g (25th and 75th percentiles, 10.13 g, 281.8 g) was significantly different than homologous sites on the contralateral limb ($Z = -2.5$, $P < 0.01$; Wilcoxon signed rank test).

Comparison of subjective reports of tactile sensitivity versus objective tactile thresholds

Although four subjects reported areas of 'more sensitive' skin outside the scar or graft area, only one subject (subject 10) showed a corresponding lowered tactile threshold. Although 11/12 subjects reported the operative site and stump tip areas were subjectively 'more sensitive' to light touch than corresponding sites on the contralateral limb, von Frey thresholds were only decreased in two of the 11 subjects, were increased in seven subjects, and were not different in two subjects (Fig. 4).

Table 4 *Number of subjects with dual percept versus number with localized heightened tactile spatial acuity of stump*

	Dual percepts	No dual percepts
Localized areas of heightened tactile spatial acuity	*n* = 3 Subjects 2, 4, 10	*n* = 3 Subjects 5, 8, 12
Normal tactile spatial acuity	*n* = 3 Subjects 3, 9, 11	*n* = 3 Subjects 1, 6, 7

Evoked phantom sensations

In six subjects, light touch of the stump evoked non-painful tactile dual percepts at both the stimulus site and referred to the phantom (Table 4). In each of these subjects there was only one limb area in which the dual percept could be induced. The quality of the referred sensation was always described as a weak, poorly localized 'awareness' of the phantom limb or a particular portion of the phantom limb to which the sensation was referred. None of the subjects could further describe the sensation.

Two-point discrimination thresholds measuring tactile spatial acuity

Two-point discrimination thresholds were not significantly different on the two limbs except for areas of scar tissue. The threshold distance at which two tactile stimuli could be reliably detected ranged between 3 and 5.5 cm at sites tested above the elbow, between 1.1 and 3 cm on the forearm and between 0.7 and 3 cm over the thenar or hypothenar eminences bilaterally. The range for the limb was 0.7–5.5 cm (median 2.5 cm bilaterally; 25th and 75th percentiles, 1.05 cm, 3.0 cm). This is within the range of normal values reported in humans (Nolan, 1982). Individual thresholds did not typically differ by more than 2 mm on repeated testing. Five of the 12 subjects (subjects 2, 4, 5, 8, 10 and 12) had localized areas of heightened tactile spatial acuity where the two-point discrimination threshold distance was smaller by 3 mm or more compared with the threshold distance on the homologous area of the intact limb. However, these 'localized areas' were restricted to the immediate scar area including the amputation site and the edges of graft tissue. In these five subjects, the median threshold at specific sites in the scar (1.25 cm; 25th and 75th percentiles, 0.7 cm, 1.5 cm) was significantly different than homologous sites on the contralateral limb ($P < 0.05$; Mann–Whitney rank sum).

Comparison of subjective reports of dual percepts versus tactile spatial acuity

Three of the six subjects in whom dual percepts could be evoked had localized (described above) stump areas of heightened tactile spatial acuity (Table 4). In two of these subjects the area of heightened spatial acuity occupied the same skin area from which dual percepts could be evoked. In the other patient, the skin surface that evoked a dual percept was several centimetres proximal to the area with heightened tactile spatial acuity.

Three of the six subjects without dual percepts also had stump areas of heightened tactile spatial acuity. The proportion of subjects who had areas of localized heightened tactile spatial acuity did not differ significantly according to the report or non-report of dual percepts ($P = 1.0$; Fisher's exact test).

Correlation between time postamputation and psychophysical variables

We calculated the Pearson correlation coefficient between time since amputation and thermal thresholds, tactile thresholds and tactile sensory acuity thresholds and skin temperature. Correlation coefficients were calculated with an overall significance level of 0.05 adjusted for multiple comparisons by the Bonferroni correction (α/number of tests) to a required P value of 0.005. There were no statistically significant correlations.

Discussion

Our method of sampling ensured that the subject cohort included only upper extremity amputees within 6 months of traumatic injury, thus without complicating disease or injury. Our data show that despite a similar injury and a similar time frame after injury, sensory findings can vary among subjects. The data provide no evidence for consistent sensory abnormalities that reflect the quality of the subjective phantom limb experience after unilateral upper extremity amputation. Therefore, we propose that phantom limb phenomena do not reflect, in any simple way, the psychophysical threshold measures of sensory function.

Subjective reports of perceptions versus measures of skin temperature and sensory thresholds

Although the mean skin temperature was significantly lower on the amputated side, there was no relationship between perceived phantom temperature and stump skin temperature. These findings are at odds with an older study by Cronholm (1951), who reported that the perceived temperature of the phantom was related to the temperature of the stump. Our findings may be a reflection of our cohort and technological advances in the accuracy and reliability of skin temperature measurement tools used in the present study. Our comparison may be limited since the interview and psychophysical testing were not necessarily completed on the same day. However, all subjects reported that the thermal quality of phantom perceptions was consistent and did not change from day to day. We did not compare pain intensity measures with limb temperature differences since we did not always complete the psychophysical testing on the same day as the interview. However, we found no evidence of a relationship between the perceived thermal quality of the phantom and actual stump skin temperature. Thus, we feel that our findings do not support a direct correlation between stump temperature and the quality of the phantom sensation.

Subjective tactile sensitivity versus measures of tactile thresholds

Our findings of normal thresholds for tactile detection and two-point discrimination at the stump are consistent with a previous study of traumatic amputees (Carlen *et al.*, 1978) but in contrast with other studies (Teuber *et al.*, 1949; Haber, 1955; Varma and Mukherjee, 1972). The discrepancy between our findings and the earlier studies may reflect differences in methodology and study population. First, we used standardized measures that improved the validity of the comparison between the stump side and the intact side. Secondly, we examined subjects at a much earlier time after amputation. Thirdly, our subjects had all undergone traumatic upper extremity amputations and did not have longstanding pre-amputation pain or coexisting medical diagnoses (diabetes, or vascular or neurological disease) that would confound sensory testing. Fourthly, earlier studies obtained measurements in lower extremity amputees (Teuber *et al.*, 1949) or measured only at the stump tip (Varma and Mukherjee, 1972). Fifthly, only three of our subjects reported that the phantom limb was intermittently perceived as shortened (telescoped). Haber (1955) reported a difference in sensory acuity (light touch, two-point discrimination, point localization) only in the stumps of upper extremity amputees who reported that the phantom limb was 'telescoped' compared with those in whom the phantom was perceived as normal size. In order to ascertain whether telescoping is a correlate of altered tactile spatial acuity, we would have to re-examine the subjects at a future date and assess the extent of telescoping of the phantom and the tactile spatial acuity of the stump. Finally, our findings may have been affected by more modern surgical techniques and postoperative care, since other more recent studies also have not detected a difference in sensory thresholds (Katz, 1992*a*; Flor *et al.*, 1998; Nikolajsen *et al.*, 2000; Vega-Bermudez and Johnson, 2002).

We did not find a relationship between thresholds for static punctate tactile stimuli and subjective reports of stump tactile sensitivity. This comparison may be limited, since the interview and psychophysical testing were not necessarily completed on the same day. However, most subjects reported that the 'stump sensitivity' was a stable phenomenon. In addition, we chose to measure static tactile thresholds in order to compare our findings with previous studies in the amputee population. However, recent studies in other neuropathic pain populations have shown that dynamic (brush-evoked) tactile thresholds and/or wind-up-like pain correlated with ongoing pain, whereas static thresholds did not (Gottrup *et al.*, 1998; Pappagallo *et al.*, 2000). Our findings extend this work in that the threshold for detection of a static tactile stimulus did not correlate with the subject's reports of perceived stump tactile sensitivity.

Mechanisms underlying postamputation pain

Thus far, there is evidence that both peripheral (Devor and Seltzer, 1999) and central (Mannion and Woolf, 2000) nervous system processes contribute to phantom sensory phenomena, but the relative contributions of each have yet to be determined (Katz, 1992*a*). Previous authors have proposed that individual phantom phenomena (both painful and non-painful) may each be mediated by unique combinations of neural substrates (Grüsser *et al.*, 2001). Following amputation and nerve transection there is nociceptor sensitization (Greenspan, 2001) and abnormal activity in the peripheral nerve (Wall and Gutnick, 1974; Nystrom and Hagbarth, 1981; Devor, 1991). Ongoing activity in nociceptive afferents may induce sensitization of dorsal horn neurons (Woolf and Mannion, 1999). In addition there is evidence of plasticity, including remapping (Merzenich *et al.*, 1984; Florence and Kaas, 1995; Wu and Kaas, 2002), changes in excitability (Schwenkreis *et al.*, 2000) and abnormal neuronal activity (Davis *et al.*, 1998; Lenz *et al.*, 1998) at many levels within the CNS.

Our findings provide useful clues about the underlying mechanisms for postamputation pain. Quantitative thermal threshold testing can provide evidence about the integrity of sensory pathways from smaller afferents that transmit information from thermal receptors. We might not have detected a significant change in thermal detection thresholds because of the low *n* and high variance in the data. This large variance may reflect the large individual differences shown in Fig. 3. However, data on individual subjects do not suggest any pattern of peripheral small fibre loss of function or generalized hyperexcitability. Tactile threshold testing can provide evidence about sensitization in the touch pathway. Abnormal tactile thresholds at the stump were restricted to skin areas in close proximity to the operated site. Even though 33% of patients reported patchy areas of sensory abnormalities in other stump regions, these were not accompanied by corresponding abnormalities in tactile thresholds. Thus, sensory testing with static stimuli showed no consistent evidence of a generalized sensitization even though all subjects had some degree of ongoing pain (either in the phantom or the stump). Spatial acuity testing can provide evidence about peripheral innervation density and/or cortical representation. Altered tactile spatial acuity was restricted to the scar and graft area and could thus reflect peripheral denervation, sprouting and hyper-innervation of theses skin areas. Finally, when taken together, our data show that the pattern of sensory abnormalities can vary between subjects with similar injuries. This heterogeneity of sensory dysfunction in subjects with similar injury was also reported in patients with post-herpetic neuralgia (Pappagallo *et al.*, 2000). Pappagallo and colleagues proposed that this heterogeneity indicated that the relative contributions of peripheral and central mechanisms to the underlying pathophysiology may vary between patients and over the course of the disease.

Jensen and colleagues reported that non-painful phantom limb experiences in lower extremity amputees change in character over the first year, exteroceptive sensations appearing later than proprioceptive sensations (Jensen *et al.*, 1984). Our subjects, who were all tested within 6 months of injury, commonly reported non-painful awareness of the position of the phantom limb. Painful sensations were commonly described as a constant spontaneous deep pain, such as cramping, squeezing and burning pain; only three subjects (subjects 2, 10 and 11) reported phantom paraesthesias (tingling). This range of symptoms is consistent with the findings of Jensen and colleagues at a similar time after injury (Jensen *et al.*, 1984). Katz (1992*a*) described a 'sympathetic–efferent somatic–afferent coupling' mechanism for non-painful phantom paraesthesias. Thus, paraesthesias may reflect autonomic activity and this may change with time after amputation.

Mechanisms underlying postamputation evoked dual percepts

Based on evidence in animals of enlarged stump representation in primary somatosensory cortex (S1) after amputation (Merzenich *et al.*, 1984; Florence and Kaas, 1995; Wu and Kaas, 2002), previous authors have proposed that evoked dual percepts can be explained by the expanded representation of the stump in S1 (Ramachandran *et al.*, 1992*b*). Tactile spatial acuity is assumed to reflect the amount of brain area devoted to the sensation (Merzenich *et al.*, 1984; Recanzone *et al.*, 1992). Improved tactile spatial and temporal acuity following sensory discrimination training correlated with S1 reorganization (Flor *et al.*, 2001). However, in the present study, improved tactile spatial acuity beyond the scar was not related to the report of tactile dual percepts. We did not find differential evidence of improved tactile spatial acuity beyond localized areas of the scar. The localized distribution of the areas of heightened tactile spatial acuity may have reflected peripheral sprouting in the immediate scar area, including the amputation site and the edges of graft tissue. If altered tactile acuity reflects S1 reorganization (Ramachandran *et al.*, 1992*a*; Flor *et al.*, 2001), we found no evidence that a simple, direct relationship exists between somatosensory remapping and dual percepts.

We propose that the perceptual consequences of S1 reorganization after amputation may not be reflected by a change in tactile spatial acuity or dual percepts, yet may still be reflected by phantom limb pain. Doetsch (1997) proposed two types of perceptual consequences of CNS reorganization: 'functional respecification' and 'functional conservation'. In the former case, sets of partially deafferented neurons that acquire new receptive fields undergo corresponding changes in perceptual meaning. Excitation of these neurons by stimulation of their novel receptive fields can thus result in a change in the location of the perceived sensation from the original (now missing) sensory field to the newly acquired fields. This reflects 'learning' and could be the basis of improved tactile spatial acuity after sensory training (Elbert *et al.*, 1997; Sterr *et al.*, 1998; Van Boven *et al.*, 2000; Flor *et al.*, 2001; Werhahn *et al.*, 2002). This reorganization is not necessarily accompanied by pain. In the present study two of our three subjects with a non-painful phantom limb (subjects 4, 5 and 6) had increased tactile spatial acuity in the scar area. Some functional respecification may have occurred in these subjects.

In contrast, the perceptual consequences of 'functional conservation' are based on the assumption that partially deafferented cortical neurons respond to novel peripheral inputs but retain their original perceptual meaning. Excitation of these neurons by stimulation of their new receptive fields will evoke the sensation formerly mediated by those neurons, and hence are still projected to the original, now missing body regions. Dual percepts could represent the perceptual consequences of functional conservation and could merely reflect reorganization elsewhere in the nervous system. One possible physiological consequence of functional conservation is a mismatch between receptive field and projection field of the neuron. For example, thalamic mapping in amputees revealed an unusually large thalamic stump representation extending into areas that normally represent the now missing limb (Davis *et al.*, 1998). In these cases, only those subjects who experienced a phantom limb had a mismatch between the receptive field and the projection field of neurons that now responded to stump stimulation. Thus functional conservation was evident in subjects with phantom phenomena. In the present study tactile spatial acuity was normal beyond the operative scar. Thus, functional conservation may be present in these patients.

In summary, data from our unselected cohort, without complicating disease, injury or pre-amputation pain, provide useful information about the somatosensory consequences of amputation. Despite a common injury and a similar time frame after injury, the sensory abnormalities differed between subjects. In the search for the mechanisms underlying phantom sensation and phantom pain, classification of phantom phenomena by the perceived sensory qualities may be misleading. Subjective thermal phenomena did not consistently reflect actual limb temperature and one could not be inferred from the other. Measures of static or punctate sensory tactile thresholds and thermal thresholds involving a comparison of the stump and the contralateral limb provided no evidence of a generalized sensitization in our subjects, all of whom had some degree of ongoing pain. Areas of heightened tactile spatial acuity were always distributed in a pattern best explained by localized peripheral sprouting at the scar. Thus in the short term (<6 months) after traumatic amputation, phantom limb sensations and pain were not related in any simple way to peripheral or segmental sensory function as measured by static tactile and temperature thresholds. A longitudinal study of a large but similar cohort is needed to evaluate the relationship between perceptual consequences of CNS reorganization, such as dual percepts and telescoping, and their relationship to phantom limb pain.

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