Illusory persistence of touch after right parietal damage: neural correlates of tactile awareness

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Summary
We studied a patient who experienced ‘palinaesthesia’, an illusion of persistent touch following tactile stimulation on the left hand, subsequent to a right parietal meningioma affecting primary somatosensory regions in the postcentral gyrus (SI) and superior parietal gyrus (Brodmann area 7), but preserving the secondary somatosensory cortex (SII) in the upper lateral sulcus. This subjective sensation was accompanied by transient increases in objective measures of tactile threshold. The patient had mild deficits in superficial tactile perception, but showed severe left-sided extinction for offsets of tactile stimuli during bilateral stimulation, but not for onsets of stimuli. Functional MRI revealed increased neural activity during palinaesthesia selectively arising within the ipsilesional–right SI cortex, but no abnormality within left SI and bilateral SII. Right SI responded to the onset of new tactile stimuli on the left hand but not to their offset. By contrast, any tactile events on either hand modulated activity in contralateral SII regions, even undetected left-sided offsets. These data demonstrate that illusory persistence of touch following stimulation on the hand may result from sustained neural activity in a restricted region of the SI cortex outlasting the offset of the actual tactile stimuli. These findings also provide direct evidence for a critical role of SI in mediating conscious somatosensory experience on contralateral parts of the body.

Keywords: sensory illusion; tactile perception; parietal cortex; fMRI; consciousness

Abbreviations: fMRI = functional magnetic resonance imaging; HRF = haemodynamic response function; LOC = lateral occipital cortex; MEG = magneto-encephalography; ROI = region of interest; SI = primary somatosensory cortex; SII = secondary somatosensory cortex; TMS = transcranial magnetic stimulation


Introduction
The existence of distinct topographically organized somatosensory areas in the human parietal cortex has long been demonstrated in patients with focal lesions (e.g. Head and Holmes, 1911; Corkin et al., 1970; Caselli, 1993; Bohlhalter et al., 2002). This anatomo-functional specialization has been further extended in healthy volunteers using imaging techniques, such as PET (Rumeau et al., 1994; Young et al., 2003), functional MRI (fMRI) (Gelnar et al., 1998 Disbrow et al., 2000; Francis et al., 2000; Ruben et al., 2001; Deuchert et al., 2002; McGlone et al., 2002) and magneto-encephalography (MEG) (Korvenoja et al., 1999; Christmann et al., 2002; Del Gratta et al., 2002). In particular, an area corresponding to the primary somatosensory cortex (SI) is located in the postcentral gyrus of the parietal lobe, whereas other regions corresponding to the secondary somatosensory cortex (SII) and associative areas are found in inferior and posterior parietal cortex (Burton et al., 1997; Disbrow et al., 2000; Ruben et al., 2001; Christmann et al., 2002; Del Gratta et al., 2002). However, the respective contribution of each of these multiple somatosensory areas to tactile awareness is largely unknown, and the exact flow of tactile information through these areas is still debated. Here we report a patient with an unusual tactile disorder suggesting that disturbances in SI activity can be selectively associated with abnormal conscious tactile experience in the absence of significant disturbances at ‘higher’ stages of cortical processing (i.e. SII).
Anatomical and physiological data indicate that the human SI is not a homogeneous area, but comprises at least four cytoarchitectonically distinct fields (areas 3a, 3b, 1 and 2), corresponding to well-defined somatotopically ordered sub-areas that are activated by stimuli on the contralateral side of the body (Geyer et al., 1999, 2000; Moore et al., 2000; Grefkes et al., 2001; Young et al., 2003). Neurons in areas 3b and 1 respond predominantly to cutaneous inputs, while neurons in areas 3a and 2 mainly receive information from the deep body tissues (Pons et al., 1992; Iwamura et al., 1993; Burton et al., 1997). Lesion studies and anatomical investigations of tactile processing have revealed a partially hierarchical organization within the postcentral somatosensory cortex, and also between SI, SII and the posterior parietal cortex (e.g. Burton and Fabri, 1995; Burton et al., 1995; for review see Kaas and Garraghty, 1991; Iwamura, 1998).

In a recent MEG study Inui and colleagues investigated the precise timing of neural activations evoked in distinct somatosensory cortical areas following a tactile stimulus, and found evidence in favour of a hierarchical sequential stream of processing through the postcentral gyrus in humans (Inui et al., 2004). However, several reports have suggested that tactile analysis may involve both serial and parallel processing within the somatosensory cortex (e.g. Gelnar et al., 1999; Hari and Forss, 1999; Ploner et al., 2000; Bodegard et al., 2001; Disbrow et al., 2001), particularly concerning information flows between SI and SII. On the one hand, the serial or ‘traditional’ model holds that somatosensory information is progressively elaborated along a serial–hierarchical stream from SI to SII, as corroborated by selective ablation experiments in the monkey (Pons et al., 1987, 1992; Garraghty et al., 1990) and MEG studies in humans (Mauguiere et al., 1997; Mima et al., 1998; Inui et al., 2004). On the other hand, a parallel-processing model postulates that somatosensory processing in SII might not need to depend on inputs from SI but perhaps receives direct separate afferents (e.g. Zhang et al., 1996; Forss et al., 1999; Simeso et al., 2003). Thus, MEG studies by Ploner and colleagues revealed simultaneous activation of SI and SII to nociceptive stimuli (Ploner et al., 1999, 2000), although superficial tactile stimuli may still obey a serial processing scheme, suggesting that the functional relationships between SI and SII may vary according to the nature of the stimulation. Simultaneous recordings in the monkey sensory cortex (areas 3b, 2, SII) using large-scale multisite electrophysiology techniques further demonstrated that different regions of SI and SII may extract information about tactile stimuli almost simultaneously, but using different representational strategies (Nicolelis et al., 1998). Moreover, some work carried out on monkeys suggests that neurons at early stages of processing within the SI cortex might be able to code for information directly underlying perceptual experience evoked by certain types of tactile stimuli (e.g. Ruiz et al., 1995; Romo et al., 1998). Using intracortical microstimulation in SI, Romo and colleagues were able to induce artificial sensations of flutter stimuli and showed that the performance of monkeys in discriminating electrically induced signals in the cortex was indistinguishable from that obtained with natural stimuli applied on the skin (Romo et al., 1998, 2003). In humans, using transcranial magnetic stimulation (TMS), Harris and colleagues also found that neuronal activity in SI may contribute not only to on-line tactile processing, but also to tactile working memory (Harris et al., 2002). Taken together, these data suggest that SI may play a critical role in conscious tactile experience and memory. However, whereas damage to SI in human patients is known to produce a loss in tactile sensation, few neurological observations have provided direct support for a role of SI activity in primary tactile awareness (Meador et al., 2002; Valenza et al., 2004).

Here, we describe a patient, KM, who experienced a rare form of non-painful tactile illusion on her left hand following a focal lesion in the right parietal cortex that selectively affected the SI region. This patient reported that the tactile sensation elicited by holding an object in her left hand often persisted after the object had been removed from the hand. We termed this disorder ‘palinaesthesia’, by analogy with palinopsia, the pathological persistence of visual images.

Palinopsia is infrequent but typically encountered after occipitoparietal or occipitotemporal lesions, and its underlying mechanisms remain largely unknown. Several authors (e.g. Jacobs, 1989; see also Critchley, 1951) distinguished between two types of palinopsia in which the visual image of an object may either (i) persist after the patient has stopped looking at the object (for a period ranging from a few seconds to several minutes), or (ii) reappear after an interval without illusion. Our patient thus presented a form of sensory persistence similar to the first type of palinopsia, but in the tactile instead of the visual domain. Palinopsia is more frequent after posterior lesions in the right hemisphere (Bender et al., 1968; Meadows and Munro, 1977; Lazaro, 1983; Maillot et al., 1993; Vaphiades et al., 1996), and different causes have been suggested for this disorder. Seizure activity may be a possible mechanism in some cases with focal brain lesions (Jacobs, 1980), although it was often attributed to some form of ‘release’ or ‘spontaneous’ neural activity subsequent to parieto-occipital damage in the absence of any seizure (Cogan, 1973). Thus, palinopsia has been observed in patients with diseases confined to the eye or the optic nerve, who had no brain lesion and did not use drugs, suggesting that a disturbance in processing early visual inputs may contribute to such illusory phenomena (Pomeranz and Lessell, 2000).

In contrast to palinopsia, the phenomenon of palinaesthesia has been much less often reported. Although this unusual disorder has already been clinically observed and mentioned in the neurological literature (e.g. Gurewitsch, 1933; Nathan et al., 1986), its neural substrates are not known. Here, we combined detailed behavioural investigation and fMRI to elucidate the role of the right parietal cortex in tactile processing during such illusory tactile persistence sensations. Our fMRI results indicate that activity in the right SI was abnormally increased during periods of palinaesthesia on the left hand, in the absence of physical stimulation. By contrast,
activity in the left SI and bilateral SII accurately reflected the actual, physical tactile stimulation. These data not only identify neural substrates associated with this unusual and disabling tactile disorder, but also provide novel evidence for a critical role of SI activity in the subjective experience of touch and possibly in tactile memory.

Methods
Case report
KM is a highly educated 65-year-old right-handed woman, who was diagnosed in 1990 with a meningioma located in the right parietal convexity that was operated five times between 1990 and 2001 because of several relapses of the tumour. After the first surgery, KM noticed mild clumsiness and a loss of dexterity with her left hand. In 2000 (before the last surgery), she presented with a new sensory complaint, i.e. palinaesthesia on the left hand. This abnormal sensation was always triggered by stimulation of the hand, as during object usage, with a subjective feeling of continuing presence and pressure of the object after releasing it, but such sensation never occurred spontaneously. She also occasionally experienced the same phenomenon under her left armpit after holding a newspaper or at the side of her left hip after carrying a shoulder bag. These abnormal sensations were annoying and uncomfortable since they often disturbed the patient in her everyday activities, but were never painful.

These symptoms remained unchanged from this time on, and were unaffected by the last surgery in 2001. She also presented with occasional partial epileptic seizures, characterized by episodes of tingling sensation spreading along her left arm that appeared without any preceding sensory stimulation and were successfully controlled by drug treatment (phenytoin and levetiracetam). These episodes were thus clearly distinguishable from the sustained and sensory-triggered palinaesthesia episodes. KM was free of seizures during the time of our investigation. The patient gave informed consent to participation in this study according to the ethics regulations of the General University Hospitals.

Thorough neurological and neuropsychological assessments were performed at the time of our neuroimaging experiment. During all sessions, KM was alert, attentive and correctly oriented. Reflexes and gait were normal. She showed a slight postural instability of her outstretched left arm and mild tactile deficits on the left hand (see below). There were no other neurological deficits. High-resolution brain MRI showed some atrophy of the right parietal lobe affecting more prominently the postcentral region, but no signs of tumour recurrence (Fig. 1). In addition, there was a T1 and T2 hypersignal in the adjacent white matter due to an ischaemic infarct during previous surgery. Figure 1 shows cortical atrophy and white matter damage affecting regions of the postcentral gyrus, including the somatosensory area 1 in the crown of the postcentral gyrus, area 3b in the rostral bank of the postcentral gyrus, and probably also area 3a lying in the fundus of the central sulcus (Geyer et al., 1999, 2000). Cortical and white matter damage is also visible in the superior parietal gyrus (Brodmann area 7) and in the superior part of the supramarginal gyrus. However, the cortex in the upper bank of the lateral sulcus (sylvian fissure) corresponding to SII appears anatomically intact. The pattern and extent of these lesions were unchanged since the last surgery. EEG recordings at the time of the present investigation did not reveal any seizure activity, either at rest or during palinaesthesia episodes. Standardized neuropsychological testing revealed mild difficulties in the recognition of complex visual objects, based on configurational information such as visuospatial position matching (Warrington and James, 1991), as well as a moderate deficit in a set-switching task (Trail Making Test, Part B; Lezak, 1995), consistent with KM’s right hemisphere lesion. She had no visuospatial neglect and no left visual or auditory extinction. Other cognitive functions were normal, including oral and written language, ideomotor praxis, arithmetic skills, executive functions, visual recognition abilities, short-term memory, and verbal and visual learning abilities.

Somatosensory function
KM provided detailed and consistent descriptions of her tactile illusion in different clinical interviews, with consistent answers and reproducible performance during different testing sessions for both the affected and the healthy hand. Palinaesthesia was localized .

![Fig. 1](http://brain.oxfordjournals.org/)

**Fig. 1** High-resolution T1-weighted MRI showing cortical atrophy in the right anterior parietal lobe and diffuse damage in the adjacent white matter. Cortical atrophy is clearly visible along the postcentral and supramarginal gyri of the right hemisphere, with thinning of the cortical layer. The three view projections are centred on the central sulcus. CS = central sulcus; L = left; LS = lateral sulcus (sylvian fissure); PCS = postcentral sulcus; R = right; SMG = supramarginal gyrus.
predominantly on the lower thanar part of the left-hand palm. It was characterized by a vivid sensation of continuous painless tactile pressure on the palm, which always followed a real tactile stimulation exerted on the hand but never arose spontaneously, and could last up to several minutes before disappearing suddenly. This sensation persisted even when KM could check visually that nothing was in her hand; it was not interrupted when KM moved her hand and was not influenced by concurrent tactile stimulations on the healthy hand. Placing a second object in the left hand during illusory tactile persistence did not modify the patient’s perception. KM could correctly report the presence of a new object in her left hand but it did not modify the initial illusory tactile sensations.

A detailed evaluation of somaesthetic functions was performed, during which the following tests were administered sequentially (with the patient keeping her eyes closed throughout each test). These somaesthetic investigations revealed the preservation of light touch/pinprick discrimination in both hands (using a metallic pin; right hand, 10/10 trials correct; left hand, 9/10); but there were some deficits in the localization of tactile stimulations applied to the left hand (as tested using a sharp wooden stick, 3/10 correct trials; right hand, 10/10) as well as an impairment in digital proprioception (detection of passive finger movements) in the left (1/10 trials) but not the right (10/10) hand. However, KM could accurately report passive movements of the left wrist and the left forearm. Two-point discrimination was tested with two sharp wooden sticks simultaneously applied on the thenar part of the palm, with distances between the two points increasing progressively by steps of 1 mm until successful discrimination; this revealed preserved performance in the right hand (3 mm) but severe impairment in the left hand (50 mm). Graphaesthesia (verbal reporting of letters and digits traced by the experimenter on KM’s palms) was preserved in the right hand (5/5 trials) but impaired in the left hand (0/5 trials). Finally, KM could not recognize familiar objects or simple three-dimensional shapes by touch, or identify the texture of objects when using her left hand; it was not interrupted when KM moved her hand and was not influenced by concurrent tactile stimulations on the healthy hand. Placing a second object in the left hand during illusory tactile persistence did not modify the patient’s perception. KM could correctly report the presence of a new object in her left hand but it did not modify the initial illusory tactile sensations.

Palinaesthesia episodes were also associated with objective modifications of tactile sensitivity. We used Rey’s aesthesiometer (Rey, 1969; for a detailed description of this device see Mayer et al., 1988) to obtain quantitative measures of the modulation of tactile thresholds (in millimetres) as a function of palinaesthesia. In brief, the aesthesiometer allows the application of a thin rod (0.6 mm in diameter) on the skin surface, through a downward mechanical movement of the rod with progressively increasing pressures, until the detection threshold is reached (Mayer et al., 1988). These stimuli were applied on the thanar region of each hand, for a total of 140 trials administered under different experimental conditions including a baseline condition (tested on both the right and left hand), as well as two additional conditions for the left hand and after palinaesthesia. All conditions were administered across three different sessions with an equal number of trials in each condition (60, 40 and 40 trials, respectively; 35 trials for each threshold measurement) (Fig. 2). On each trial, the aesthesiometer’s cylinder was first applied on the skin surface (contact base ~1 cm²), and the rod pressure was then progressively increased by moving the rod in successive steps of 0.05 mm. A trial terminated when the subject detected the rod on her skin, and the next trial started after a rest period of at least 20 s. These stimulations alone did not trigger any palinaesthesia sensation.

At baseline, the mean tactile threshold in the right hand was in the normal range (0.75 mm), whereas this was moderately defective in the left hand (0.88 mm; for normative data see Rey, 1969). A baseline intermanual comparison (prior to any stimulation) revealed significantly higher tactile thresholds in the left than the right hand (t = 2.46, P = 0.02). More critically, following stimulation of the hand (by grabbing an object for a few seconds), tactile thresholds were significantly increased on the left hand concomitantly with the palinaesthesia phenomenon (1.03, moderately defective range), in comparison with the baseline condition (t = 2.10, P = 0.04) and with a post-palinaesthesia condition performed after the illusory sensation had ceased (0.89 mm, moderately defective range; t = 2.34, P = 0.02). In contrast, left tactile thresholds were equivalent in the baseline and post-palinaesthesia conditions (respectively 0.88 versus 0.89 mm, t = 0.15, P = 0.88).

![Fig. 2 Tactile discrimination thresholds measured with an aesthesiometer. Experimental conditions of tactile stimulation included a baseline resting condition tested on both the intact right hand and the affected left hand, a palinaesthesia condition tested on the left hand after the experimenter had stimulated KM’s left palm with an object, and a post-palinaesthesia condition tested on the left hand once the persistent illusory sensation had vanished (35 trials for each threshold measure, obtained across three separate sessions). These measures revealed not only an increased baseline threshold for the left hand compared with the right hand, but also a significant increase on the left hand during the transient palinaesthesia episodes. Data shown here were averaged across the different sessions in which the same pattern was reliably reproduced.](http://brain.oxfordjournals.org/organ/gy.png)
**fMRI study**

We examined the neural substrates of KM’s illusory tactile sensation using whole-brain fMRI and a voxel-by-voxel analysis with SPM99 (Friston et al., 1995). We first conducted three successive experimental scanning sessions, in which tactile stimuli were delivered on either the right or left hand, using a custom-made device (Fig. 3A) to trigger brief episodes of palinaesthesia when applied to the left hand. These experimental sessions allowed us to compare epochs of sustained illusory tactile sensation with epochs of rest without any subjective sensation (Fig. 3B). We next performed two hand-localizer runs to identify somatosensory regions responding to soft tactile stimulation on either the normal or the pathological hand. A high-resolution anatomical MRI scan was also acquired.

During the experimental fMRI scanning, tactile stimuli were delivered on each hand using two identical MRI-compatible devices (Fig. 3A) controlled by two experimenters standing on each side of KM. These stimulation devices were designed to exert a reproducible moderate pressure on KM’s palm using a lever system. During behavioral pilot tests prior to fMRI scanning, tactile stimulation with the lever was calibrated by adjusting its weight in order to reliably induce transient palinaesthesia on the left hand (typically ~20–30 s). They were never reported as painful or unpleasant by KM.

Experimenters controlling the stimulation device received instructions to let the lever fall down, leave it applied on the hand, and then pull it back to the upper position, with a precise timing given via a computer screen that was located in the scanning room. Presentation of these instructions and synchronization of the tactile events with the scanner acquisition was precisely controlled by Cogent 2000 (http://www.vislab.ucl.ac.uk/Cogent/). Experimenters were trained prior to scanning to apply the stimulation with regularity, and were counter-balanced across successive scanning runs with regard to which hand they were stimulating, in order to prevent any systematic difference related to the manipulation of the lever device. The effectiveness of this device was again confirmed by subsequent debriefing with KM, who reported a consistent occurrence of palinaesthesia during a few tens of seconds after each lever stimulation of the left hand. KM was reminded to close her eyes before the beginning of each run to avoid any visual interference, although in fact the stimulation device, the experimenters, and the instruction screen remained out of her sight during scanning.

Each experimental run (369 s each) consisted of three blocks of four trials (four onsets, four offsets) on the right hand and three blocks of four trials on the left hand delivered in a pseudorandom order. Each stimulation block was immediately followed by a block of rest without stimulation (28 s each block). Intervals between the onset and offset of stimulation were randomly jittered (Fig. 3B), with a mean duration (onset-to-offset interval) of 3.5 s (range 2.5–4.5 s). This jittering allowed us to complement our block-related analysis with an examination of the event-related responses (Price et al., 1999). The intertrial interval was 7 s (onset-to-onset interval).

Two additional scanning runs were performed to obtain a left and right hand-localizer sequence (207 s each). During each of these runs, one hand was stimulated by repeatedly rubbing a soft tissue-sponge on KM’s palm at 1 Hz. By using this gentle stimulation delivered exclusively to one hand in each run, we sought to minimize any contamination of the somatosensory responses by palinaesthesia. KM’s report confirmed that this tactile stimulation did not elicit any robust palinaesthesia episodes. Four blocks of hand stimulation were interleaved with four blocks of rest without stimulation (20 s each block). All experimental or localizer runs started only when KM reported a complete disappearance of any persisting sensation that might have been induced during preceding scanning runs.

**MRI data collection**

Scanning was performed on a 1.5 T Intera Philips (Philips, Best, The Netherlands) whole-body MRI system, with standard head coil configuration. Multi-slice T2*-weighted fMRI images were obtained with an EPI GRE sequence [TE (echo time)/flip angle = 40 ms/80°, FOV (field of view) = 250 mm, matrix = 128 \(\times\) 128 \(\times\) 30, voxel size = 1.95 \(\times\) 1.95 \(\times\) 4 mm]. The volume of acquisition covered the whole brain except the lower part of the cerebellum. Repetition times (TR) for the main experimental runs and the hand-localizer runs were 2560 and 3000 ms, respectively. After discarding the four initial scans (to ensure magnetization steady state), each time-series from the experimental and hand-localizer runs comprised 140 and 65 volume images, respectively. A high-resolution structural volume was obtained with a 3D GRE T1-weighted sequence (TR/TE/flip angle = 15 ms/5 ms/30°, FOV = 250 mm, matrix = 256 \(\times\) 256, voxel size = 0.977 \(\times\) 0.977 \(\times\) 1.25 mm) and later co-registered to the functional images.
fMRI data analysis
Statistical Parametric Mapping SPM99 (http://www.fil.ion.ucl.ac.uk/spm/) was used for image processing and statistical analyses. All functional volumes were spatially realigned to the first image of the first experimental session, time-corrected with reference to the middle slice, smoothed with a standard isotropic 8 mm FWHM (full-width half-maximum) Gaussian kernel. Time-series from each voxel were high-pass filtered (1/140 Hz cut-off) to remove low-frequency noise and signal drift. The fMRI series were then submitted to a single-subject fixed-effects analysis using the general linear model applied at each voxel across the whole brain (Friston et al., 1995).

For both the experimental and localizer runs, each condition of interest was modelled by boxcar waveforms convolved with a canonical haemodynamic response function (HRF), and included in a multiple regression analysis. Since our hypothesis was that the persistent tactile sensation would be associated with differential neural activity during rest periods that followed left-hand stimulation, compared with rest periods following right-hand stimulation, different rest blocks were modelled in the multiple regression analysis that corresponded to periods after left-hand and after right-hand stimulation. Thus, the design matrix for the main experimental acquisition included three sessions, with two stimulation conditions (left and right hand) and two rest conditions (post-left and post-right). Note that block duration (28 s) was adjusted based on the average duration of palinaesthesia as elicited by the lever device, such that the post-left ‘rest’ condition could capture any neural activity persisting after left-hand stimulation. Each localizer run was analysed using two regressors of interest (stimulation and rest), similarly for each hand.

Data from the experimental sessions were also analysed using an event-related design to examine any differential activity evoked by the onsets and offsets of tactile stimuli. Importantly, we minimized the correlation between pairs of successive stimulation events by randomly jittering the time interval between onsets and offsets from 2.5 to 4.5 s (see above). In addition, the average intertrial interval (3.5 s) differed from the TR (2.56 s), resulting in a distributed sampling over peristimulus time that ensured maximum efficiency for the detection of small and transient activations (Price et al., 1999). Onset and offset times were modelled separately for each hand as four regressors convolved with a canonical HRF. A complementary event-related analysis was performed using a linear combination of the HRF and its temporal derivative to capture any temporal shifts possibly due to the variability of our experimental events (Henson et al., 2002), but this analysis indicated no significant influence of the temporal derivative in the regression model, suggesting that the HRF timing alone could successfully capture signal changes due to tactile onsets and offsets.

In all analyses, realignment parameters of head motion correction were added as regressors of no interest to capture any residual movement-related artefacts. Parameter estimates for each regressor were calculated at each voxel by a least-squares fit to the data. Statistical parametric maps of the t statistic were generated from linear contrasts between conditions, across all sessions.

Finally, to complement the functional localizer data and anatomical landmarks used to identify somatosensory areas in the patient, we also performed a normalization transformation on the activation coordinates found in KM, allowing a comparison with coordinates in previous neuroimaging studies of healthy people. Independently of the functional analyses, KM’s brain volume was normalized to the Montreal Neurological Institute (MNI) template using a cost-function mask excluding the area of the lesion, so that the lesion did not bias the spatial transformation (Brett et al., 2001), and the MNI coordinates were then converted to Talairach space. Using this transformation matrix, we were able to locate the peak of SI activity in KM’s in normalized Talairach coordinates, and compare with findings in healthy subjects.

Results
In the following single-subject fMRI analyses, we report all regional activations that surpassed a statistical threshold of \( P < 0.001 \) uncorrected, except when corrections by volumes of interest are mentioned (at \( P < 0.05 \) corrected).

Hand-localizer scan
Two localizer scans were performed to identify SI regions in each hemisphere, independently of the experimental sessions, and with minimal (left-hand run) or no (right-hand run) contamination by palinaesthesia.

Right hand areas (healthy side)
Tactile stimulation of the right hand (stimulation > rest) led to increased fMRI response in the left postcentral gyrus (contralateral SI; \( Z = 4.09 \), cluster size = 28), as well as in a symmetrical region of the right hemisphere (ipsilateral SI; \( Z = 3.77 \), cluster size = 9) (Fig. 4A). In addition, ipsilateral SII was activated (\( Z = 3.20 \)) as well as contralateral SII, but at a lower threshold (\( Z = 2.53 \)) (Fig. 4A, lower panel). A region of interest (ROI) centred on the left SI was saved as a mask image (120 voxels at a threshold level of \( P < 0.01 \)) to be used in our analyses of the main experimental runs.

Left hand areas (affected side)
Several regions showed an increased response to stimulation of the left hand, including the right postcentral gyrus (contralateral SI; \( Z = 3.83 \), cluster size = 15) (Fig. 4B), the left orbital gyrus (\( Z = 5.15 \), cluster size = 58) and the right inferior frontal gyrus (\( Z = 3.54 \), cluster size = 15). At a lower threshold, activation in SII regions was also detectable (right SII, \( Z = 3.45 \); left SII, \( Z = 3.07 \)) (Fig. 4B, lower panel). A mask image was again created for the ROI centred on the right SI region (117 voxels at a threshold level of \( P < 0.01 \)).

For either the right- or left-hand stimulation, no significant activation was observed in thalamic nuclei (even at low statistical thresholds).

Brain response to lever stimulation blocks
The aim of the main block-design fMRI experiment was to identify the cerebral correlates of tactile sensation either in the
presence or in the absence of actual stimulation. Four conditions could be compared: right-hand stimulation, left-hand stimulation, rest periods following right-hand stimulation, and, most critically, rest periods following left-hand stimulation (i.e., associated with palinaesthesia).

Right hand > rest (intact side)

Functional maps disclosed several brain regions that were more activated during stimulation of the right hand compared with the immediately following rest periods. These included the left postcentral gyrus (contralateral SI; \(Z = 3.93, P < 0.01\) corrected for the right-hand localizer volume) (Fig. 5A), where activity selectively increased during right tactile stimulation only, as shown by the mean parameter estimates of activation (Fig. 5C) and the peristimulus time course of responses over the entire stimulation period (Fig. 5E). Increased activity also occurred bilaterally in two regions of the upper bank of the lateral sulcus or sylvian fissure (see Fig. 6), including left SII (\(Z = 4.05\)) and right SII (\(Z = 4.38\)), plus a slightly more posterior area (\(Z = 4.36\) right, 4.04 left) that may correspond to the caudal somatosensory region described by Disbrow and colleagues (Disbrow et al., 2000).

In addition, activation during right-hand blocks was also observed in the left lateral occipital complex (LOC) (\(Z = 4.11\)), right inferior frontal gyrus (\(Z = 4.30\)), left cerebellum (\(Z = 4.82\)) and a region of the left precentral gyrus presumably corresponding to the primary motor area M1 (\(Z = 4.41\)). The latter activation could not be associated with overt hand movements, since KM’s hands were tightly attached to the board by a rubber band to prevent any actual hand or finger movements during scanning.

Left hand > rest (affected side)

When contrasting left-hand stimulation versus rest periods that immediately followed left-hand stimulation, no differential activation was detected in the right contralateral SI region, even at low threshold (\(P < 0.01\), uncorrected). By contrast, increased activity was observed bilaterally in SII regions (right, \(Z = 4.36\); left, \(Z = 4.21\)).

The lack of differential response in SI when comparing real left-hand stimulation with immediately following rest could relate to the illusory persistence of tactile sensation that occurred in the latter condition. In fact, during rest periods following left-hand stimuli, activity within the right-hemisphere SI area remained relatively high, as shown in Fig. 5D and F. In a subsequent contrast, we formally tested this hypothesis by comparing the left-hand stimulation blocks to rest periods following right-hand stimulation, which occurred later in time (i.e., at least 40 s after the end of left-hand stimulation blocks) with a reduced or no tactile persistence any more. This new contrast disclosed a significant activation of SI in the right hemisphere (\(Z = 3.53, P < 0.01\) corrected for the left-hand localizer volume) (Fig. 5B). This comparison also revealed additional activations in the right hemisphere, including the inferior frontal gyrus (\(Z = 4.53\)) and SII (\(Z = 4.02\)). In the left hemisphere, activations were found in the LOC (\(Z = 3.92\)), fusiform gyrus (\(Z = 3.86\)) and cuneus (\(Z = 3.44\)).

This pattern of results suggests that neural activity elicited by the stimulation of the left hand persisted in SI and in several other brain regions after termination of the tactile stimulation. In contrast to this persistent activity observed in the right SI and some visual regions, which returned to baseline only after a delay of 40 s or more, activity in SII regions decreased as soon as the left-hand stimulation ceased (Fig. 6B and C).

Post-left rest > post-right rest

To further investigate regional activity associated with the palinaesthetic sensation following left-hand stimulation, we directly compared the post-left with the post-right rest periods (i.e., all without any actual tactile stimulation). As expected from the inspection of the parameter estimates and peristimulus time course of activity extracted from...
right SI (see above) (Fig. 5D and F), this contrast revealed a significant increase in the right SI during the rest blocks after left-hand stimulation ($Z = 3.49, P < 0.01$ corrected for the ROI volume from the left-hand localizer). Increased activity was also found in the left LOC and fusiform region ($Z = 4.10$), left cuneus ($Z = 3.95$), as well as right posterior parietal cortex ($Z = 3.54$) and right medial temporal gyrus ($Z = 3.58$). This differential neural activity during rest blocks that followed left-hand stimulations therefore paralleled the subjective phenomenon of palinaesthesia.

Note that the post-right rest > post-left rest contrast revealed some increases in bilateral precentral gyrus, left middle frontal gyrus and left insula ($P < 0.001$, uncorrected), but did not reveal any increase in fMRI signal in the primary or secondary somatosensory regions.

**Brain response to stimulation onsets and offsets**

Finally, we used an event-related approach to determine whether the somatosensory regions revealed above by our
block-design analysis might show a differential response to the stimulation lever falling down on the palm (stimulation onset) or being pulled back up (stimulation offset). Figure 7 shows the parameter estimates of event-related responses to these contralateral tactile events on each hand, extracted at the voxels corresponding to SI and SII in each hemisphere (peaks of activity identified in the previous epoch-related analysis). Critically, the right SI responded to contralateral onsets but not to contralateral offsets; whereas the left SI responded to both event types on the contralateral hand. In both hemispheres, SII responded to both contralateral onsets and offsets; an apparent slight difference in magnitude between right and left SII response to contralateral stimulus offsets was not significant ($t = 0.4, P = 0.35$).

**Comparison with SI and SII in healthy brain**

Using the normalization matrix (see Methods), the peak of SI activity in KM’s normalized intact (left) hemisphere was located at Talairach coordinates $x, y, z = -49, -26, 44$ [similar to findings in healthy subjects (Burton et al., 1997; Spiegel et al., 1999; Truloisson et al., 2001; Christmann et al., 2002; McGlone et al., 2002); mean (SD) for these studies: $x, y, z = -48.7 (3.1), -21.0 (2.2), 48.10 (4.1)$]; the anterior cluster in the right lateral sulcus corresponded to the normal SII location [$x, y, z = -44, -28, 15$ (similar to Ruben et al., 2001; Christmann et al., 2002; Del Gratta et al., 2002; Disbrow et al., 2000); mean (SD) for these studies: $x, y, z = -46.0 (5.8), -20.2 (2.2), 15.1 (1.7)$]; whereas a more caudal cluster (coordinates $x, y, z = -58, -43, 16$) presumably corresponded to the caudal somatosensory area described by Disbrow and colleagues (Disbrow et al., 2000). This confirms that our stimulation protocol effectively activated SI and SH regions as identified in previous neuroimaging studies.

**Discussion**

We studied a patient, KM, who suffered from a focal right parietal damage and exhibited a rare phenomenon of tactile persistence—palinaesthesia—on her left hand. Detailed clinical testing revealed that KM had mild deficits of superficial touch in the left hand (primarily affecting two-point discrimination or tactile thresholds), with impaired graphesthesia, and astereognosia. KM also showed a striking phenomenon of left tactile extinction that exclusively affected the perception of offsets (but not onsets) of stimuli. The palinaesthesia phenomenon was distressing for the patient, with an illusory persistence of tactile sensations triggered by the manipulation of objects that could often disturb her everyday activities.

Our detailed investigations provided a number of important observations. We were able to demonstrate that palinaesthesia was associated with a concomitant increase in tactile thresholds for the affected left hand, providing an objective measure of transient somatosensory dysfunction during the illusory sensation. Sustained SI activity during palinaesthesia may have interfered with new incoming inputs, and thus increased detection thresholds. More critically, the vividness and reproducibility of palinaesthesia in KM provided a unique opportunity to use fMRI methods to identify neural correlates of the subjective experience of touch in the absence of actual sensory inputs.

**Sustained activity in right SI**

Tactile stimulation on either hand produced a reliable fMRI response in the contralateral postcentral gyrus, during both the hand-localizer and the main experimental scans, consistent with the hand representation in SI found for healthy volunteers (e.g. Rumeau et al., 1994; McGlone et al., 2002). These data demonstrate a relative preservation of the right SI despite substantial cortical atrophy in the vicinity of this region, and are consistent with KM’s ability to detect tactile stimuli on the affected hand.

Although responsive to stimulation of the left hand, right SI activity showed an abnormal time course. Unlike the left intact SI, whose activity decreased as soon as the contralateral stimulation ceased, as expected, activity in right SI persisted during the ‘rest’ periods that followed contralateral tactile stimulation. Thus, SI activity actually decreased only during the later rest periods (e.g. ‘true rest’ after right-hand stimulation) (Fig. 5D and F). Furthermore, activity in the right SI was also significantly increased when we directly compared rest periods following left-hand stimuli with rest periods following right-hand stimuli (even though no physical stimuli were delivered during either rest period). Not only does this pattern directly demonstrate that our fMRI approach was successful in revealing selective foci of neural activity associated with palinaesthesia periods, but it suggests that KM’s palinaesthesia might correlate with abnormal persistence of activity in SI, triggered by preceding stimulation, and therefore indicate a dysfunction at the earliest cortical stage of somatosensory processing.
This increased activity in SI during vivid tactile illusion of touch, outlasting the presence of a real physical stimulus, converges with the recent work carried out on monkeys by Romo and colleagues (Romo et al., 1998; for review see Romo and Salinas, 2003). These authors demonstrated that intracortical microstimulation applied to SI neurons could induce an artificial sensation of flutter stimuli that the monkeys could not distinguish from a natural tactile stimulation. Taken together, these electrophysiological findings and the present neuroimaging results in our patient provide direct evidence that neural activity in the SI cortex alone may trigger a subjective perceptual tactile experience for certain types of stimuli.

**Preserved responses in bilateral SII regions**

In addition to SI, SII regions showed increased activation during blocks of real tactile stimulations. However, unlike right SI, bilateral SII regions were always more active during real stimulation than during subsequent rest, including in the damaged hemisphere (Fig. 6), reflecting actual stimulus input rather than subjective sensation.

Bilateral SII response to unilateral tactile stimulation is consistent with previous imaging data in healthy volunteers (Hari and Forss, 1999; Ruben et al., 2001; Del Gratta et al., 2002; Deuchert et al., 2002; Simoes et al., 2003). Physiological results in monkeys have also shown a high percentage of neurons with bilateral receptive fields in SII (Robinson and Burton, 1980; Burton and Carlson, 1986) and strong callosal connections between SII in each hemisphere (Krubitzer et al., 1998). In addition, stimulation of the contralateral hand in hemispherectomized patients may produce activation of the ipsilateral SII but not the ipsilateral SI (Bittar et al., 2000), suggesting ipsilateral projections to SII. Our fMRI findings of distinct patterns of activity in SI and SII therefore provide new evidence that activity in the primary and second somatosensory cortices in humans may be dissociated. These data are consistent with proposals that somatosensory processing does not follow a strict serial pathway from SI to SII (Hari and Forss, 1999; Iwamura, 1998).

Importantly, our findings in KM suggest that activity in SI alone can be sufficient to elicit a vivid tactile illusion of touch, while activity in SII remains apparently unaffected. In addition, since SII is thought to be involved in complex processing of shape and texture information (Jiang et al., 1997; Bohlhalter et al., 2002), a pathological persistence of activity in SII but not SII during palinaesthesia seems consistent with the subjective sensation of the presence of an object in the affected hand as described by KM, without a more detailed sensation of its particular shape or surface.

Moreover, KM showed marked difficulties in fine tactile perception, such as two-point discrimination and haptic object recognition, supporting the view that some deficits in the recognition of objects by touch can result from damage to SI, despite relatively intact SII, presumably due to impaired extraction of surface properties of tactile objects (Roland et al., 1998; Moore et al., 2000). Lesions in SII and the posterior parietal cortex may cause more severe deficits due to additional impairments in processing the geometrical or spatial structure of objects (Valenza et al., 2001; Bohlhalter et al., 2002). Thus, our study also provides the first functional imaging investigation of a tactile deficit predominantly associated with SI dysfunction.

However, although SII was anatomically preserved and showed a relatively normal pattern of responses, in contrast to clear abnormalities in SI, we cannot entirely exclude any abnormality in SII function. Left SII activity appeared somewhat weaker than right SII during the hand localizer scan, while right SII responses to left stimulus offsets were somewhat smaller than left SII responses, but importantly these differences were not statistically significant, and clearly unlike the striking SI abnormalities. Furthermore, only SI showed the critical pattern of sustained activity during post-stimulation periods, in parallel to the palinaesthesia phenomenon.

**Brain responses to stimulation onsets and offsets**

Using an event-related analysis, we could further examine the transient neural responses evoked in somatosensory regions by both onsets and offsets of the lever stimulation. We found that the right SI reliably responded to contralateral stimulation onsets (lever falling down on the palm) but not to offsets (release of the pressure exerted by the lever). By contrast, SI in the intact left hemisphere and bilateral SII responded to all contralateral onset or offset events. This lack of activation of the right SI to stimulus offsets may parallel KM’s inability to detect the withdrawal of left-side stimulations during the clinical extinction tests, and provides another objective substrate for her subjective experience of persistent sensations after touching an object. However, this does not necessarily imply that she could not detect the offset of the unilateral tactile stimulations during scanning (despite illusory persistence). It is unclear why clinical testing showed impaired detection of left-sided offsets only during bilateral simultaneous stimulation, while right SI activity showed lack of neural responses even to the unilateral left offsets, but we speculate that, in the absence of a second simultaneous concomitant stimulus, residual activation outside SI (e.g. SII) might be sufficient for the patient to report unilateral left offset events (Valenza et al., 2004). In addition, a striking finding was that, unlike SI, SII in the damaged right hemisphere could still respond to tactile offsets on the left hand, although these were presumably not perceived and failed to influence SI activity. This suggests that any signal indicating the interruption of current sensory inputs may normally need to reach SI to afford awareness of the stimulus change, but here did not do so despite activating SII.

These data provide novel support for proposals that SI activity might be critically involved in tactile awareness (Meador et al., 2002; Valenza et al., 2004). Increased activity in SI may also correlate with phantom sensations after...
limb amputation in humans (Lotze et al., 2001; Roux et al., 2001), and with the perceived rather than physical characteristics of tactile stimuli in optical imaging studies in non-human primates (Chen et al., 2003). Such a role of SI in conscious tactile experience thus appears to parallel similar proposals suggesting a crucial role of V1 in conscious visual experience (Polonsky et al., 2000; Pins and Ffytche, 2003; Tong, 2003).

**Distributed networks involved in conscious tactile perception**

We note that other brain areas besides the primary somatosensory cortex also showed persistent activity associated with palinaesthesia (i.e. after left-hand stimulation), including the fusiform and LOC. The latter visual area was also activated by real tactile stimulations on the right and left hands. This may accord with recent findings (Amedi et al., 2001; Amedi et al., 2002) that in healthy volunteers visual areas in LOC can be activated by both visual and haptic presentations of objects. Such activation may reflect a multimodal perceptual network, providing stored visual information about objects that can be accessed via both vision and touch. We would like to suggest that persisting activity in the LOC during palinaesthesia might similarly reflect an object-related response elicited by the abnormal activation of SI during or after tactile stimulation of the affected hand, underlying KM’s vivid feeling of holding an ‘object’ in the hand. These visual activations might in turn provide new evidence that the LOC is implicated in object representation even during tactile perception.

While our data provide compelling evidence for specific neural substrates of palinaesthesia, we can only speculate about the exact neurophysiological mechanisms implicated in sustained SI activity. Increased fMRI response may reflect an increase in the number of neurons firing, in the rate of firing, or in local synchrony of firing (Rees et al., 2000; Fries et al., 2001; Logothetis et al., 2001). In addition, SI is not a unitary area but includes several subdivisions with distinct functional roles (Moore et al., 2000; Young et al., 2003), beyond the anatomical resolution of fMRI. Whereas neurons in areas 3a and 2 receive information from deep body tissues, neurons in areas 3b and 1 respond to stimulation of cutaneous receptors (Pons et al., 1992; Iwamura et al., 1993; Burton et al., 1997). Moreover, distinct cortical domains within area 1 respond to pressure, flutter and vibratory stimuli applied to the same location (Friedman et al., 2004). In our experiment, stimulation onsets probably activated both cutaneous and deep receptors sensitive to fast transients (due to the strong impact of the stimulation lever), whereas offsets probably produced a weaker activation (lever up-lifted with a slower acceleration) that might activate a different neuronal population with different sensitivities (for comparable differences see also Burton et al., 1997). Although we did not specifically design our experiment to distinguish between the different functional subdivisions of SI, we would like to suggest that palinaesthesia might have resulted from a functional disconnection between different subregions of SI, or between SI and other related regions (e.g. in higher-level parietal or subcortical regions). Impaired processing of offsets (as shown by our event-related analysis) might result from a relative dysfunction in SI subregions such as 3b or 1 (which were anatomically most severely damaged), together with preserved processing of inputs in other subregions, which could underline preserved responses to onsets and persistent activity associated with palinaesthesia after the cessation of tactile stimulation.

Some damage to white-matter fibres adjacent to SI could also have contributed to prevent reset or inhibition signals received from other regions, thus disrupting reciprocal influences between SI and SII (Burton et al., 1995; Cauller et al., 1998) or between SI and distant brain regions (Schnitzler et al., 1995; Korvenoja et al., 1999). It is possible that such release from control influences led to increased activity in the disconnected or deafferented SI modules (McCormick et al., 2003). Furthermore, a recent study using TMS in humans showed that neural activity in SI may not only reflect on-line processing of tactile stimuli, but also underlie the maintenance of sensory traces during tactile working memory (Harris et al., 2002; see also Romo and Salinas, 2003). SI activity may thus directly contribute to the continuity and stability of tactile signals that seem to be required for conscious sensory experience. An alternative explanation for palinaesthesia might therefore involve some abnormal maintenance of tactile memory traces following recent stimulation, rather than a primary perceptual experience or a direct consequence of a perceptual deficit in detecting tactile offsets. It is worth noting that mechanisms similar to those described above, such as an abnormal activation of memory traces, have been proposed in the visual modality to account for palinopsia (Bender et al., 1968; Cummings et al., 1982; Vaphiades et al., 1996; see also Super et al., 2001), but neurophysiological data have only rarely been provided for such visual phenomena (Ffytche et al., 1998).

**Conclusions**

This case study enabled us to determine the behavioural and neural correlates of a rare tactile illusory sensation (palinaesthesia) following right parietal damage. This phenomenon was reliably triggered by left-hand stimulation, and provided the opportunity to experimentally dissociate the neural response to actual physical stimulation from the subjective tactile experience. Our fMRI data revealed sustained activity in SI contralateral to the affected hand, even in the absence of tactile inputs, with a lack of response to stimulation offsets, but no such marked functional abnormalities in the SII response to mechanical stimulation by the lever-like device. Palinaesthesia was also associated with sustained activity in left visual areas including the LOC, suggesting that concomitant activation in associative visual cortices may contribute to the vivid illusory sensation of holding an object in the affected hand. These data provide new insights into the
distinct roles of the SI and SII in conscious tactile experience, and perhaps tactile memory. Although rare, palinaesthesia needs to be recognized as it may be disabling in everyday life. Furthermore, a better understanding of neural mechanisms involved in abnormal somatosensory processing and awareness may have important implications for other frequent clinical disorders when such abnormalities are associated with pain or phantom sensation disorders.

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References
Garraghty PE, Pons TP, Kaas JH. Ablations of areas 3b (SI proper) and 3a of somatosensory cortex in marmosets deactivate the second and parietal ventral somatosensory areas. Somatosen Mot Res 1990; 7: 125–55.


Moores DJ, Stimpson R, Friston KJ, Crolley G, Friston KJ. The critical relationship between the timing of stimulus presentation and data acquisition in blocked designs with fMRI. Neuroimage 1999; 10: 36–44.


