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Seeing or not seeing where your hands are

Received: 29 December 1998 / Accepted: 24 September 1999 / Published online: 8 March 2000
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Abstract Previous findings have demonstrated the existence of a visual peripersonal space centered on the *hand* in humans and its modulatory effects on tactile perception. A strong modulatory effect of vision on touch perception was found when a visual stimulus was presented near the hand. In contrast, when the visual stimulus was presented far from the hand, only a weak modulatory effect was found. The aim of the present study was to verify whether such cross-modal links between touch and vision in the peripersonal space centered on the hand could be mediated by proprioceptive signals specifying the current hand positions or if they directly reflect an interaction between two sensory modalities, i.e., vision and touch. To this aim, cross-modal effects were studied in two different experiments: one in which patients could see their hands and one in which vision of their hands was prevented. The results showed strong modulatory effects of vision on touch perception when the visual stimulus was presented near the seen hand and only mild effects when the vision of the hand was prevented. These findings are explained by referring to the activity of bimodal neurons in premotor and parietal cortex of macaque, which have tactile receptive fields on the hand, and corresponding visual receptive fields in the space immediately adjacent to the tactile fields. One important feature of these bimodal neurons is that their responsiveness to visual stimuli delivered near the body part is reduced or even extinguished when the view of the body part is prevented. This implies that, at least for the hand, the vision of the hand is crucial for determining the spatial mapping between vision and touch that takes place in the peripersonal space. In contrast, the proprioceptive

signals specifying the current hand position in space do not seem to be relevant in determining the cross-modal interaction between vision and touch.

Key words Peripersonal space · Tactile extinction · Cross-modal interaction · Spatial coding · Proprioceptive information

Introduction

Some brain-damaged patients do not have a deficit in processing an isolated stimulus on the affected side. Their deficit only emerges when stimuli are presented on both sides simultaneously; in this case, the previously detectable contralesional stimulus is now extinguished by the competing ipsilesional stimulus. This phenomenon has been called “extinction”.

An accredited interpretation of extinction views the deficit as a result of an unbalanced competition between simultaneous targets for access to limited attentional resources (Ward et al. 1994; Desimone and Duncan 1995; di Pellegrino et al. 1997a). Due to the lesion, stimuli presented on the contralesional side have lower competitive weights relative to stimuli presented in the ipsilesional side. As a result of this uneven competition, contralesional stimuli weakly activate the contralesional space and, therefore, they are extinguished due to the competition with the stimuli presented in the intact ipsilesional space.

It has been shown that extinction may occur within different sensory modalities (unimodal extinction): visual (Làdavas 1990; Ward et al. 1994; di Pellegrino and De Renzi 1995), auditory (De Renzi et al. 1984), and tactile (Bender 1952; Gainotti et al. 1989; Moscovitch and Behrmann 1994; Vallar et al. 1994). More recently, however, it has been shown that the competition between concurrent targets for attention operates also across spatial representations based on different sensory modalities (Mattingley et al. 1997; di Pellegrino et al. 1997b; Làdavas et al. 1998a, 1998b).

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More specifically, Làdavas and colleagues (di Pellegrino et al. 1997b; Làdavas et al. 1998a, 1998b) showed that the competition between left and right space representations in one modality, which is the distinctive feature of extinction patients, can be modulated (i.e., reduced or exacerbated) by the activation of an intact spatial representation in a different modality. In patients with a right-hemisphere lesion and reliable tactile extinction, a visual stimulus presented near the *ipsilesional* hand (or face) inhibited or interfered with the processing of a tactile stimulus delivered on the *contralesional* hand (or face) (cross visual-tactile extinction) to the same extent as did an ipsilesional tactile stimulation (unimodal extinction). Furthermore, a visual stimulus presented in the proximity of the *contralesional* hand (or face) improved the detection of a left tactile stimulus: i.e., under bilateral tactile stimulation, patients were more accurate in reporting the presence of a left tactile stimulus when a simultaneous visual stimulus was presented near the left hand (Làdavas et al. 1998a) or the left side of the face (Làdavas et al. 1998b). In contrast, weak modulatory effects of vision on touch perception were observed when a visual stimulus was presented far from the patient's hand (or face). Likewise, left tactile detection on tactile bilateral stimulation did not improve when visual stimuli were presented distant from the contralesional affected hand (or face).

These results show that visual and tactile spatial representations are coded by an integrated (visuo-tactile) system responsible for processing tactile stimuli and visual stimuli presented near the body, i.e., in the peripersonal space. When competition is biased in favor of the right tactile space representation, as the case in a patient with left tactile extinction, the activation of a left peripersonal space by a visual stimulus improves left tactile stimulus detection (cross-modal visual-tactile facilitation). In contrast, the activation of a right peripersonal space by a visual stimulus produces a deficit in the detection of a single left tactile stimulus (cross-modal visual-tactile extinction).

Neurophysiological studies on monkeys help to understand the nature of the mechanism underlying the cross-modal effects found in the previous studies and to clarify how such a mechanism operates to coordinate visual and tactile representations of space. Single-cell recording studies in monkeys have shown that parietal areas 7b and VIP, premotor area 6, and the putamen, a large subcortical nucleus forming part of the basal ganglia, appear to represent visual space near the body (Rizzolatti et al. 1981; Duhamel et al. 1991; Graziano and Gross 1993, 1995). These areas have tactile neurons that also respond to visual stimuli: their bimodal cells have visual receptive fields that match in space the location of the tactile receptive fields and are confined in depth to a region near the animal. Because the tactile fields are arranged somatotopically, the associated visual receptive fields form a map of the visual space immediately around the body, which moves when the body parts move; thus, peripersonal space is coded in body-part

centered coordinates and not in retinal or other egocentric reference systems.

These areas provide an integrated (visuo-tactile) system for coding peripersonal space, and, as a consequence of this sensory integration, the activation of these bimodal neurons by a visual stimulus presented near the hand (or face) also activates the corresponding somesthetic representation of the hand (or face). The simultaneous activation of the somatosensory representation of the left hand (or face) by a tactile stimulus and of the right hand (or face) by a peripersonal visual stimulus produces an extinction of those stimuli presented in the weaker representation, i.e., the left hand (or left side of the face). Likewise, the stimulation of the visual space near the left hand (or face) results in the enhancement of the damaged (and hence weak) somatosensory representation of the left hand (or face). This stimulation is, thus, able to correct the abnormal bias towards the ipsilesional hand (or face) representation, and, as a consequence, left tactile extinction improves substantially.

Single-neurons studies have also shown that visuo-tactile bimodal cells are less active when visual stimuli are administered far from the hand, i.e., in the extrapersonal space (Gentilucci et al. 1988; Graziano and Gross 1995; Fogassi et al. 1996a). This neurophysiological evidence is consistent with the impressive reduction of cross-modal extinction, and the absence of visuo-tactile facilitation, found when the visual stimulus was presented far from the hand, at the level of patient's eyes or far from the face (Làdavas et al. 1998a, 1998b).

One important feature of some bimodal neurons is that their responsiveness to visual stimuli delivered near the body part is reduced or even extinguished when the view of this body part is prevented (Graziano et al. 1994; MacKay and Crammond 1987). This is particularly evident for bimodal neurons with tactile receptive fields located on the hand (MacKay and Crammond 1987); their best visual response is evoked when the hand is under visual control. This implies that, at least for the hand, the proprioceptive signals specifying the current hand position in space are irrelevant in determining the spatial mapping between vision and touch.

In contrast, some other bimodal neurons still show a visual response even though the vision of the body part is prevented. This is particularly evident for bimodal neurons with tactile and visual receptive fields located on the face or the shoulder, that is, on body segments whose direct vision is normally precluded. For these neurons, the preferred visual response is evoked when the visual stimulus has a particular direction and their responsiveness does not change as a function of the direct view of the body part. For instance, in VIP, the majority of neurons show selective direction activity: their visual responses are a function of the projected point of impact of the stimulus on the body (Duhamel et al. 1998). For these neurons, the spatial location of the tactile receptive field is probably mediated by proprioceptive information.

In light of these neurophysiological findings, it is important to assess whether the cross-modal effect found

by Lådavas and colleagues (Lådavas et al. 1998a) between tactile and visual peripersonal space centered on the hand is mainly mediated by the vision of the hand or by the proprioceptive information related to the hand position in space. To this aim, cross-modal visual-tactile effects were studied in two different experiments: one in which the vision of the hand was allowed, and one in which it was prevented. Since bimodal neurons centered on the hand vary their responsiveness primarily with direct vision of the hand, with their activation being higher when the vision of the hand is allowed, strong cross-modal effects are expected when the visual stimulus is presented near the seen hand. In addition, only a mild cross-modal effect should be found when the visual stimulus is presented near the unseen hand. In contrast, if the cross-modal effect is primarily mediated by the proprioceptive information related to the hand position in space, then no difference between the two experiments is expected.

Materials and methods

Subjects

We identified ten patients with contralesional tactile extinction without confounding variables of primary sensory dysfunction, visual and tactile neglect, anosognosia, or other mental defects. They were fully alert, lucid and co-operative. All of them had suffered a right-hemisphere stroke, as determined by cranial CT scan. Characteristics of patients are outlined in Table 1. Some of the patients (see Table 1) also participated in a previous study by Lådavas et al. (1998a). For the present study, they were tested again in all conditions 1 or 2 months later. All patients were tested after giving informed consent.

Primary tactile and proprioceptive sensations were intact. The absence of visual neglect was assessed by using three cancellation tests (Albert's lines, bell cancellation, and letter cancellation tests) and several conventional tasks (i.e., text and word reading, line bisection, copying of complex figures, drawing by memory). Visual extinction was assessed by using the conventional "confrontation" test. A finger wiggle was applied above the dorsal surface of one or the other of the patient's hand, or on both sides simultaneously. Patients had to report how many stimuli had been detected (one, two, or none). Three out of ten patients showed a mild left visual extinction on double simultaneous stimulation (less than 20%), but they performed well on single-stimulus presentation.

Tactile extinction was assessed by applying a light touch to the dorsum of the right or the left of the patient's hand, or to both hands simultaneously with the patient's eyes closed. Patients had to report how many stimuli had been presented (one, two, or none) and the side on which they had been applied. All patients showed tactile extinction, but they performed well on single-stimulus presentation.

Procedure

Patients, tested individually, sat at a table in front of the experimenter at an approximate distance of 60 cm. Their hand, palm-down and fingers spread apart, rested on the table surface at a separation distance of 40 cm, with each hand located in its own hemispace. Patients angled their head and eyes slightly downward to fixate a dot marked on the table surface at a distance of 25 cm from the front edge of the table and aligned with the subject's midsagittal axis. Depending on experimental condition, patients' hands were either in view or their vision was prevented by a card-

Table 1 Clinical data on right brain-damaged patients. *F* Frontal lobe, *P* parietal lobe, *T* temporal lobe, *I* insula, *C* caudate nucleus, *Pu* putamen, *Ic* internal capsule

Patient	Sex	Age	Years of schooling	Months post-stroke	Lesion site
M.L. ^a	F	47	5	3	P, T, I
A.F. ^a	F	71	12	9	F, P, T
G.C. ^a	M	66	5	5	P, T
B.C. ^a	F	69	5	5	P, T, C, Ic
P.T. ^a	M	65	10	3	T, Ic
A.M. ^a	M	62	18	2	C, Pu
M.P.	M	42	13	6	P, T, Ic
A.D.	F	57	8	4	F, P, T
M.M. ^a	M	72	19	38	C, Pu
A.V. ^a	M	71	5	2	F

^a These patients also participated in Lådavas et al.'s (1998a) study. For the present study, they were retested in all conditions 1 or 2 months later

board shield (21 cm wide × 28 cm deep × 10 cm tall). The cardboard shields were open at the distal ends to deliver unseen tactile stimuli. Before and during each trial, the experimenter ensured that the patient was gazing at the fixation dot.

Tactile stimuli consisted of a brief flexion-extension of the examiner's index finger, touching lightly the dorsal surface of finger III of the patient's hand. Visual stimuli consisted of a single brief flexion of the experimenter's index finger, and they were delivered just above the dorsum of the patients' finger III, except for condition 4. In this condition, visual and tactile stimuli were presented in homologous locations on the two sides, with the patient's ipsilesional hand being placed behind her/his back.

There were four types of trials within each experimental condition: a single left stimulus only, a right stimulus only, bilateral stimuli (double simultaneous stimulation), or no stimulation at all ("catch trials"). Catch trials were included to assess the extent to which patients guessed on trials in which no stimulus was given. In each experimental condition, there were ten trials for each type of stimulation. Trials were given in a different pseudo-random order within each experimental condition, which was carried out twice. The order of conditions varied pseudo-randomly across subjects and sessions.

Two experiments were run: one in which patients' could see their hands (experiment 1; see also Lådavas et al. 1998a) and one in which the hands were not within the patients' view (experiment 2). The order of the experiments was counterbalanced across subjects, such that half of the patients started with experiment 1 and the other half with experiment 2. In each experiment, patients were tested in four different conditions, which were given in separate blocks. Thus, in all conditions of experiment 2, tactile stimuli were delivered just inside the distal end of the shield, out of the patient's view. In experiment 2, visual stimuli were identical to those used in experiment 1, except that were presented just above the shield, which covered the patient's hands.

Condition 1 (tactile stimulation)

This condition was identical in both experiments 1 and 2 (see Fig. 1) and was aimed at assessing the presence of unimodal tactile extinction. To test for the presence of pure tactile extinction, patients are usually blindfolded or their eyes are closed, so that the vision of the tactile stimuli delivered by the experimenter is impeded. In the present study, patients were tested with their eyes open and their hands occluded from vision with the screen. This was done in order to make unimodal and cross-modal visuo-tactile conditions more comparable. To this aim, tactile stimuli were applied to patient's hands, which were each placed beneath a cardboard shield that prevented direct view of the patient's hand. In

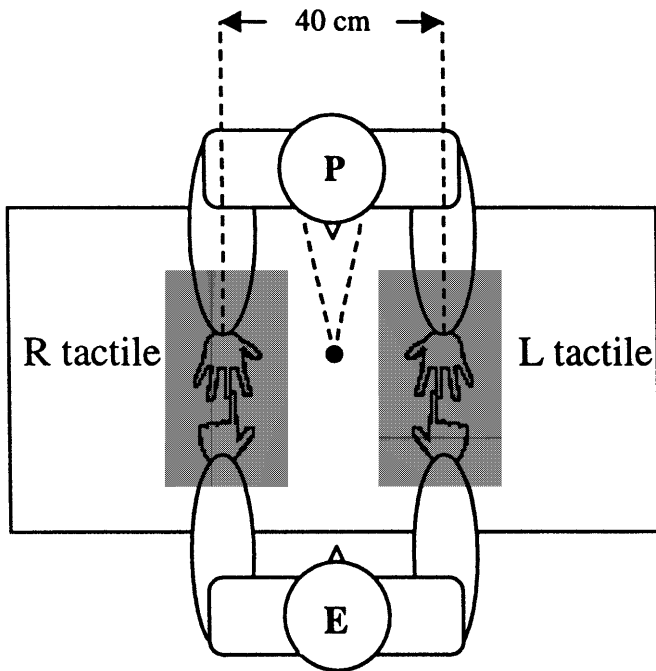
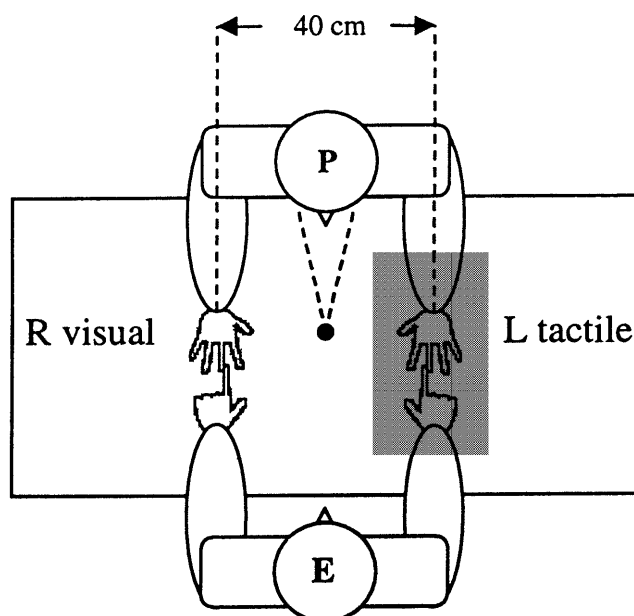


Fig. 1 Condition 1: schematic drawing of the experimental set-up. The patient (*P*) was seated at a table in front of the experimenter (*E*). The patient's hands rested on the table surface and were occluded from vision using cardboard shields (grey rectangles). The filled circle on the table indicates the point of fixation. The figure also reports the type of stimulation (e.g., tactile) that was presented to the right (*R*) or to the left (*L*) hand of the patient

this condition, patients were told that they would feel a light touch on one or the other hand, or on both hands simultaneously, and that occasionally they would feel nothing at all. Patients were instructed to respond verbally to what they had *felt* with the words "left", "right", "both" or "none". The verbal response was always accompanied by a head movement towards the left or right or both. This was done to check for a possible confusion in using spatial terms.



Condition 2 (right visual peripersonal space and left tactile stimulation)

This condition was aimed at assessing the presence of cross-modal visuo-tactile extinction between right visual peripersonal stimuli and left tactile stimuli. In experiment 1, the right hand was in the patient's view, whereas the left hand was screened with the shield. A tactile stimulus was given to the left hand and a visual stimulus near the right hand. In experiment 2, both hands were screened by the shield. The visual stimulus was presented near the unseen right hand, just above the surface of the cardboard shield (see Fig. 2).

Patients were told that they would *feel* a light touch on their left hand only, or that they would *see* a finger movement near the right hand only, or they would *feel* a touch on the left hand and *see* a finger movement near the right hand simultaneously. Patients were told that occasionally they would neither feel nor see anything.

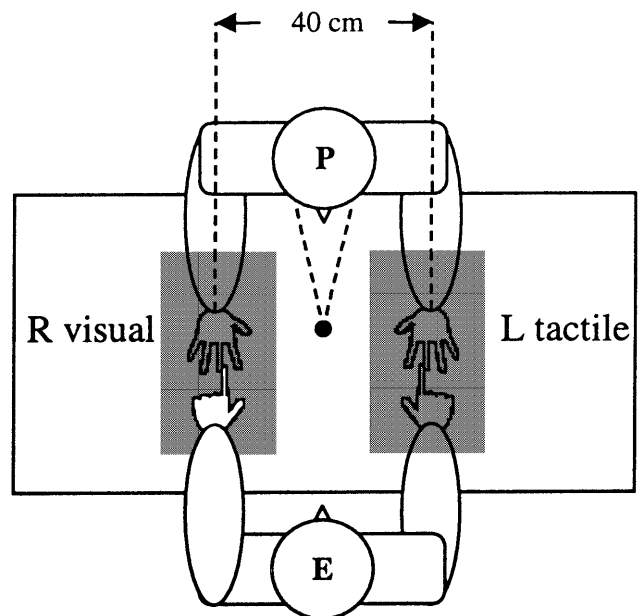
Condition 3 (right visual extrapersonal space and left tactile stimulation)

This condition was performed in order to test the presence of visuo-tactile extinction between right visual extrapersonal stimuli and left tactile stimuli located in homologous locations. In both experiment 1 and 2, the right hand was placed behind the patient's back, whereas the left hand was occluded from the view with the shield. The tactile stimulus was given to the left hand, whereas the visual stimulus was presented in a homologous location on the right side of the table surface (experiment 1) or just above the top edge of the shield (experiment 2) (see Fig.3).

In this condition, patients were told that they would *feel* a light touch on their left hand only, or they would *see* a finger movement on the right side only, or they would *feel* a touch on the left hand and *see* a finger movement on the right side simultaneously. As in the previous condition, they were informed that occasionally they would neither feel nor see anything.

In conditions 2 and 3, patients were asked to respond verbally to what they had *felt* or *seen*, with the words "left", "right", "both" or "none". As in condition 1, verbal response was always accompanied by a head movement towards left or right or both.

Fig. 2 Condition 2: schematic drawing of the experimental set-up of experiment 1 (*left*) and experiment 2 (*right*). Abbreviations as in Fig. 1



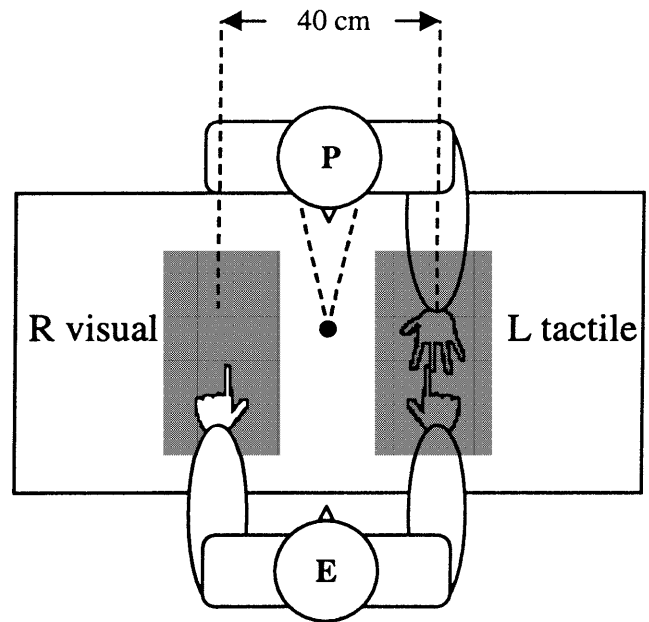
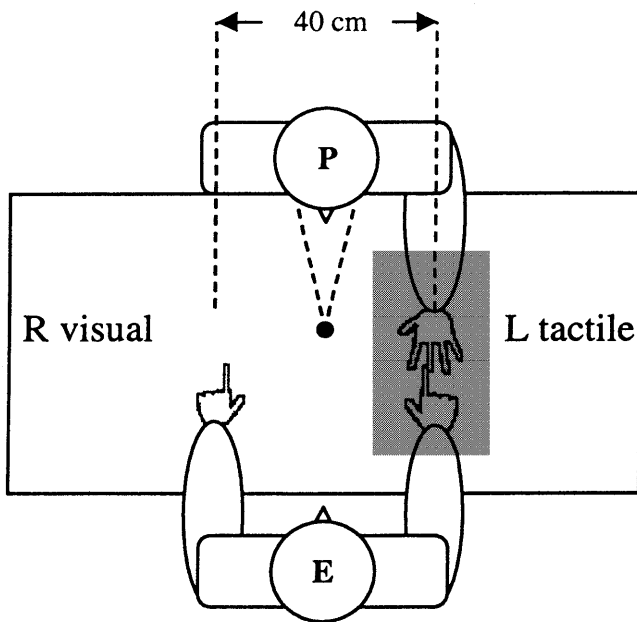


Fig. 3 Condition 3: schematic drawing of the experimental set-up of experiment 1 (*left*) and experiment 2 (*right*). In this condition, the right patient's hand was placed behind his back. Abbreviations as in Fig. 1

Condition 4 (left visual peripersonal space and bilateral tactile stimulation)

This condition was performed in order to test whether presenting a left visual stimulus near the left hand enhance the detection of tactile stimulus on the left (affected) hand. In experiment 1 the left hand was in the patient's view, whereas the right hand was screened with the shield. In experiment 2, the vision of both hands was prevented. A tactile stimulus was given to the left (or right) hand or to both hands simultaneously. The visual stimulus was

given only near the left hand. In experiment 2, the visual stimulus was delivered by a second experimenter just above the top edge of the shield (see Fig. 4).

Patients were told that: (1) they would feel a touch on the right (or left) hand, (2) they would see a finger movement near the left hand touching the left hand *and* feel a touch on the right hand, (3) they would see a finger movement near the left hand *and* feel a touch on the right hand, or (4) they would see a finger movement near the left hand. The last two types of trials (3 and 4) were in-

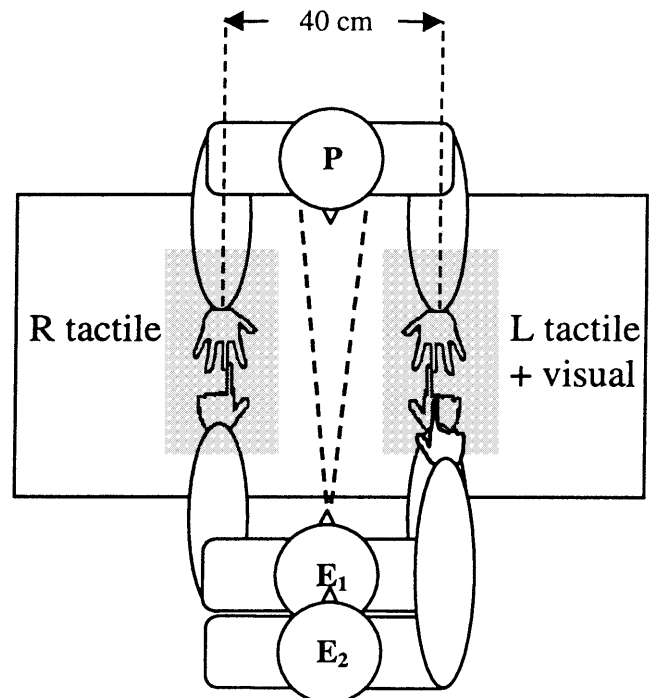
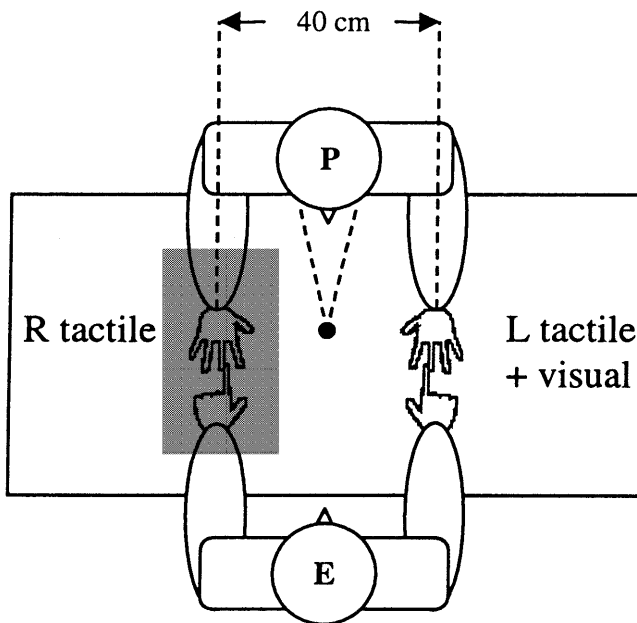


Fig. 4 Condition 4: schematic drawing of the experimental set-up of experiment 1 (*left*) and experiment 2 (*right*). Bilateral tactile stimulation was delivered by one experimenter (E_1) and simultaneous visual stimulation by a second experimenter (E_2). Other abbreviations as in Fig. 1

cluded to control for the possibility that patients erroneously reported the presence of a left visual stimulus instead of a tactile stimulus. This was necessary because, in condition 4, patients were asked to respond verbally only to what they had *felt*.

Each trial comprised the following steps: first the experimenter ensured that the patient was fixating the central dot. Next, he started the trial by saying “ready” and then delivered the stimulus or stimuli that were appropriate for the condition being tested. In condition 4 of experiment 2 the presentation of visuo-tactile stimuli was preceded by a third examiner saying “ready: one, two, three, four”, following a 4/4 tempo. In order to keep the timing of visual and tactile stimuli synchronous, both examiners delivered the stimuli on “four”, observing the rhythmic beats. Following stimulation, patients either responded spontaneously with an appropriate verbal label or, if they failed to respond, they were encouraged by the experimenter to make one of the four possible responses (i.e. left, right, both, or none). No feedback was given on accuracy.

Results

In both unimodal and cross-modal conditions, all patients performed at or near ceiling on trials consisting of unilateral left or right stimulus presentation. This result shows that tactile sensation was sufficient for a correct single-stimulus detection and that patients rarely made spurious “both” responses. Patients almost never produced false alarms in the no-stimulation trials (less than 3%). The data on these catch trials, which were included to prevent guessing in the absence of detection, indicates that they used the “none” response correctly. Moreover, they did not erroneously report the presence of the visual stimulus when they were instructed to report only the tactile stimulus (see condition 4 of both experiments).

Cross-modal extinction was evaluated by comparing the percentage of correct responses to single left tactile stimulation (condition 1) to those made in bilateral stimulation, i.e., right visual stimulus and left tactile stimulus (conditions 2 and 3). A reduction of contralesional detection in bilateral stimulations compared with unilateral stimulation indicates cross-modal extinction. Moreover, in order to test the hypothesis that the cross-modal inhibition effect is reduced when the view of the hand is prevented, the percentages of correct responses in the two experiments were compared. The percentage of left correct tactile detection made by the patients are shown in Fig. 5.

A repeated-measure Anova with experiment (experiment 1 and 2) and condition (unilateral, bilateral tactile stimulation, visuo-tactile stimulation in peripersonal space, and visuo-tactile stimulation in extrapersonal space) as within-subjects factors revealed a significant main effect of condition [$F(3,27)=17.52$, $P<0.0001$]. Post-hoc analysis showed that patients were significantly more accurate in detecting a left tactile stimulus on unilateral than on bilateral tactile presentation [92% (SD=8) and 47.5% (SD=32) of accuracy, respectively, $P<0.0001$]. Likewise, subjects performed better on single tactile stimulation (92%) than when a right visual stimulus was simultaneously presented near the right hand [46.4% (SD=23), $P<0.0001$] or far from the hand

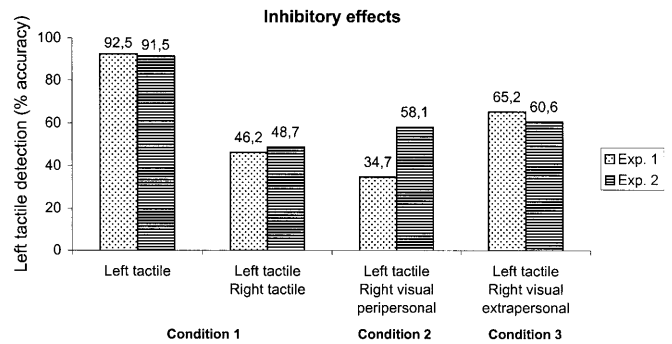


Fig. 5 Inhibitory effects. The graph shows mean percentage of correct detection of the left tactile stimulus in experiment 1 and experiment 2 as a function of type of stimulation. *R* right hand, *L* left hand

in a homologous position as the left tactile stimulus [62.9% (SD=24), $P<0.0005$].

Moreover, the interaction experiment \times condition was also significant [$F(3,27)=5.41$, $P<0.005$], showing that cross-modal inhibitory effect was mainly present in experiment 1 and not in experiment 2. The cross-modal effect found in experiment 1 when the visual stimulus was presented near the right hand [34.7% (SD=23)] was significantly different from the effect found when the visual stimulus was presented far from the hand in a position homologous to the tactile stimulus [65.2% (SD=18) $P<0.0002$]. Furthermore, both cross-modal effects were significantly different from the effect observed in the unimodal tactile extinction [46.2% (SD=33); $P<0.04$ and $P<0.01$, respectively].

In contrast, in experiment 2, the cross-modal effect found when the visual stimulus was presented near the right hand [58.1% (SD=24)] was not significantly different from the effect found when the visual stimulus was presented far from the hand in a position homologous to the tactile stimulus [60.6% (SD=28)]. Both cross-modal effects were not significantly different from the effect observed in the unimodal tactile extinction.

Moreover, and more relevant to the aim of the present study, when the percentages of correct responses for each experimental condition in the two experiments were compared, it was found that the only significant difference was that related to the condition in which the visual stimulus was presented near the hand, with the cross-modal inhibition being stronger under vision (experiment 1 =34.7% of correct responses) than in the no-vision condition (experiment 2 =58.1% of correct responses) ($P<0.001$). No other comparison between the two experiments for each experimental condition was significant.

Cross-modal facilitation was evaluated by comparing the percentage of correct responses to bilateral tactile stimulation (condition 1) with those made under bilateral visuo-tactile stimulation, i.e., bilateral tactile stimulation and left visual stimulation (condition 4). An increase in contralesional detection under bilateral stimulation in this latter condition indicates cross-modal facilitation. In addition, a stronger cross-modal facilitatory effect is ex-

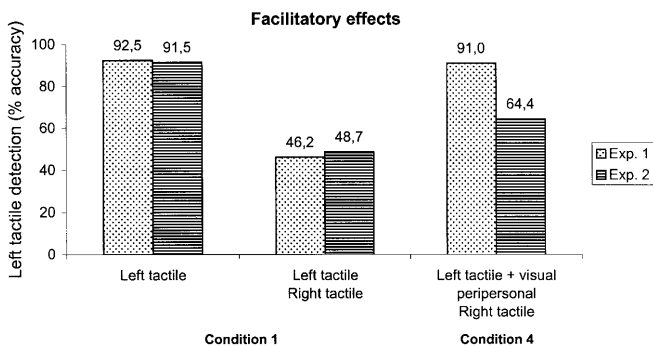


Fig. 6 Facilitatory effects. The graph shows mean percentage of correct detection of the left tactile stimulus in experiment 1 and experiment 2 as a function of type of stimulation. *R* right hand, *L* left hand

pected when the patients' hand is under visual control (experiment 1). Figure 6 shows the percentage of left correct tactile detection as a function of the different types of trials.

A repeated-measure Anova with experiment (experiment 1 and experiment 2) and condition (unilateral, bilateral tactile stimulation, and bilateral tactile stimulation + left peripersonal visual stimulus) as within-subjects factors showed a significant main effect of experiment [$F(1,9)=10.77$, $P<0.01$] and condition [$F(2,18)=18.33$, $P<0.0001$]. Patients were more accurate in performing the tasks when the hand was in full vision than without visual control (76.6% vs. 68.2% of correct responses). Tactile extinction [47.5% ($SD=32$)] was reduced when a simultaneous visual stimulus was presented near the left hand [77.7% ($SD=23$), $P<0.001$].

However, the interaction experiment \times condition was also significant [$F(2,18)=8.02$, $P<0.003$], showing that the cross-modal facilitatory effect was larger in experiment 1 than in experiment 2. In experiment 1, under bilateral tactile stimulation, patients were more accurate in detecting a left tactile stimulus when a visual stimulus was presented near the left hand [91% ($SD=14$)] than in the unimodal bilateral tactile condition [46.2% ($SD=33$), $P<0.0001$]. Moreover, when a visual stimulus was presented near the left hand (91%), the accuracy in detecting left tactile stimuli under bilateral tactile stimulation was not significantly different from that found in unilateral tactile stimulation [92.5% of correct responses ($SD=8$)]. In other words, left tactile stimulus detection became normal or close to normal when a visual stimulus was presented near the left hand.

In experiment 2, when the visual stimulus was presented near the left unseen hand [64.4% ($SD=32$)], the performance was significantly better than in the bilateral tactile condition [48.7% ($SD=31$) $P<0.01$]. However, the performance in the cross-modal condition (64.4%) was significantly worse than in the unilateral tactile stimulation [91.5% ($SD=7$), $P<0.0001$]. Moreover, when the percentages of correct responses in the two experiments for each condition were compared, it appeared clearly that the only significant difference was that related to the

condition in which the visual stimulus was presented near the left hand. Patients were more accurate in reporting a left tactile stimulus when they were able to see the visually stimulated hand than when the hand was not under the patient's view (91% vs. 64.4%, $P<0.0003$). No other comparison between the two experiments for each experimental condition was significant.

Discussion

The present study confirms previous results from our laboratory (Làdavas et al. 1998a, 1998b) showing the existence of a visual peripersonal space coded in body-part-centered coordinates in man and its modulatory effect on tactile-stimulus detection. In addition, it extends the results by showing that the cross-modal links between touch and visual peripersonal space around the hand are strongly mediated by the vision of the hand and much less by the proprioceptive information related to the hand position. Patients with tactile extinction failed to report a single contralesional tactile stimulus when a visual stimulus was presented in the peripersonal space of the ipsilesional hand. However, this cross-modal inhibitory effect was mainly present when the patient could see the visually stimulated hand. Indeed, when the vision of the right hand was prevented, the cross-modal inhibitory effect, although still present, was not significantly different from that found when the right visual stimulus was delivered far from the hand, i.e., in the extrapersonal space. In other words, when the vision of the hand was prevented, it was no longer possible to obtain a differential cross-modal effect between the visual stimulation of peripersonal and extrapersonal space. These findings imply that the proprioceptive information related to the position of the hand is not crucial for differentiating the peripersonal from the extrapersonal space, at least in simple tactile detection tasks, such as that used in the present study.

The relevance of the vision of the hand in determining a cross-modal effect between touch and vision also comes from the facilitatory cross-modal effect, which appeared to be stronger when the patient could see the contralesional hand. When the left visual stimulus was presented near the seen left hand, the facilitatory effect was so powerful that the contralesional tactile extinction disappeared.

This finding is in accordance with recent results reported by Halligan and colleagues (Halligan et al. 1996, 1997) in brain-damaged patients with dense hemisensory loss of the upper limb. These patients reported having felt a tactile sensation on the affected hand only if they were allowed to see the hand being touched by the experimenter. In one patient, simply the vision on the screen of the affected hand being touched produced reports of tactile sensation on the affected hand, even if no real touch occurred (Halligan et al. 1997). The present results, besides being in accordance with Halligan et al.'s findings, also explain the lack of *strong* cross-modal

links between vision and touch found by Mattingley et al. (1997) by using a paradigm in many ways analogous to our own. These authors studied the cross-modal interactions between vision and touch in three neurological patients suffering from both visual and tactile extinction, and found a *mild* cross-modal inhibitory effect when visual stimuli were presented either far from the ipsilesional hand or near the ipsilesional hand, without a significant difference between these two conditions. However, in Mattingley et al.'s study, visual stimuli were always presented while the patients' view of the hand was occluded. Mattingley et al.'s (1997) results are, thus, consistent with the results of the present study, which show that only a *mild* cross-modal inhibitory effect is obtained when patients could not see their hand. In our study, a *strong* cross-modal inhibitory effect was found only in the condition in which patients could see their hand being visually stimulated in the peripersonal space.

These results are entirely compatible with the visual responses exhibited by bimodal neurons, illustrated in animal work. Arm-centered bimodal neurons have been shown to respond best to visual stimuli located in a region of space within 5–20 cm from the skin surface. These neurons can also be activated by visual stimuli located at larger distances (up to 2 m) or when the vision of the arm is prevented, but, in these latter cases, their response is much reduced or extinguished (MacKay and Crammond 1987; Graziano et al. 1994). That is, bimodal neurons vary their responsiveness primarily as a function of the distance of the visual stimulus from the body surface and by the direct vision of the arm. Their activation is higher at closer distances and when the vision of the arm is allowed. Therefore, the functional activity of these neurons explain the strong cross-modal effect found when the visual stimulus is presented near the seen hand and the mild cross-modal effect found when the visual stimulus is presented in the extrapersonal space (Làdavas et al. 1998a) or near the unseen hand (present study), which are fully consistent with the neurophysiological findings.

It is important to stress that, in order to find the effects described in the present and previous studies (Làdavas et al. 1998a, 1998b), at least some of the bimodal areas responsible for the visual peripersonal space coding should be intact. A lesion of most of these areas would prevent the construction of a visual peripersonal space in which the integration between vision and touch occurs.

Thus, a convergent series of studies in monkeys and man seems to suggest that cross-modal links between touch and vision in the peripersonal space around the hand critically depend on the vision of the hand more than on the proprioceptive signals specifying the current hand positions. Therefore, visual peripersonal space surrounding the hand can be conceived of as the result of the interaction between *two main* sensory modalities, i.e., vision and touch.

There are, however, examples in which cross-modal interactions between two sensory modalities are modulated by a third modality, e.g., proprioception. Làdavas et

al. (1998b) found strong cross-modal effects between touch and vision in the peripersonal space surrounding the face, which is never under a subject's visual control. Thus, this seems to be a particular case, in which the relevant information about the spatial location of the tactile receptive field may be mediated by proprioception. Due to the fact that the face cannot be visually experienced by a subject, the characteristic of bimodal cells responsible for coding visual peripersonal space centered on the face may be functionally different from that of bimodal neurons coding peripersonal space centered on the hand. Indeed, in the case of bimodal neurons with tactile receptive fields on the face, the best visual response is evoked by a stimulus approaching the body surface along a precise trajectory that would ideally bring the stimulus in contact with the tactile receptive field. The main variable affecting the neurons' discharge seems to be the direction of the approaching stimulus with respect to the tactile receptive field (Duhamel et al. 1998); in other words, these neurons are directionally selective. In contrast, in the case of bimodal neurons with tactile receptive fields on the hand, the best visual response is evoked by a stimulus approaching the seen hand.

The visuo-tactile abilities of bimodal neurons are hardwired, and the spatial calibration between visual and tactile receptive fields might develop through experience (see Salinas and Abbot 1995). In the case of bimodal neurons with tactile receptive field on the hand, the integration probably occurs with a visual stimulus repeatedly approaching and touching the seen hand. The fact that experience has been built with the hand under vision control might explain a sort of resistance of this integrated visuo-tactile system to change the response properties according to the environmental conditions, i.e., when the hand is not under the control of vision. In order to respond to this particular condition, the adaptation might require many trials of training or be limited to a critical period early in life. It will be interesting to test, in monkeys, whether these bimodal neurons can change their response properties with an appropriate and long-lasting training early in life.

Some evidence of this sort of plasticity early in life has been shown in mice by Benedetti (1995). To test the formation of topographic maps, he connected two cutaneous regions of the body of new-born mice by implanting an artificial bridge of pig hair. Through this procedure, the mechanical fusion of the ear with either the shoulder or the nose was produced. By recording from the superior colliculus, the author found somatosensory-visual bimodal neurons with visual receptive fields extending into the portion of visual space where the artificial bridge was directed. These results show that an experience-dependent interaction between visual and somatosensory inputs occurs during development and that early exposure to abnormal visual-somatosensory experience modifies the organization of multisensory neurons (see also Benedetti and Ferro 1995).

An interesting issue is understanding the functional role of a visual peripersonal space centered in body-

partcentered coordinates. One way to address this question is to try to understand the functional organization of these bimodal neurons. Cells in the putamen, the VIP area, and the inferior area 6 (PMv) have motor functions as well as sensory functions. Indeed, the same neurons often have both sensory and motor activity and many of them respond only when the animal makes a voluntary movement (Rizzolatti et al. 1981; Alexander 1987; Fogassi et al. 1996a). The interesting point is that the same neuron that controls body movements on the basis of cutaneous information can also do it on the basis of visual information. This could allow the neuron to localize the stimulus, even when the skin is not stimulated, and to produce an appropriate movement in response to it. These neurons can, therefore, encode the distance and direction from a body part to a nearby visual stimulus. Such information specifies the distance and direction that the body part must move to reach or avoid the stimulus (Bruce 1990; Fogassi et al. 1996b). Arm and visual neurons are, in this way, useful for guiding the arm toward or away from nearby stimuli. Bimodal neurons with receptive fields located on the face are useful for guiding the head. Graziano et al. (1997) have recently found that 63% of the "face + visual cells" responded during voluntary movement of the head. This is a very important function because, also for a very "simple" action such as that of avoiding a stimulus coming towards the face or the hand, reaching to grasp an object, or getting food into the mouth, we need to know the position of the visual stimulus relative to the head, hand, or both. Thus, this information is most likely provided by the bimodal visuo-tactile neurons described in the physiological studies. Direct evidence of the notion that these areas encode the location of sensory stimuli and generate the motor responses to those stimuli comes from a study by Rizzolatti et al. (1983), in which lesions of PMv disrupted the monkey's ability to avoid or to bite nearby visual stimuli. Surgical ablation of this area caused neglect *only* for peri-personal space around the animals' mouth (peribuccal space) and abolished mouth grasping or licking responses to contralesional tactile and peripersonal visual stimuli.

Other evidence also supports the hypothesis that reaching with the arm may be controlled in an arm-centered co-ordinate system. Caminiti et al. (1990), recording from PMv and dorsal premotor cortex, found that neurons responded best as the monkey reached objects in a particular direction; that is, the neurons had a motor field. When the arm was moved to a different position, the motor field also moved, rotating with the arm. Thus, the motor fields are arm-centered, just as the visual receptive fields of bimodal neurons are arm- or body-part-centered. Psychophysical studies in humans also indicate that visually guided reaching may be organized in arm-centered coordinates. Normal subjects wearing displacing prisms are able to adapt to the prisms by repeatedly pointing towards visual targets. However, Paillard (1991) showed that each body part, i.e., the hand, the forearm, and the upper arm, could be separately adapted.

All these studies suggest that arm movements may be organized in an arm-centered coordinate frame.

To summarize, we suggest that the processing of space is not unitary, but is strongly modular and dispersed among several brain areas and several coordinate systems. In particular, our study suggests the existence of a system that controls both visual and tactile inputs within peripersonal space, and it shows how this system is functionally separated from the one that controls visual information in the extrapersonal space.

Acknowledgements This work was supported by grants from MURST and CNR to Elisabetta Làdavas.

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