Face or Hand, Not Both: Perceptual Correlates of Reafferentation in a Former Amputee

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Summary

The topography of the somatosensory maps of our body [1] can be largely shaped by alterations of peripheral sensory inputs [2, 3]. Following hand amputation, the hand cortical territory becomes responsive to facial cutaneous stimulation [4–7]. Amputation-induced remapping, however, reverses after transplantation, as the grafted hand (re)gains its sensorimotor representation [8]. Here, we investigate hand tactile perception in a former amputee by touching either grafted hand singly or in combination with another body part. The results showed that tactile sensitivity recovered rapidly, being remarkably good 5 months after transplant. In the right grafted hand, however, the newly acquired somatosensory awareness was strikingly hampered when the ipsilateral face was touched simultaneously, i.e., right face perception extinguished right hand perception. Ipsilateral face-hand extinction was present in the formerly dominant right hand 5 months after transplant and eventually disappeared 6 months afterwards. Control conditions' results showed that right hand tactile awareness was not extinguished either by contralateral left face and left hand stimulation or ipsilateral stimulation of the arm, which is bodily close to, but cortically far from, the hand. We suggest that ipsilateral face-hand extinction is a perceptual counterpart of the remapping that occurs after allograft and eyewitnesses the inherently competitive nature of sensory representations.

Results and Discussion

We had the opportunity to investigate C.D., a 33-year-old man who was the recipient of the world’s first double hand transplant [9]. Touches were delivered in single (SS) or double simultaneous (DSS) stimulation to different body parts in six experimental conditions (Figures 1A–1F), which also included no-stimulation catch trials (CT). The subject was asked to verbally report and localize all the sensations he felt. The results for each condition are reported in Figure 1. At the time of the investigation, i.e., 5 months after the surgery, C.D.’s tactile sensitivity of both hands was already remarkably good. In the first session, the experimental testing revealed highly accurate detection of single touches, as C.D. perceived nearly 100% of SS on both grafted hands. Strikingly, somatosensory perception of the right hand was largely reduced (45% correct) when the right face was concurrently stimulated (p < 0.001 by Fisher’s exact test), although it was nearly perfect (95% correct) when the right hand was stimulated alone in the same block of trials (Figure 1A). In more than half of the right face and hand DSS, C.D. reported that only the right face had been touched. Facial stimulation severely interfered with the perceptual awareness of real touches of the hand, although C.D. tended to favor right hand sensations when the hand was not actually touched. Following single stimulation of the right face, C.D. erroneously reported double right face and hand touches (25% of SS), as well as right hand touches in no-stimulation catch trials (30% of CT).

Neither face-hand extinction nor illusory sensations were manifest at the time of testing when the left face and left hand were similarly stimulated (Figure 1E). Control conditions indicated that the phenomenon of right hand extinction under face and hand DSS was highly selective for the spatial arrangement of tactile stimuli and was not due to a perceptual deficit of the newly sensed right versus left grafted hand. Indeed, C.D.’s ability to perceive touches delivered to his right hand was completely preserved (100% correct) when a concurrent touch was also delivered to the face, but a few centimeters away on the left contralateral side (Figure 1B). On the other hand, right face stimulation did not extinguish touches simultaneously delivered to the left hand (Figure 1F). Furthermore, no sign of extinction emerged for the right hand (90% correct) when tactile perceptual rivalry was tested between the two homologous grafted hands (Figure 1C). Taken together, these findings rule out potential accounts of right face-hand extinction in terms of higher sensitivity to the facial stimulation and deficient orientation of attention to the right grafted hand. Most critically, right hand tactile perception was also tested while the ipsilateral right arm was concurrently touched (well above the graft line) instead of the patient’s right face (Figure 1D). In this alternative arrangement of ipsilateral DSS, touches delivered to the right arm did not interfere with the detection of tactile stimuli delivered to the right hand (90% correct), and this clearly shows that ipsilateral face-hand extinction depends upon topographical relationships between body parts at a central rather than peripheral level.

When right face-hand extinction was reevaluated in a second session the same day, C.D.’s performance was virtually identical (Figure 1A), the loss of somatosensory
Figure 1. Schematic View of the Experimental Setup, Conditions, and Results

(A–F) The figure illustrates the six experimental conditions ([A]–[F], upper panels) and the corresponding results ([A]–[F], lower panels). Upper row: The site(s) stimulated on the right (R) and left (L) sides of the subject’s body; the spatial arrangement of tactile stimuli is indicated for each condition. Different body parts could be stimulated singly or simultaneously. The tactile detection accuracy of simultaneous stimulation is represented by a color code: yellow for accurate tactile perception (>85% correct), and blue and yellow for reduced tactile perception (85% correct). Lower row: Each panel shows the mean percentage of accuracy in reporting the stimulation delivered to the hand, face, or arm as a function of single (SS) or double simultaneous stimulation (DSS). The mean percentage of accuracy obtained in the second session is reported in brackets, but only when differing from the first session. Significant differences determined by the one-tailed Fisher test are indicated by a star. The subject’s mean accuracy in responding to no stimulation catch trials (CT) is also indicated as a percentage. Note that false alarms in (A), (B), and (C) were always reported as stimulation of the right hand. A signal detection analysis \( d' \) was conducted on C.D.’s discriminative ability to perceive right hand touches under DSS across different experimental conditions (A–D); the \( d' \) value obtained in (A) significantly differed from those of the remaining conditions \( p < 0.05 \) in all comparisons) and confirmed the selectivity of right face-hand extinction. The analysis did not reveal any significant shift in the subject’s response criterion \( p > 0.05 \) in all comparisons).

 awareness being highly significant (SS: 90% versus DSS: 45% of accuracy, \( p < 0.003 \)). Again, right face and hand sensations following single stimulation of the right face (30% of SS) were observed only within this condition, at variance with C.D.’s tendency to report right hand touches in no-stimulation catch trials. Signal detection analysis \( d' \) confirmed the selective interference exerted by the right face upon right hand perception, with no shift in response criterion (Figure 1).

Finally, C.D. was resubmitted to the same protocol 6 months afterwards (i.e., 11 months after transplant). At that time, his tactile sensitivity was further ameliorated at both hands; inasmuch, he was able to accurately detect even lighter touches. Interestingly, C.D.’s ability in perceiving right hand touches under face-hand DSS was also substantially increased when compared to the first session (DSS: 45% versus 80%, \( p < 0.03 \)). In this follow-up examination, right face-hand extinction was no longer significantly present (SS: 100% versus DSS: 80%), thus showing the transient nature of this perceptual phenomenon. Similarly, single facial stimulation did not evoke any tactile sensations in the right hand, and illusory touches were no longer reported in CT.

Far from being static, somatosensory maps’ extension and topography in the mature brain are dynamically modulated and maintained over time by competitive processes that are dependent upon neuronal activity [3, 10]. Consistent with observations in macaques [4], following hand amputation in humans, the cortical representation of the face markedly intrudes into the missing hand area, the deprived hand area becoming responsive to the face [6, 7]. Several studies have shown that the perceptual consequences of such map reorganization are surprising [11–14] and, unfortunately, are most often characterized by excruciating phantom hand pain [6]. As another perceptual instance, some amputees may experience face-to-phantom hand-referred sensations: i.e., when subjects’ faces are touched on the same side of the missing limb, they feel non-painful touches emanating from the phantom hand [5, 7, 11, 13]. A recent review [15] anecdotally reported the case of one patient whose referred sensations could be suppressed by touching her normal hand, that is by providing tactile stimulation to the homologous body part on the contralateral side. At variance with all of these previous findings, here we report for the first time a perceptual phenomenon emerging after reafferentation of a previously deprived hand representation. As revealed by a longitudinal fMRI study performed on C.D. by some of us [8], motor and somatosensory representations of both grafted hands had (re)occupied the “normal” hand region almost entirely at the time of the present investigation. The reconquest of cortical territory toward the classical somatotopic location of the hand area was characterized by a progressive mediolateral shift that unveiled a major reorganization in the dominant right hand rather than in the left hand (10 mm versus 6 mm). The wider cortical remapping of C.D.’s preferred right hand, besides suggesting a major facial “invasion” of hand cortical territory in the left rather than right hemisphere, may explain the finding that the phenomenon of face-hand extinction was selective for the right domi-
Figure 2. Schematic View of Topographic Changes in the Somatosensory Cortex

(A–D) The figure illustrates (A) the homuncular somatosensory topography, with the usual spatial relationships between the face (yellow) and hand (blue) area, and schematically summarizes the changes that may occur at the cortical level following (B) hand amputation and (C and D) transplant, on the basis of animal and human studies on neural plasticity. After hand amputation (B), the cortical territory formerly devoted to the hand representation becomes responsive to somatosensory stimulation of the face, whose representation is said to “invade” the hand area [3–7]. The proximal representation of the arm and stump also shifts laterally into the hand area (not shown). Following hand transplantation (C), the hand starts (re)gaining its lost territory and produces an overlapping face-hand area (blue and yellow) that is responsive to tactile inputs delivered to either body parts, despite their physical discontinuity in the external space [10, 16, 19]. Owing, at least in part, to the newly established somatosensory inputs, the hand representation progressively segregates from the face area (D) and returns to the almost original somatotopy [8, 17–21]. This figure was modified from [1].
nont hand. In fact, since both hands were grafted at the same time and a smaller, but substantial, cortical remapping occurred for the nondominant hand [8], we did expect to find signs of face-hand extinction also for the left hand. In light of the temporary nature of this perceptual phenomenon, which we demonstrated here for the right hand, the possibility remains open that spatial asymmetries in cortical reorganization between the dominant and nondominant hand may bring about asynchronous manifestations of behavioral phenomena. Future studies on double- as well as single-hand transplantees would hopefully clarify whether ipsilateral face-hand extinction also occurs on the left nonpreferred side and, in this case, whether it may precede or follow that on the right preferred side. Also consistent with fMRI evidence showing that the canonical hand cortical territory had been newly devoted to the grafted hands, here we found that somatosensory perception was well re-established at both hands. Furthermore, hand tactile awareness was unambiguous enough to largely withstand the interference potentially exerted by concurrent tactile events in a wealth of spatial combinations. The only relevant exception was the simultaneous stimulation of the face and the hand on the right side, where tactile perception did not appear to be sufficiently unambiguous to allow perceptual awareness of face and hand inputs at the same time.

This is the pattern of results one would expect if the formerly deafferented hand area, once reafferented, were competing with the “invading” facial representation for a more appropriate sensory control of the transplanted hand. Both in animals and humans, a regenerating or transplanted nerve reclaims its lost cortical territory and overturns the deafferentation-induced topographical changes to regain the (almost) original somatotopy [8, 16–18] (Figure 2). During this second-order remapping, two physically distant, but cortically adjacent, body parts (face and hand) seem to compete for cortical representation and give rise to a temporary overlapping (face-hand) area that, until complete segregation, receives multiple conflicting inputs from both body parts [16, 19, 20]. We suggest that the new behavioral finding reported here is a perceptual counterpart of this competitive “filling in” of the receptor sheet. This view is strongly supported by the high somatotopic selectivity characterizing ipsilateral face-hand extinction and by the successive substantial reduction of the phenomenon, which the segregation process would imply [19, 21]. While the nature of the competitive process that is responsible for ipsilateral face-hand extinction might be difficult to ascertain on a purely behavioral basis, the present findings suggest that somatosensory awareness may depend on a low level of uncertainty for attributing neuronal activation to the corresponding body part. In the case of a newly sensed hand, neuronal activity evoked in the overlapping face-hand area might be labeled as “hand” when the hand is stimulated alone and might be labeled as “face” when ambiguity is higher due to simultaneous stimulation of the face, which might benefit from wider and less ambiguous cortical activation.

Perceptual correlates of cortical reorganization are often temporarily manifest and may undergo long-term major modifications [22]. Indeed, the extent of cortical reorganization can be rather stable in a short space of time, whereas the concomitant patterns of sensory perception may change rapidly [23], eventually subsiding in a few months [24]. The findings we obtained by using a simple face-hand test, originally introduced to reveal extinction as a sign of neurological deficits [25, 26], clearly support the notion that sensory awareness from a given body part might depend on the level of competitive (re)activation assigned to the representation of that body part. The high topographic selectivity of reduced tactile perception points to the intimately rival nature of cerebral representations [27] and shows that this concept applies within, as well as between, hemispheres.

Reorganization of sensory, as well as motor, maps is almost ubiquititary in the mature brain and occurs at subcortical and cortical levels [28]. While the mechanism underlying remapping remains uncertain (e.g., changes in synaptic strength, unmasking of existing connections, sprouting of new connections [see, 10]), our findings clearly demonstrate that perceptual effects that parallel the occurrence of cerebral plastic changes following transplantation can be disclosed behaviorally. Such perceptual markers can thus be exploited to keep track of the temporal evolution of functional aspects of neural plasticity [29] and can be used in future studies to reveal their precise timing as well as possible temporal asymmetries between dominant versus nondominant hand reaferenceation.

Experimental Procedures

This study focused on the somatosensory perceptual abilities of C.D., a 33-year-old man who, 4 years after traumatic amputation of both hands (3 cm above wrists, following an accidental explosion while handling fireworks), sustained a bilateral hand transplant in Lyon, France. Informed consent was obtained from the subject, and the study was approved by the local human ethics committee. Right handed prior and after amputation (1996) and transplant (2000), C.D. experienced vivid, painless phantom limb sensations bilaterally until hand graft, and the right phantom hand was perceived as dominant. A first evaluation of C.D.’s tactile sensitivity, performed 4 months after surgery, revealed that his tactile perception was rapidly recovering, but was not sufficiently restored to allow a fully reliable examination. The experimental investigation started 1 month later, when he was able to reliably detect tactile stimulation delivered on the dorsum of either grafted hand (i.e., he consistently reported more than 85% of single touches). At the time of the present study, neither supernumerary nor spontaneous “phantom” sensations were experienced by the subject, who remained alert and collaborative during all testing sessions.

The subject, his hands resting palm down on a table, sat blindfolded in front of the experimenter. Tactile stimuli were brief (<1 s), light touches silently delivered to the right and/or left hemibody through synthetic probes analogous to Semmes-Weinstein monofilaments. In the first two sessions (5 months after surgery), a pair of probes that required a force of 60 g for the monofilament to buckle was used and provided indenting stimulation of nearly constant force across trials. In the third follow-up examination (11 months after surgery), lighter touches were also delivered with an additional pair of probes (40 g). The different sites stimulated in the six experimental conditions are indicated in Figure 1. Single (SS) or double simultaneous (DSS) stimulations were applied to the dorsum of the hand, to the perioral part of the jaw, or to the arm (just above the biceps-belly), in different combinations according to the following experimental conditions: (a): right hand, right face, both; (b): right hand, left face, both; (c): right hand, left hand, both; (d): right hand, ...
right arm, both; (e): left hand, left face, both; (f): left hand, right face, both. The order of the conditions, run in separate blocks, was randomized. In each condition, a total of 60 trials, 20 for each type of single and double stimulation, were pseudorandomly presented. To control for paraesthesia and possible subject’s guessing strategies, all conditions also included ten catch trials (CT) in which no stimulation was given. Before each condition, the subject was informed about which parts of his body could be stimulated, singly or together. He was also informed that, on some occasions, no stimulation would occur. Immediately before each trial, the subject was verbally prompted by the experimenter to summon his attention to the next upcoming event (also in case of no stimulation CT). He was instructed to verbally report and localize any tactile sensation he felt by naming the site(s) and side(s) of perceived stimulation.

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