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Synaesthesia in phantom limbs induced with mirrors

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SUMMARY

Although there is a vast clinical literature on phantom limbs, there have been no experimental studies on the effects of visual input on phantom sensations. We introduce an inexpensive new device – a 'virtual reality box' – to resurrect the phantom visually to study such inter-sensory effects. A mirror is placed vertically on the table so that the mirror reflection of the patient's intact hand is 'superimposed' on the felt position of the phantom. We used this procedure on ten patients and found the following results.

1. In six patients, when the normal hand was moved, so that the phantom was perceived to move in the mirror, it was also felt to move; i.e. kinesthetic sensations emerged in the phantom. In D.S. this effect occurred even though he had never experienced any movements in the phantom for ten years before we tested him. He found the return of sensations very enjoyable.
2. Repeated practice led to a permanent 'disappearance' of the phantom arm in patient D.S. and the hand became telescoped into the stump near the shoulder.
3. Using an optical trick, impossible postures – e.g. extreme hyperextension of the fingers – could be induced visually in the phantom. In one case this was felt as a transient 'painful tug' in the phantom.
4. Five patients experienced involuntary painful 'clenching spasms' in the phantom hand and in four of them the spasms were relieved when the mirror was used to facilitate 'opening' of the phantom hand; opening was not possible without the mirror.
5. In three patients, touching the normal hand evoked precisely localized touch sensations in the phantom. Interestingly, the referral was especially pronounced when the patients actually 'saw' their phantom being touched in the mirror. Indeed, in a fourth patient (R.L.) the referral occurred only if he saw his phantom being touched: a curious form of synaesthesia.

These experiments lend themselves readily to imaging studies using PET and fMRI. Taken collectively, they suggest that there is a considerable amount of latent plasticity even in the adult human brain. For example, precisely organized new pathways, bridging the two cerebral hemispheres, can emerge in less than three weeks.

Furthermore, there must be a great deal of back and forth interaction between vision and touch, so that the strictly modular, hierarchical model of the brain that is currently in vogue needs to be replaced with a more dynamic, interactive model, in which 're-entrant' signalling plays the main role.

1. INTRODUCTION

Since the time when they were originally described by Silas Wier-Mitchell (1872), 'phantom limbs' have evoked considerable interest and there have been literally hundreds of clinical case studies (Henderson & Smyth 1948; Livingstone 1945; Cronholm 1951; Melzack 1992). There has, however, been an unfortunate tendency within the medical profession to regard them as enigmatic clinical curiosities and, with a few notable exceptions (Teuber *et al.* 1949), almost no systematic psychophysical work has been done on the patients. In this article we will describe several novel experimental approaches to phantom limbs and will argue that they illustrate certain important principles underlying the functional organization and plasticity of the normal human brain (Ramachandran *et al.* 1992; Ramachandran 1993, 1995).

Some patients with phantom limbs experience vivid movements in their phantom. For example, the phantom might attempt to fend off a blow, wave goodbye, break a fall or even shake hands (Ramachandran 1994). Many other patients, however, report that the phantom is 'frozen' in a specific position and that they cannot generate voluntary movements in it even with intense effort. The reason for these differences is obscure and needs careful investigation. In our own experience, however, at least three factors seem to play a main role.

1. If an arm has been paralysed, as a result of a peripheral nerve lesion, before amputation, then the phantom tends to be 'paralysed' as well and tends to occupy the same position as the arm did before amputation. Elsewhere, we have dubbed this phenomenon 'learned paralysis' (Ramachandran 1994).
2. Immediately following a non-traumatic surgical amputation (e.g. for a tumour) subjects find they can usually generate voluntary movement in the phantom. With the passage of time, however, this ability is lost in many (but not all) patients.
3. When a phantom is extremely painful – as it sometimes is – the patient finds it difficult to move the arm because even an attempt to generate movements can amplify the pain. This may be analogous to the

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defensive, reflexive immobilization of an intact limb that occurs following any painful injury to the limb.

It is tempting to assume that the pain that arises from attempts to move the phantom is a simple consequence of neuromas being irritated by muscle activity in and around the stump. This can't be the whole story, however, because we have sometimes seen such effects when the patient attempts to move a single digit (e.g. the thumb) following an amputation well above the elbow. We may conclude, therefore, that more interesting central factors must be involved.

Some patients also experience involuntary movements in their phantom: such as a clenching spasm of the hand. ('As though the nails are digging into my palm': as one patient told us.) Voluntary 'unclenching' is often effective in relieving the spasm, but the patients usually find this very difficult to do: because they have no voluntary control over the phantom.

What exactly does it mean to say that a patient has volitional control of a phantom arm? One possibility is that messages from the motor cortex in the front part of the brain continue to be sent to the muscles in the hand even though the hand is missing. After all, the part of the brain that controls movement doesn't 'know' that the hand is missing. It is likely that these movement commands are simultaneously monitored by the parietal lobes which are concerned with body image. In a normal person, messages from the frontal lobe are sent either directly or via the cerebellum to the parietal lobes which monitor the commands and simultaneously receive feedback from the arm about its position and velocity of movement. There is, of course, no feedback from a phantom arm; but the monitoring of motor commands might continue to occur in the parietal lobes, and thus the patient vividly feels movements in the phantom.

But how can a phantom – a nonexistent limb – be paralysed? One possibility is that during the months preceding the amputation the brain had 'learned' that the arm was paralysed, i.e. every time that the message went from the motor cortex to the arm, the brain received visual feedback that the arm was not moving. This contradictory information is somehow stamped into the neural circuitry of the parietal lobes so that the brain 'learns' that the arm is fixed in that position. Therefore, when the arm is amputated the brain still 'thinks' the arm is fixed in the previous position and the net result is a paralysed phantom limb (Ramachandran 1993, 1994, 1995).

A similar sequence might occur following a surgical amputation, except that instead of receiving contradictory information (that the arm is immobile) the subject simply receives no feedback confirming that the command has been obeyed. Therefore, immediately after amputation the subject can still generate volitional movements in the phantom, but with the passage of time: this ability is lost because of the prolonged absence of confirming sensory feedback.

If this hypothesis of learned paralysis is correct, would it be possible to unlearn the phantom paralysis? To do this, every time the patient sends a message to the phantom arm, he would need to receive a visual feedback message that his arm is indeed moving correctly. But how can this happen when the patient doesn't even have an arm? To enable the patient to perceive real movement in a nonexistent arm, we constructed a 'virtual reality box'. The box is constructed by placing a vertical mirror inside a cardboard box with the roof of the box removed (figure 1). The front of the box has two holes in it through which the patient inserts his 'good arm' and his phantom arm. The patient is then asked to view the reflection of his normal hand in the mirror, thus creating the illusion of observing two hands, when in fact the patient is only seeing the mirror reflection of the intact hand. If he now sends motor commands to both arms to make mirror symmetric movements he will literally see his phantom hand resurrected and obeying his commands, i.e. he receives the positive visual feedback informing his brain that his phantom arm is moving correctly. Would this somehow revive sensations of movement and of voluntary control over the phantom?

Figure 1. The mirror-box. A mirror is placed vertically in the centre of a wooden or cardboard box whose top and front surfaces have been removed. The patient places his normal hand on one side and looks into the mirror. This creates the illusion that the phantom hand has been resurrected.

We tried this experiment on patient D.S. who had his left arm amputated nine years before we saw him (see table 1 for clinical details). He looked inside the mirror-box and, with his eyes shut, tried to make bilateral mirror-symmetric movements. As expected, the right arm felt like it was moving but the phantom remained 'frozen as in a cement block'. As soon as he looked in the mirror, however, he exclaimed that he experienced vivid sensations of movement originating

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from the muscles and joints of his phantom left arm (Ramachandran 1994). We then removed the mirror and verified that, as before, he could no longer feel his phantom moving even if he tried mirror symmetric movements. ('It feels frozen again,' he said.) Patient D.S. also tried moving his index finger and thumb alone while looking in the mirror but, this time, the phantom thumb and index finger remained paralysed: they were not revived. (This is an important observation for it rules out the possibility that the previous result was simply a confabulation in response to unusual task demands.) Thus, it would appear that there had been a temporary inhibition or 'block' of neural circuits that would ordinarily move the phantom and the visual feedback could overcome the block.

Our purpose in this paper is to provide additional details on patient D.S. and to report preliminary results from nine other patients whom we have studied using the same procedure.

2. PATIENTS

Ten upper limb amputees were studied. They were either referred to us by colleagues in the orthopedics department or were recruited by contacting local prosthesis manufacturers and by placing ads in newspapers. A complete neurological work-up and 'mental status' examination was done on all patients. They were all neurologically intact (except for the sequelae of the avulsion). Patient D.S. had a left Horner's Syndrome. Patient R.L. had sustained a subdural hematoma 30 years before our testing him but this did not leave any residual neurological defects. Additional clinical details pertinent to the amputation are given in table 1.

3. METHODS

Our 'virtual reality box' was constructed by simply placing a 2″ by 2″ mirror vertically inside the middle of a cardboard box, so that it was perpendicular to the patient's chest and its upper end was almost touching the chin. The top and face of the box were removed to afford the patient full view of the reflection of his normal hand in the mirror. For patients with a shoulder level disarticualtion, a much taller mirror was used.

The patients were first questioned carefully about the clinical and medical history pertaining to the amputation (table 1). Following this they were asked questions about the extent to which they could generate volitional movements in the phantom and the duration and frequency of involuntary

Table 1. *Clinical history of patients used in the study*

(All patients underwent a thorough neurological evaluation to rule out CNS pathology and to ensure that their 'mental status' was normal. Patients R.L., P.N., R.T., J.P. and B.D. experienced frequent involuntary clenching spasms in the phantom. In four of them (R.L., P.N., J.P. and R.T.), clenching spasms were relieved when they used the mirror-box (see text). In one (R.T.), the spasms casued 'the fingernails to dig into my phantom palm,' and these sensations also went away each time that the spasm went away. Perhaps the two sensations – clenching and nail digging – had been linked in R.T.'s brain by a Hebbian learning mechanism, so that relieving one also relieves the other. Sensations that were apparently unrelated to the clenching – such as burning pain – were completely unaffected by the mirror procedure.

Patient P.N. said the hand was usually in exactly the same peculiar semi-flexed position that she had last seen it just before it was avulsed: a curious form of sensory 'flashbulb memory'.

Patient B.D. did not show any intermanual referral of sensations whether or not he used the mirror-box. Also, he could not generate any movements in the phantom, whether or not he used the box, and there was no relief from pain. (It's frustrating Doctor. I can see it move; I want it to move but it doesn't feel like it's moving!)

Patients D.B., J.P. and D.S. also referred sensations from the lower face region to the phantom hand, as in some of the patients whom we had studied previously (Ramachandran *et al.* 1992*a*). Patient L.C. experienced phantom pain only very rarely.

patient	age	pathology	location	time of testing
K.S.	73	car accident crush injury	left arm 5 cm above elbow	2 years after amputation
J.P.	31	self inflicted amputation	to right forearm 5 cm below elbow	5 months after amputation
R.L.	56	melanoma infiltrating brachial plexus	right upper limb disarticulation at shoulder 1 year after onset of melanoma	2 months after amputation
P.N.	48	arm crushed in car accident	left hand 8 cm below elbow	7 months after amputation
R.T.	55	sarcoma infiltrating ulnar nerve	left arm 6 cm above elbow	7 months after amputation
P.N.N.	40	airplane propeller cut off arm	right arm above elbow	8 years and 3 months after amputation
D.B.	23	car accident, crush injury	left arm, disarticulation of shoulder	3 years after amputation
D.S.	28	brachial plexus avulsion	left above elbow amputation 1 year after avulsion	9 years after amputation
B.D.	29	brachial plexus avulsion	right above elbow amputation 2 years after avulsion	3 months after amputation
L.C.	23	crush injury following train accident	right forearm below elbow	19 days after amputation

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movements such as 'clenching spasms'. They were also asked to provide detailed descriptions of the pain they experienced in the phantom.

The mirror-box was then shown to the patient and he/she was asked to put the real arm on one side of the mirror and the phantom on the other side. He was then asked to gradually move his real arm around until its mirror image matched the felt position of the phantom. (Patients found this easy to do, with some practice.)

After this the patient was asked to close their eyes and to generate mirror symmetric movements, for example, 'Pretend you are conducting an orchestra'. Typically, they would experience the real arm moving – responding to the command – but the phantom remained completely 'frozen' (except in one patient, J.P.). The patient then opened his eyes and looked in the mirror while performing exactly the same task. Patient's responses were noted either by an assistant or by a video-camcorder for subsequent analysis. Some of the patients also took the mirror-box home and continued the experiments on their own.

Because the patients were tested in a clinical setting it was often not possible to adhere to a very strict testing protocol. For the most part, tactile stimuli were delivered by simply using a cotton-bud (Q-tip). In two patients (J.P. and D.B.), some of the testing was done using Semmes monofilaments (Lafayette instruments) to obtain touch thresholds.

4. RESULTS

For practical reasons we could not use exactly the same protocol on all patients and there were minor differences in testing procedures. For this reason the patients will be described individually.

(*a*) *Patient R.T.*

Mr R.T. was an intelligent, 55-year-old engineer who had an infiltrating sarcoma in his left arm that produced a painful ulnar nerve palsy. Six months later his arm was amputated 6″ above the elbow (see table 1). When we examined him seven months after the amputation, he experienced a vivid phantom arm that was of normal length but apparently paralysed, i.e. he could not generate voluntary movements in it except with prolonged, intense effort. His hand frequently went into an involuntary, clenching spasm (with 'fingernails digging into the palm') and it took him half an hour or more to voluntarily unclench it. We verified also that Mr R.T. was otherwise completely intact neurologically and that his mental status was normal.

It occurred to us that if one could somehow enable the patient to generate voluntary movements in his phantom he might be able to unclench it during the spasms. To achieve this, we used the mirror-box to convey a visual illusion to the patient that his phantom arm had been resurrected. When he then looked into the right side of the vertical mirror from above the box, he could see the reflection of his right hand and this created a vivid visual illusion that his left arm had been resurrected. We then asked him to simultaneously send motor commands to both hands as if to perform mirror symmetric movements, e.g. clenching and unclenching of the fist, extension and flexion of the wrist or circular movements: as if conducting an orchestra. The very first time he tried this the patient exclaimed with considerable surprise, that all his movements had 'come back': that he now vividly experienced muscle and joint movements in his phantom! For example, at the time of his first visit his phantom fist was clenched and he was unable to unclench it voluntarily with his eyes closed even if he unclenched his other fist. When he looked in the box, however, he was immediately able to unclench his phantom: much to his surprise and delight. The procedure was repeated several times with identical results.

We then repeated the experiment on eight different occasions when patient R.T. had spasms. On four of these occasions, he tried in vain for the first five minutes to unclench the fist with his eyes closed and the spasm remained unabated. But as soon as he looked in the box, he could unclench the hands and the spasm vanished completely. The hand then remained unclenched, even outside the box, for several hours until the next spasm occurred spontaneously. On those occasions when he did not use the box at all, the clenching spasms usually continued for 40 minutes or more.

(*b*) *Patient P.N.*

Our second patient, Mrs P.N. was a 48-year-old lady who had a traumatic amputation of her left hand just below the elbow. When we examined her seven months after the amputation, she too was experiencing clenching spasms of her left hand along with a 'burning pain' in the fingers. Again, she could not voluntarily extend her phantom fingers even if she made mirror symmetric movements with her normal hand and even if she looked inside the box and tried to visualize her phantom moving while her eyes were shut. When she opened her eyes, however, she could immediately produce the movements. Furthermore, the unclenching that she induced produced immediate relief from the 'tight feeling' in the fingers, but, unfortunately, did nothing to alleviate the burning pain. This is an important observation for it not only rules out placebo effects, but implies that only some kinds of discomfort may be relieved by the procedure. The direct comparison between eyes-closed and eyes-open condition was repeated eight times (distributed over a week) with identical results each time.

(*c*) *Patient R.L.*

A 'control' procedure was adopted on our third patient, Mr R.L., a 56-year-old man who had a right fore-quarter disarticulation following a melanoma that had begun infiltrating his brachial plexus. (The patient was otherwise neurologically intact in spite of having sustained a right subdural hematoma 30 years ago.) Two months after the amputation he experienced frequent clenching spasms and involuntary writhing movements in his phantom hand: so that his fingers often adopted uncomfortable positions (e.g. 'digging in the palm' as in R.T. and P.N.). Like the other patient,

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he found his inability to generate voluntary movements in his hand very frustrating. As a 'placebo' control, we instructed R.L. and his spouse on the use of a TENS (transcutaneous electrical simulator) mounted on his normal (left) forearm. Whenever the spasms and abnormal postures occurred, he was asked to rotate the dial on the unit until he just began to feel a tingling in his left arm. We told him that this would immediately restore voluntary movements in the phantom and provide relief from the spasms. (We also informed him that the procedure had proven effective on several patients.) Mr R.L. returned the following day after having tried the procedure on five different occasions and he reported, with a hint of annoyance, that the device was useless. We then demonstrated the use of the mirror-device to him and, although initially skeptical, he exclaimed, like the other patients, that this instantly restored voluntary movement in his phantom: so that his clenching spasms were relieved. Taking the device home, he tried the procedure six times and reported that it had been effective every time in eliminating the spasms. When questioned specifically about the pain he said the 'digging sensation' associated with the spasms disappeared every time, but that tingling paraesthesias remained largely unaffected.

It is difficult to explain these results in terms of our current knowledge of neuroscience. One possibility is that when motor commands are sent from the premotor and motor cortex to the clenched hand, they are normally damped by error feedback from proprioception. If the limb is missing, however, such damping is not possible: so that the motor output is amplified even further: and this overflow or 'sense of effort' itself may be experienced as pain. Perhaps the mirror simply provides extraneous visual feedback to unclench the hand – through visual capture – so that the clenching spasm is abolished.

But why would the 'nails digging' sensation also disappear along with the spasm? This is even more difficult to explain but one might suppose that the two sensations, 'nails digging' and the 'clenching', are linked in the brain, even in normal individuals, by a Hebbian learning mechanism so that abolishing one leads to the elimination of the other as well. What we are dealing with here, then, might be a primitive form of sensory learning that could conceivably provide a new way of experimentally approaching more complex forms of memory and learning in the adult brain.

The reactivation of pre-amputation memories in the phantom has been noted before (Katz & Melzack 1990) but there has been very little systematic work and the significance of the findings for understanding normal memory functions appears to have gone largely unrecognized. One of our patients, for example, reported that before amputation, the arthritic joint pains in her fingers would often flare-up when the weather was damp and cold. Remarkably, whenever the air became humid the same pains would recur in her phantom fingers! Also, when her hand went into a clenching spasm in the evening, the thumb was usually abducted and hyper-extended ('sticking out') but on those occasions when it was flexed into the palm, the spasm was accompanied by the unmistakable feeling of her thumb-nail digging into the fifth digit's pad. The curious implication of this observation is that even fleeting sensory associations may be permanently recorded in the brain; these memory traces may be ordinarily 'repressed', but may become unmasked by the de-afferentation. (Also, surprisingly, access to the traces may be gated by the felt position of the phantom thumb.)

(*d*) *Patient D.S.*

Can the illusory voluntary movements in the phantom be restored permanently? We explored this in a fourth patient, D.S., who had sustained a brachial plexus avulsion 10 years ago and an arm amputation 6″ above the elbow, a year following the avulsion. At the time when we first saw him he was neurologically normal (except for a left Horner's syndrome) and experienced a vivid 'paralysed' phantom arm that was painful, of normal length, and fixed in the position that it was in before the amputation. Even with repeated, intense voluntary effort he could not generate the slightest flicker of movement in his phantom.

We asked the patient to try our 'virtual reality box'. He was first instructed to place both his normal arm and his phantom arm into the box, close his eyes and to try to move both hands. He reported, as expected, that he could move his right hand inside the box but that his phantom was 'frozen'. We then asked him to open his eyes, look at the reflection of his hand in the mirror and try the same procedure, so that he could 'see' his phantom come to life and move in response to his commands. A few seconds later he exclaimed, with considerable surprise, 'mind-boggling. My arm is plugged in again; it's as if I am back in the past. All these years I have often tried to move my phantom several times a day without success, but now I can actually feel I'm moving my arm, Doctor. It no longer feels like it's lying lifeless in a sling'. We then removed the mirror and verified that, as before, he could no longer feel his phantom moving if he closed his eyes and tried mirror symmetric movements. ('It feels frozen again,' he said.) Patient D.S. also tried moving his index finger and thumb alone while looking in the mirror but, this time, the phantom thumb and index finger remained paralysed: they were not revived. This is an important observation for it rules out the possibility that the previous result was simply a confabulation in response to unusual task demands. Thus it was as though there had been some temporary inhibition or 'block' of the neural circuits that would ordinarily move the phantom and the visual feedback could be used to overcome this block. And the remarkable thing is that these somatic sensations could be revived in an arm that had never experienced such sensations in the preceding ten years.

We wondered, however, whether such movements could be restored permanently with repeated practice using the box. He therefore took the box home and practiced for 15 minutes-a-day for a few weeks. A follow-up interview conducted a week later revealed that although the mirror effect could still be elicited

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vividly, the phantom remained paralysed, i.e. no movements without the box. Three weeks later, however, a remarkable effect occurred. The patient telephoned us and pointed out to us, with considerable surprise, that his phantom arm had 'disappeared completely' and that all he had were the fingers and part of the palm dangling from the stump near the shoulder. Furthermore, he could now generate voluntary movements in his phantom fingers: something he could never achieve before our 'therapy' (e.g. he could make a 'precision' grip with his thumb and index finger). Patient D.S. was very surprised by all this because he had never heard of the clinical phenomenon of 'telescoping', but he seemed pleased because his phantom pain in the elbow, that he used to experience several times a day, had now disappeared along with the elbow. D.S. then stopped using the box, but six months later a follow up interview revealed that these effects were permanent. What we had achieved, therefore, may be the first known case of an 'amputation' of a phantom limb!

What caused patient D.S.'s phantom to be paralysed in the first place and why should the mirror produce those remarkable effects? It seems likely that when commands are sent from the premotor/motor cortex to the limbs, they are monitored simultaneously by the parietal lobes (perhaps after cerebellar relay), where one constructs a dynamic 'body image' (Critchley 1966; Brain & Walton 1969; Heilman 1985). In normal individuals, visual and proprioceptive feedback signals get sent back to these same areas for comparing intention and performance. If the feedback is contradictory (e.g. if the arm is paralysed or missing) the phantom eventually becomes immobile but restoring the feedback (e.g. using the virtual reality box) revives mobility in the phantom. However, if the device is used for a long time, the resulting flood of conflicting sensory information (e.g. from vision versus proprioception), may cause the signals from the limb to be 'gated' so that the arm disappears. Also, as a bonus, the pain disappears as well. (The fingers may persist because they are over-represented in the sensory cortex.) These conjectures can all be tested using modern imaging techniques such as PET or fMRI.

(*e*) *Visual feedback without moving the intact arm*

In the experiments described so far, the patient simultaneously attempts mirror symmetric movements with both arms and this is effective in temporarily restoring 'voluntary control' over the phantom. But notice that in these cases there are also two other potential sources of information besides the visual feedback: namely the proprioceptive feedback from the intact limb and the motor commands to the intact limb. These could be conveyed via the corpus callosum to the hemisphere that controls the phantom and may therefore contribute to the 'revival' of movements in the paralysed phantom. It is clear that in these patients at least, this information in not sufficient for producing phantom sensations. (Recall that even if mirror symmetric movements are attempted, they do not evoke sensations of movements in the phantom if the eyes are closed.) But is it possible that they are necessary?

To explore this we adopted a simple modification of our basic procedure: instead of using the patient's intact hand, we used the experimenter's corresponding hand to produce the mirror reflection. For practical reasons we were able to try the experiment only on two of our patients: P.N. N. and K.S. In both cases, movements were vividly experienced in the phantom even though they did not send motor commands to either hand. Apparently the visual cue was sufficiently compelling that it created a vivid feeling of joint movements in the phantom whether or not the patient moved the contralateral hand (and even though no commands were sent to the phantom). Patient K.S. noted, however, that the joint sensations were less vivid when the experimenter's hand was used than when he himself moved his fingers. (And this was not because of a lack of perfect resemblance between the patient's hand and the experimenter's since a gloved hand produced the same result.) We may conclude, therefore, that even though movements of the normal hand are not necessary for inducing movements in the phantom, they may nevertheless contribute to the sensations.

(*f*) *Induction of anatomically impossible finger positions in the phantom*

By using the experimenter's hand one can also convey the illusion that the patient's phantom fingers have adopted abnormal or 'anatomically impossible' positions. What would be the feelings generated in the phantom by such a procedure?

We tried this in P.N.N. and K.S. Ordinarily, if the patient places (say) her phantom on the right side of the mirror, the experimenter places his gloved left hand on the left side of the mirror. This creates the illusion of a resurrected gloved phantom. If the patient has 'placed' her phantom palm-down on the table, the experimenter would, obviously, also place his left hand palm down. But consider what would happen if the experimenter places his gloved right hand with the palm up on the table. To the subject this will look almost identical to the left hand palm down. If the experimenter then flexes his index finger or opposes the thumb, the patient will see his phantom perform an anatomically impossible hyperextension or opposition of these fingers.

We tried this four times on P.N.N.'s index finger. Each time she said she distinctly felt – and not just saw – the finger bending backwards. ('One would have thought that it should feel peculiar Doctor, but it doesn't. It feels exactly like the finger is bending backwards: like it isn't supposed to. But it doesn't feel peculiar or painful or anything like that'.) It would be interesting to repeat this result with a larger number of patients and with other types of 'impossible' movements. For example, would it be possible to induce an anatomically impossible lengthening of the arm using a Fresnel lens?

The result on patient K.S. was especially intriguing. In him, when we did exactly the same experiment with

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the thumb bending backward: he winced. ('Hey, it felt like an invisible hand was grabbing and pulling my thumb backward: producing a painful tugging sensation.') This is a remarkable result, for it suggests that at least under some conditions, even the mere visual appearance of a bending phantom thumb can evoke pain! This result flatly contradicts the view held by the A.I. community that the brain is composed of a number of autonomous 'modules' that sequentially perform various 'computations' on the sensory input. (Stuart Sutherland once described black-boxology as a branch of cognitive psychology that 'uses the ostentatious display of flow-diagrams as a substitute for thought.') Indeed, our results are much more consistent with the dynamic, interactive view of the brain proposed by Edelman (1993) and his colleagues.

(*g*) *Patient R.L.; intermanual referral of tactile sensations*

Next, we wondered whether other types of sensations can also be 'referred' from the normal hand to the phantom in the presence of visual feedback. (Such intermanual transfer of sensations to the phantom can occasionally be seen even without visual feed back (see, for example, Ramachandran 1994), but we wondered whether the effects might be enhanced by visually resurrecting the phantom.) We instructed patient R.L. to place his phantom on the right side of the mirror and look into the mirror at the reflection of his left hand so that the reflection was superimposed on the felt position of the phantom. When we then asked him to close his eyes and touched or stroked individual fingers of his left hand with a Q-tip, he reported that he felt the touch only in his left hand and there was no referral to his phantom. However, as soon as he opened his eyes and looked into the mirror, he exclaimed with some surprise, that he could clearly feel the tactile sensations in the exact mirror symmetric location on his phantom. (We compared eight 'eyes closed' trials interleaved with eight 'eyes open' trials and the referral was seen in all of the former and none of the latter.) However, when we dabbed ice cold water (0°) or hot water (86°) on his normal hand he reported feeling only the dabbing on the phantom: the temperature was not carried over. This is important for it rules out confabulation as a possible explanation of these effects. For if the patient was confabulating why should only touch be referred and not temperature? We conclude, therefore, that we are clearly dealing with a genuine sensory phenomenon. Certain Bimodal cells in the Parietal cortex described recently by Graziano *et al.* (1994) that have visual and tactile receptive fields 'superimposed' on the hand might provide a neural substrate for these curious effects.

(*h*) *Patient J.P.*

A second patient, J.P., also referred sensations from the normal hand to the phantom right hand. In him, the referral occurred even without the mirror-box, although he found that the sensations were much more vivid when the box was used.

Patient J.P. had suffered a traumatic amputation of his right arm, 45 days before we tested him. (See table 1) After verifying first that he was neurologically intact and that his 'mental status' was normal, we blindfolded him and touched various parts of his body and asked him where he experienced the sensations. When we touched individual points of the intact (left) limb, he reported that he could clearly feel the sensations on the corresponding mirror-symmetric location of the phantom hand. Similarly, a vibrator applied to the left hand was felt simultaneously as 'vibration' in the other hand. Fifteen touch stimuli were then delivered to the fingers in random order and accurate intermanual referral was seen every time. Furthermore, when we stroked his hand with a knee hammer over 5 cm, he experienced a corresponding excursion on the phantom. 16 stimuli were delivered, eight on the dorsum and eight on the palm. (Four being transverse and four coaxial.) Of these 16, the eight co-axially ones were referred to the phantom with the direction of movement, speed and location (palm versus dorsum) being 'carried over' faithfully. The transversely applied stimuli, however, were never referred to the phantom. We also tried passively dipping the intact fingers in either ice-cold (0°) water or hot water (86°). Interestingly, the patient reported that he could feel the 'dipping' consistently but on none of the 16 trials did he experience the heat or cold being referred to the phantom; it was felt only on the left hand. Finally, when we applied pinpricks to the normal hand he reported feeling a distinct skin indentation on the phantom but the pain was not carried over; on all eight trials it was felt only on the intact hand. No referral of sensations occurred from any other part of the body but, as in some of our other patients, stimuli delivered to the ipsilateral face were felt in the phantom hand. The intermanual referral effects remained stable across four successive testing sessions separated by one week intervals. Identical effects were also observed in the second patient L.C.: referral of touch, vibration and 'dipping' but not of temperature.

These effects cannot be the result of confabulation for four reasons. First, the patients themselves often experienced considerable surprise when they noticed these phenomena. Second, recall that there was referral of sensations such as touch, 'scraping,' 'dipping,' and vibration, but no referral of heat and cold. (If the patients were confabulating, why should they refer touch but not temperature and why should this be consistent across patients?) Third, although the sensations were felt immediately in the normal hand (as expected), there was often a slight delay (2–4 s) before it was experienced in the phantom and an echo like a persistence of the sensation in the phantom even after the stimulus was removed in the real hand. This was consistent across trials and across patients and, again, it is hard to see why it should occur if they were confabulating. And finally, recall that in J.P. coaxial movements on the hand were referred to the phantom but not transverse movements; a result that implies, once again, that one is dealing with a genuine sensory phenomenon. We suggest that the effects arise from activation of preexisting commissural connections. The

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reason temperature and pain were not referred intermanually may be that there are no commissual pathways concerned with these modalities. (See below, under summary and conclusions.)

We then asked J.P. to repeat the same procedure using the mirror-box so that his phantom was visually resurrected. He exclaimed almost immediately that this made the sensations much more vivid and intense. There appeared to be some attenuation of the referred sensation in the phantom when the eyes were closed, but when the hand was made visible in the mirror the sensations seemed as intense in the phantom as in his intact hand! And finally, by substituting the experimenter's left hand in the box, we were able to convey the visual illusion to the patient that the phantom was being touched, without touching his normal hand, and in this case, no referral occurred (zero out of eight trials). We may conclude, therefore, that even though visual 'confirmation' can enhance referred sensations, visual cues by themselves are not sufficient (at least in this one patient) to generate tactile sensations in the phantom. (Recall that visual cues were sufficient to generate proprioceptive sensations in the phantom).

In a more formal experiment, thresholds for referral of sensation (eyes open versus closed) were determined by a staircase procedure using Semmes monofilaments (Lafayette instruments). Each filament was applied to the normal hand and the patient was asked whether or not he could feel it. The filament number (strength) was then progressively increased (or decreased) until the patient could just feel (or stop feeling) the sensation. The stimulus was always applied to the normal hand and data were obtained for ten 'reversals' for each of four experimental conditions. In condition 1, we obtained simple touch thresholds for sensations felt in the normal hand when the eyes were closed. In condition 2, we obtained thresholds for sensations felt in the phantom hand (with stimuli applied to the normal hand and with eyes closed). In condition 3, thresholds for referral to the phantom were obtained while the patient watched his phantom being 'touched' in the mirror. (Strictly speaking this is not a formal 'threshold' measurement because the patient could always see when he was being touched and when he wasn't. However, in practice, we found that this problem could be overcome by instructing the patient to report 'yes' only when he actually felt the touch sensation.) And finally, we had the patient watching his normal hand while thresholds were obtained for sensations in that same hand.

The thresholds for the four conditions were: 3.84; 5.09; 4.68; and 3.84. Thus the threshold for referral to the phantom was clearly higher than for the normal hand itself, even when the eyes were closed; in other words, there were many trials in which the touch was felt on the normal hand but not referred to the phantom. (This finding provides yet another argument against confabulation). Furthermore, when the eyes were open so that he could 'see' the phantom being touched, the threshold was lowered considerably (condition 3; 4.68) which confirms our earlier informal observations that the referred sensations were much more vivid when the phantom was visually resurrected. And finally, the results of condition (4) imply that the enhancement of referral seen in (3) is not simply the effect of 'suggestion'; i.e. it was not a simple result of a criterion shift caused by his being able to see his phantom being touched. For if criterion effects were to play a role, a reduction in touch thresholds should also have been seen in the normal hand when the patient watched himself being touched.

Patient J.P. was sufficiently impressed with these effects that he decided to take the box home and try it as a therapeutic device. Whenever he experienced pain in his phantom fingers, he asked his twin brother to rub or massage his intact fingers while he watched the phantom being rubbed in the mirror. He reported to us two weeks later that he had tried the procedure at least two dozen times and it was effective each time in producing relief from pain, with the pain disappearing for about 2–3 h after the massage was applied. Obviously the experiment needs to be repeated double-blind, but if the result holds up it may have tremendous therapeutic potential for treating at least some types of phantom pain.

(*i*) *Patient D.B.*

Patient D.B. was a 23-year-old right handed man whose left arm was disarticulated at the shoulder following a crush injury to his arm in a car accident. We tested him three years after the amputation.

Results were very similar to what we observed in patient J.P. First, we blindfolded him, touched various parts of his body randomly and asked him what he experienced. During this initial testing session he referred sensation from the lower left face region to the phantom finger but there was no intermanual referral and no referral from any other part of the body to the phantom. We then had him look in the mirror and, this time, he reported with considerable surprise that he could actually feel his phantom being touched as he watched it being touched. And again, as in J.P., if the experimenter's hand replaced the patient's left hand, this effect did not occur suggesting that both the visual and the tactile input must be simultaneously present for the referral to occur.

During the second testing session on the following day, however, he reported intermanual referral even with his eyes closed but emphasized the sensations were amplified considerably if he also saw the phantom being touched in the mirror. Again, as in patient J.P., this cannot be the result of effects of suggestion because temperature (e.g. 'ice cold' and heat) were not referred whether or not he looked in the mirror. Also, the patient experienced considerable surprise that sensations applied to one hand were felt in the other. ('If it's all in the mind, why doesn't the ice feel cold in the phantom, Doctor?' he asked me.)

Again, we also conducted a more formal experiment on D.B. using Semmes monofilaments. Touch thresholds were determined for the normal (right) hand as well as for the referral of sensations to the phantom using a staircase procedure (eight reversals for each session). When D.B. closed his eyes, the touch threshold for his right hand was 3.98 (mean) whereas the

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'threshold' for referral to the phantom was 4.74. When he looked in the mirror, however, his threshold for referred sensations was 4.08. Once again, these data confirm that the referral was more pronounced when the patient could actually see his phantom being touched.

(*j*) *Control condition*

Finally, we also tried using the mirror-box procedure on four control subjects. They were instructed to place their hands on either side of the box and to look at the mirror reflection of (say) the left hand superimposed on the right hand: which was hidden by the mirror. On eight separate trials, each subject was asked to perform various types of movement with the other hand. (Prompting the subject was also ineffective in eliciting such sensation.) We also tried touching and stroking the left hand so that the subject could 'see' his/her other hand being touched and, again, this did not produce any referred sensations. We conclude, therefore, that the effects we have discovered are unique to phantom limbs.

It is worth noting, however, that even though none of the four subjects actually experienced the finger movements or the touching or stroking in the hand hidden from view, they all reported that the discrepancy felt odd and one of them noticed, in addition, that there was a very transient tingling sensation in that hand.

Also, although our mirror-box was effective only in the amputees, there are other circumstances in which kinesthetic sensations can be induced visually even in normal subjects (Rock & Harris 1967; Nielsen 1963). For example, if a small object is palpated while being viewed through a magnifying lens it not only looks larger – as expected – but feels larger as well, an effect that Rock has dubbed 'visual capture'. What we have seen in our amputees may therefore be regarded as a very amplified version of essentially the same phenomenon. Specifically, we suggest that the reason these visual capture effects are so much more vivid in amputees is that there are no countermanding signals from the amputated arm that would ordinarily contradict the visual signals.

5. CONCLUSIONS

Until about a decade ago, it was widely believed that no new neural connections can emerge in the adult mammalian brain: a dogma that was challenged by a number of pioneering studies on monkeys by Merzenich *et al.* (1983), Kaas *et al.* (1981), Pons *et al.* (1991) and Wall (1977). By using MEG (magnetoencephalophy), we showed recently that, consistent with these animal studies, reorganization also occurs on a massive scale in adult humans (Ramachandran 1993; Yang *et al.* 1994). For example, in four patients, after amputation of an arm, the sensory input from the face was found to have 'invaded' the adjacent hand territory in the sensory homunculus. Furthermore, in some of these amputees sensory stimuli applied to the face were perceived to simultaneously arise from the missing phantom hand; an effect that might be a direct perceptual correlate of the 'remapping' observed in the cortex. It remains to be seen, however, whether this effect occurs as a result of sprouting new axons or from unmasking pre-existing connections. We have seen the effect in one amputee just four weeks after amputation (Ramachandran *et al.* 1992), a result that would not be easy to reconcile with the sprouting hypothesis.

In the present study, three of the ten patients clearly referred sensations from the face to the phantom (patients J.P., D.S. and D.B.). It is unclear why the other patients did not have a map on the face but one possibility is that some compensatory changes occur in higher areas that lead to the deletion of anomalous sensations. Indeed, we have seen at least one patient with clear MEG evidence of remapping i.e. the face input had expanded into the hand region: but he did not refer sensations from the face to the phantom. It is possible that with the passage of time this patient had 'learned' to ignore the referred sensation because of the continuous absence of visual feedback.

The most striking observation reported in the present study, however, is the systematic, topographically organized referral of sensations intermanually from the normal hand to the phantom, an effect that occurred even without the mirror in three patients and only when the mirror was used, in the fourth. In L.C. this effect was seen in just 19 days, suggesting that new and precisely organized pathways – connecting the two cerebral hemispheres – can emerge with surprising rapidity even in the adult brain. What the functional role of such 'reserve troops' might be in the normal human brain remains wholly unclear but the observation could be regarded as unequivocal proof that such organized pathways can emerge under appropriate circumstances. Clearly, this must involve the activation of pre-existing commissural connections because there can be no question of axons sprouting over such large distances.

More specifically, we suggest that even in normal individuals, sensory input from (say) the left thumb might project not only to the right hemisphere but – via unidentified commissural pathways – to mirror symmetric points in the other hemisphere Calford 1991. This latent input may ordinarily be too weak to express itself, but when the right hand is amputated this input may become either disinhibited or progressively strengthened so that touching the left hand evokes sensations in the right hand as well. Perhaps there are no commissural pathways concerned with pain and temperature; which might explain why these sensations are not referred. In patient R.L., however, the reactivation may not reach threshold unless visual 'confirmation' is provided, using the mirror.

It is noteworthy that some of our patients also reported a disappearance of pain as soon as they used the mirror to unclench the hand and patient D.S. noted that his elbow pain had disappeared – for the first time in ten years – as a result of the 'telescoping'. Given the notorious susceptibility of pain to 'placebo' and suggestion, however, these effects need to be repeated on a large number of subjects using double-blind trials to see if the effect is a specific consequence

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of the visual feedback. Until such experiments are done, the procedure certainly should not be regarded as a 'treatment' for phantom pain.

It is worth emphasizing, also, that not all our patients experienced these effects. Our eighth patient (B.D.) had his arm amputated after a brachial avulsion and his phantom was in a permanently clenched, painful spasm when we saw him. He was very eager to participate and spent nearly a half an hour with our mirror trying to 'move' his paralysed arm and making every effort to unclench his fist. Yet in spite of his strenuous efforts he could not generate even a flicker of movement in the phantom. ('It's frustrating Doctor: I can see it move. I want it to move, but it doesn't move!') The tenth patient (K.S.) could move his phantom when he used the mirror but, even with prolonged use of the box, there was no relief from the continuous pain he experienced.

Whether these techniques prove clinically useful or not, however, we may draw four main conclusions based on these experiments.

1. The referral of sensations from the intact arm to the phantom, an observation that implies that new pathways that are precisely organized and functionally effective can emerge in the adult human brain in less than three weeks.

2. The mirror-box may provide a useful new tool for exploring inter-sensory effects in phantom limbs. Although there is a vast clinical literature on phantom limbs, such inter-sensory effects have never been explored before, perhaps because no simple technique was available for studying them. The stage is also set now for using currently available imaging techniques (fMRI and PET) in conjunction with the mirror-box for investigating these effects in detail.

3. The immediate restoration of vivid illusory movements in the phantom using a mirror; including the 'opening' of a tightly clenched phantom fist. This effect demonstrates that 'modules' concerned with vision and proprioception must interact to a much greater extent than previously assumed. It is especially interesting that such movements could be restored in a phantom that had been 'paralysed' for over ten years.

4. A total of three hours of visual experience distributed over three weeks, in patient D.S., permanently altered his body image, eliminated his elbow pain and restored his ability to move his fingers. This finding also demonstrates the tremendous lability of neural connections in the adult human brain and it may have some therapeutic implications for stroke-rehabilitation.

A more general implication of these observation is that we must give up a strictly hierarchical, modular view of the brain – the legacy of classical AI – and replace it with a more dynamic, interactive model in which 're-entrant' signalling may play an important role.

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