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**CHAPTER 2: "Knowing Where to**

My intention is to tell  
of bodies changed  
to different forms.

The heavens and all below them,  
Earth and her creatures,  
All change,  
And we, part of creation,  
Also must suffer

Ovid

Tom Sorenson vividly recalls the horrifying circumstances that led to the loss of his arm. He was driving home from soccer practice, tired and hungry from the exercise, when a car in the opposite lane swerved in front of him. Brakes squealed, Tom's car spun out of control and he was thrown from the driver's seat onto the ice plant bordering the freeway. As he was hurled through the air, Tom looked back and saw that his hand was still in the car, "gripping" the seat cushion—severed from his body like a prop in a Freddy Krueger horror film.

As a result of this gruesome mishap, Tom lost his left arm just above the elbow. He was seventeen years old, with just three months to go until high school graduation.

In the weeks afterward, even though he knew that his arm was gone, Tom could still feel its ghostly presence below the elbow. He could wiggle each "finger," "reach out" and "grab" objects that were within arm's reach. Indeed, his phantom arm seemed to be able to do anything that the real arm would have done automatically, such as warding off blows, breaking falls or patting his little brother on the back. Since Tom had been left-handed, his phantom would reach for the receiver whenever the telephone rang.

Tom was not crazy. His impression that his missing arm was still there is a classic example of a phantom limb—an arm or leg that lingers indefinitely in the minds of patients long after it has been lost in an accident or removed by a surgeon. Some wake up from anesthesia and are incredulous when told that their arm had to be sacrificed, because they still vividly feel its presence.<sup>1</sup> Only when they look under the sheets do they come to the shocking realization that the limb is really gone. Moreover, some of these patients experience excruciating pain in the phantom arm, hand or fingers, so much so that they contemplate suicide. The pain is not only unrelenting, it's also untreatable; no one has the foggiest idea of how it arises or how to deal with it.

As a physician I was aware that phantom limb pain poses a serious clinical problem. Chronic pain in a real body part such as the joint aches of arthritis or lower backache is difficult enough to treat, but how do you treat pain in a nonexistent limb? As a scientist, I was also curious about why the phenomenon occurs in the first place: Why would an arm persist in the patient's mind long after it had been removed? Why doesn't the mind simply accept the loss and "reshape" the body image? To be sure, this does happen in a few patients, but it usually takes years or decades. Why decades—why not just a week or a day? A study of this phenomenon, I realized, might not only help us understand the question of how the brain copes with a sudden and massive loss, but also help address the more fundamental debate over nature versus nurture—the extent to which our body image, as well as other aspects of our minds, are laid down by genes and the extent to which they are modified by experience. The persistence of sensation in limbs long after amputation had been noticed as far back as the sixteenth century by the French surgeon Ambroise Paré, and, not surprisingly, there is an elaborate folklore surrounding this phenomenon. After Lord Nelson lost his right arm during an unsuccessful attack on Santa Cruz de Tenerife, he experienced compelling phantom limb pains, including the unmistakable sensation of fingers digging into his phantom palm. The emergence of these ghostly sensations in his missing limb led the sea lord to proclaim that his phantom was "direct evidence for the existence of the soul." For if an arm can exist after it is removed, why can't the whole person survive physical annihilation of the body? It is proof, Lord Nelson claimed, for the existence of the spirit long after it has cast off its attire.

The eminent Philadelphia physician Silas Weir Mitchell<sup>2</sup> first coined the phrase "phantom limb" after the Civil War. In those pre-antibiotic days, gangrene was a common result of injuries and surgeons sawed infected limbs off thousands of wounded soldiers. They returned home with the phantoms, setting off new rounds of speculation about what might be causing them. Weir Mitchell himself was so surprised by the phenomenon that he published the first article on the subject under a pseudonym in a popular magazine called Lippincott's Journal rather than risk facing the ridicule from his colleagues that might have ensued had he published in a professional medical journal. Phantoms, when you think about it, are a rather spooky phenomenon.

Since Weir Mitchell's time there have been all kinds of speculations about phantoms, ranging from the sublime to the ridiculous. As recently as fifteen years ago, a paper in the Canadian Journal of Psychiatry stated that phantom limbs are merely the result of wishful thinking. The authors argued that the patient desperately wants his arm back and therefore experiences a phantom—in much the same way that a person may have recurring dreams or may even see "ghosts" of a recently deceased parent. This argument, as we shall see, is utter nonsense.

A second, more popular explanation for phantoms is that the frayed and curled-up nerve endings in the stump (neuromas) that originally supplied the hand tend to become inflamed and irritated, thereby fooling higher brain centers into thinking that the missing limb is still there. Though there are far too many problems with this nerve irritation theory, because it's a simple and convenient explanation, most physicians still cling to it.

There are literally hundreds of fascinating case studies, which appear in the older medical journals.

Some of the described phenomena have been confirmed repeatedly and still cry out for an explanation, whereas others seem like far-fetched products of the writer's own imagination. One of my favorites is about a patient who started experiencing a vivid phantom arm soon after amputation—nothing unusual so far—but after a few weeks developed a peculiar, gnawing sensation in his phantom. Naturally he was quite puzzled by the sudden emergence of these new sensations, but when he asked his physician why this was happening, the doctor didn't know and couldn't help. Finally, out of curiosity, the fellow asked, "Whatever happened to my arm after you removed it?" "Good question," replied the doctor, "you need to ask the surgeon." So the fellow called the surgeon, who said, "Oh, we usually send the limbs to the morgue." So the man called the morgue and asked, "What do you do with amputated arms?" They replied, "We send them either to the incinerator or to pathology. Usually we incinerate them."

"Well, what did you do with this particular arm? With my arm?" They looked at their records and said, "You know, it's funny. We didn't incinerate it. We sent it to pathology."

The man called the pathology lab. "Where is my arm?" he asked again. They said, "Well, we had too many arms, so we just buried it in the garden, out behind the hospital."

They took him to the garden and showed him where the arm was buried. When he exhumed it, he found it was crawling with maggots and exclaimed, "Well, maybe that's why I'm feeling these bizarre sensations in my arm." So he took the limb and incinerated it. And from that day on, his phantom pain disappeared.

Such stories are fun to tell, especially around a campfire at night, but they do very little to dispel the real mystery of phantom limbs. Although patients with this syndrome have been studied extensively since the turn of the century, there's been a tendency among physicians to regard them as enigmatic, clinical curiosities and almost no experimental work has been done on them. One reason for this is that clinical neurology historically has been a descriptive rather than an experimental science.

Neurologists of the nineteenth and early twentieth centuries were astute clinical observers, and many valuable lessons can be learned from reading their case reports. Oddly enough, however, they did not take the next obvious step of doing experiments to discover what might be going on in the brains of these patients; their science was Aristotelian rather than Galilean.<sup>3</sup> Given how immensely successful the experimental method has been in almost every other science, isn't it high time we imported it into neurology?

Like most physicians, I was intrigued by phantoms the very first time I encountered them and have been puzzled by them ever since. In addition to phantom arms and legs—which are common among amputees—I had also encountered women with phantom breasts after radical mastectomy and even a patient with a phantom appendix: The characteristic spasmodic pain of appendicitis did not abate after surgical removal, so much so that the patient refused to believe that the surgeon had cut it out! As a medical student, I was just as baffled as the patients themselves, and the textbooks I consulted only deepened the mystery. I read about a patient who experienced phantom erections after his penis had been amputated, a woman with phantom menstrual cramps following hysterectomy, and a gentleman

who had a phantom nose and face after the trigeminal nerve innervating his face had been severed in an accident.

All these clinical experiences lay tucked away in my brain, dormant until about six years ago, when my interest was rekindled by a scientific paper published in 1991 by Dr. Tim Pons of the National Institutes of Health, a paper that propelled me into a whole new direction of research and eventually brought Tom into my laboratory. But before I continue with this part of the story, we need to look closely at the anatomy of the brain—particularly at how various body parts such as limbs are mapped onto the cerebral cortex, the great convoluted mantle on the surface of the brain. This will help you understand what Dr. Pons discovered and, in turn, how phantom limbs emerge.

Of the many strange images that have remained with me from my medical school days, perhaps none is more vivid than that of the deformed little man you see in Figure 2.1 draped across the surface of the cerebral cortex—the so-called Penfield homunculus. The homunculus is the artist's whimsical depiction of the manner in which different points on the body surface are mapped onto the surface of the brain—the grotesquely deformed features are an attempt to indicate that certain body parts such as the lips and tongue are grossly over-represented.

**Figure 2.1** (Image not reproduced in this .pdf

[(a) The representation of the body surface on the surface of the brain (as discovered by Wilder Penfield) behind the central sulcus. There are many such maps, but for clarity only one is shown here. The homunculus (“little man”) is upside down for the most part, and his feet are tucked onto the medial surface (inner surface) of the parietal lobe near the very top, whereas the face is down near the bottom of the outer surface. The face and hand occupy a disproportionately large share of the map. Notice also that the face area is below the hand area instead of being where it should—near the neck—and the genitals are represented below the foot. Could this provide an anatomical explanation for foot fetishes? (b) A whimsical three-dimensional model of the Penfield homunculus—the little man in the brain—depicting the representation of body parts. Notice the gross over-representation of mouth and hands. Reprinted with permission from the British Museum, London.]

The map was drawn from information gleaned from real human brains. During the 1940s and 1950s, the brilliant Canadian neurosurgeon Wilder Penfield performed extensive brain surgeries on patients under local anesthetic (there are no pain receptors in the brain, even though it is a mass of nerve tissue). Often, much of the brain was exposed during the operation and Penfield seized this opportunity to do experiments that had never been tried before. He stimulated specific regions of the patients' brains with an electrode and simply asked them what they felt. All kinds of sensations, images, and even memories were elicited by the electrode and the areas of the brain that were responsible could be mapped.

Among other things, Penfield found a narrow strip running from top to bottom down both sides of the brain where his electrode produced sensations localized in various parts of the body. Up at the top of

the brain, in the crevice that separates the two hemispheres, electrical stimulation elicited sensations in the genitals. Nearby stimuli evoked sensations in the feet. As Penfield followed this strip down from the top of the brain, he discovered areas that receive sensations from the legs and trunk, from the hand (a large region with a very prominent representation of the thumb), the face, the lips and finally the thorax and voicebox. This "sensory homunculus," as it is now called, forms a greatly distorted representation of the body on the surface of the brain, with the parts that are particularly important taking up disproportionately large areas. For example, the area involved with the lips or with the fingers takes up as much space as the area involved with the entire trunk of the body. This is presumably because your lips and fingers are highly sensitive to touch and are capable of very fine discrimination, whereas your trunk is considerably less sensitive, requiring less cortical space. For the most part, the map is orderly though upside down: The foot is represented at the top and the outstretched arms are at the bottom. However, upon close examination, you will see that the map is not entirely continuous. The face is not near the neck, where it should be, but is below the hand. The genitals, instead of being between the thighs, are located below the foot.<sup>4</sup>

These areas can be mapped out with even greater precision in other animals, particularly in monkeys. The researcher inserts a long thin needle made of steel or tungsten into the monkey's somatosensory cortex—the strip of brain tissue described earlier. If the needle tip comes to lie right next to the cell body of a neuron and if that neuron is active, it will generate tiny electrical currents that are picked up by the needle electrode and amplified. The signal can be displayed on an oscilloscope, making it possible to monitor the activity of that neuron.

For example, if you put an electrode into the monkey's somatosensory cortex and touch the monkey on a specific part of its body, the cell will fire. Each cell has its territory on the body surface—its own small patch of skin, so to speak—to which it responds. We call this the cell's receptive field. A map of the entire body surface exists in the brain, with each half of the body mapped onto the opposite side of the brain.

While animals are logical experimental subjects in which to examine the detailed structure and function of the brain's sensory regions, they have one obvious problem: Monkeys can't talk.

Therefore, they cannot tell the experimenter, as Penfield's patients could, what they are feeling. Thus a large and important dimension is lost when animals are used in such experiments.

But despite this obvious limitation, a great deal can be learned by doing the right kinds of experiments. For instance, as we've noted, one important question concerns nature versus nurture: Are these body maps on the surface of the brain fixed, or can they change with experience as we grow from newborns to infancy, through adolescence and into old age? And even if the maps are already there at birth, to what extent can they be modified in the adult?<sup>5</sup>

It was these questions that prompted Tim Pons and his colleagues to embark on their research. Their strategy was to record signals from the brains of monkeys who had undergone dorsal rhizotomy—a procedure in which all the nerve fibers carrying sensory information from one arm into the spinal cord are completely severed.<sup>6</sup> Eleven years after the surgery, they anesthetized the animals, opened their skulls and recorded from the somatosensory map. Since the monkey's paralyzed arm was not sending messages to the brain, you would not expect to record any signals when you touch the monkey's

useless hand and record from the "hand area" of the brain. There should be a big patch of silent cortex corresponding to the affected hand.

Indeed, when the researchers stroked the useless hand, there was no activity in this region. But to their amazement they found that when they touched the monkey's face, the cells in the brain corresponding to the "dead" hand started firing vigorously. (So did cells corresponding to the face, but those were expected to fire.) It appeared that sensory information from the monkey's face not only went to the face area of the cortex, as it would in a normal animal, but it had also invaded the territory of the paralyzed hand!

The implications of this finding are astonishing: It means that you can change the map; you can alter the brain circuitry of an adult animal, and connections can be modified over distances spanning a centimeter or more.

Upon reading Pons's paper, I thought, "My God! Might this be an explanation for phantom limbs?" What did the monkey actually "feel" when its face was being stroked? Since its "hand" cortex was also being excited, did it perceive sensations as arising from the useless hand as well as the face? Or would it use higher brain centers to reinterpret the sensations correctly as arising from the face alone? The monkey of course was silent on the subject.

It takes years to train a monkey to carry out even very simple tasks, let alone signal what part of its body is being touched. Then it occurred to me that you don't have to use a monkey. Why not answer the same question by touching the face of a human patient who has lost an arm? I telephoned my colleagues Dr. Mark Johnson and Dr. Rita Finkelstein in orthopedic surgery and asked, "Do you have any patients who have recently lost an arm?"

That is how I came to meet Tom. I called him up right away and asked whether he would like to participate in a study. Although initially shy and reticent in his mannerisms, Tom soon became eager to participate in our experiment. I was careful not to tell him what we hoped to find, so as not to bias his responses. Even though he was distressed by "itching" and painful sensations in his phantom fingers, he was cheerful, apparently pleased that he had survived the accident.

With Tom seated comfortably in my basement laboratory, I placed a blindfold over his eyes because I didn't want him to see where I was touching him. Then I took an ordinary Q-tip and started stroking various parts of his body surface, asking him to tell me where he felt the sensations. (My graduate student, who was watching, thought I was crazy.)

I swabbed his cheek. "What do you feel?"

"You are touching my cheek."

"Anything else?"

"Hey, you know it's funny," said Tom. "You're touching my missing thumb, my phantom thumb."

I moved the Q-tip to his upper lip. "How about here?"

"You're touching my index finger. And my upper lip."

"Really? Are you sure?"

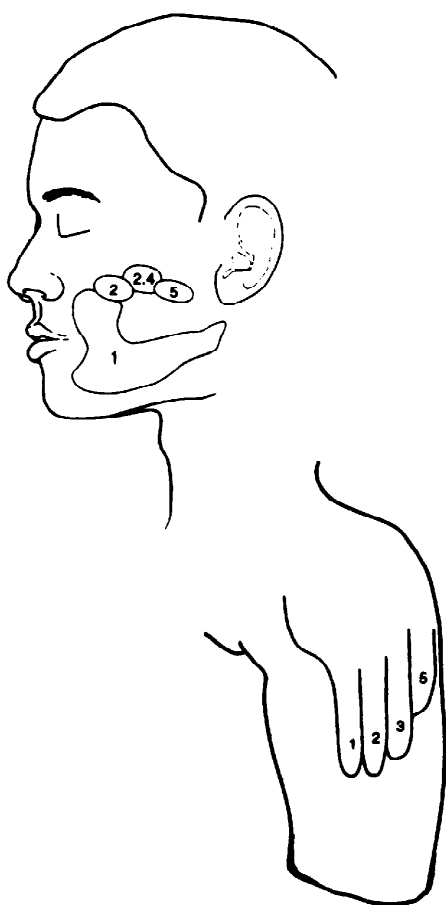
"Yes. I can feel it both places."

"How about here?" I stroked his lower jaw with the swab.

"That's my missing pinkie."

I soon found a complete map of Tom's phantom hand—on his face! I realized that what I was seeing was perhaps a direct perceptual correlate of the remapping that Tim Pons had seen in his monkeys. For there is no other way of explaining why touching an area so far away from the stump—namely, the face—should generate sensations in the phantom hand; the secret lies in the peculiar mapping of body parts in the brain, with the face lying right beside the hand.<sup>7</sup>

I continued this procedure until I had explored Tom's entire body surface. When I touched his chest, right shoulder, right leg or lower back, he felt sensations only in those places and not in the phantom. But I also found a second, beautifully laid out "map" of his missing hand—tucked onto his left upper arm a few inches above the line of amputation (Figure 2.2). Stroking the skin surface on this second map also evoked precisely localized sensations on the individual fingers: Touch here and he says, "Oh, that's my thumb," and so on.



**Figure 2.2** [Points on the body surface that yield referred sensations in the phantom hand (this patient's left hand had been amputated prior to our testing him.) Notice that there is a complete map of all the fingers (labelled 1 to 5) on the face and a second map on the upper arm. The sensory input from these two patches of skin is now apparently activating the hand territory of the brain (either in the thalamus or in the cortex). So when these points are touched, the sensations are felt to arise from the missing hand as well.]

Why were there two maps instead of just one? If you look again at the Penfield map, you'll see that the hand area in the brain is flanked below by the face area and above by the upper arm and shoulder area. Input from Tom's hand area was lost after the amputation, and consequently, the sensory fibers originating from Tom's face—which normally activate only the face area in his cortex—now invaded the vacated territory of the hand and began to drive the cells there. Therefore, when I touched Tom's face, he also felt sensations in his phantom hand. But if the invasion of the hand cortex also results from sensory fibers that normally innervate the brain region above the hand cortex (that is, fibers that originate in the upper arm and shoulder), then touching points on the upper arm should also evoke sensations in the phantom hand. And indeed I was able to map out these points on the arm above

Tom's stump. So, this sort of arrangement is precisely what one would expect: One cluster of points on the face that evoke sensations in the phantom and a second cluster on the upper arm, corresponding to the two body parts that are represented on either side (above and below) of the hand representation in the brain.<sup>8</sup>

It's not often in science (especially neurology) that you can make a simple prediction like this and confirm it with a few minutes of exploration using a Q-tip. The existence of two clusters of points suggests strongly that remapping of the kind seen in Pons's monkeys also occurs in the human brain. But there was still a nagging doubt: How can we be sure that such changes are actually taking place—that the map is really changing in people like Tom? To obtain more direct proof, we took advantage of a modern neuroimaging technique called magneto-encephalography (MEG), which relies on the principle that if you touch different body parts, the localized electrical activity evoked in the Penfield map can be measured as changes in magnetic fields on the scalp. The major advantage of the technique is that it is non-invasive; one does not have to open the patient's scalp to peer inside the brain.

Using MEG, it is relatively easy in just a two-hour session to map out the entire body surface on the brain surface of any person willing to sit under the magnet. Not surprisingly, the map that results is quite similar to the original Penfield homunculus map, and there is very little variation from person to person in the gross layout of the map. When we conducted MEGs on four arm amputees, however, we found that the maps had changed over large distances, just as we had predicted. For example, a glance at Figure 2.3 reveals that the hand area (hatched) is missing in the right hemisphere and has been invaded by the sensory input from the face (in white) and upper arm (in gray). These observations, which I made in collaboration with a medical student, Tony Yang, and the neurologists Chris Gallen and Floyd Bloom, were in fact the first direct demonstration that such large-scale changes in the organization of the brain could occur in adult humans.

**Figure 2.3** (Image not reproduced in this .pdf

[Magneto-encephalography (MEG) image superimposed on a magnetic resonance image (MRI) of the brain in a patient whose right arm was amputated below the elbow. The brain is viewed from the top. The right hemisphere shows normal activation of the hand (hatched), face (black) and upper arm (white) areas of the cortex corresponding to the Penfield map. In the left hemisphere there is no activation corresponding to the missing right hand, but the activity from the face and upper arm has now “spread” to this area.]

The implications are staggering. First and foremost, they suggest that brain maps can change, sometimes with astonishing rapidity. This finding flatly contradicts one of the most widely accepted dogmas in neurology—the fixed nature of connections in the adult human brain. It had always been assumed that once this circuitry, including the Penfield map, has been laid down in fetal life or in early infancy, there is very little one can do to modify it in adulthood. Indeed, this presumed absence of plasticity in the adult brain is often invoked to explain why there is so little recovery of function after brain injury and why neurological ailments are so notoriously difficult to treat. But the evidence from Tom shows—contrary to what is taught in textbooks—that new, highly precise and functionally

effective pathways can emerge in the adult brain as early as four weeks after injury. It certainly doesn't follow that revolutionary new treatments for neurological syndromes will emerge from this discovery right away, but it does provide some grounds for optimism.

Second, the findings may help explain the very existence of phantom limbs. The most popular medical explanation, noted earlier, is that nerves that once supplied the hand begin to innervate the stump.

Moreover, these frayed nerve endings form little clumps of scar tissue called neuromas, which can be very painful. When neuromas are irritated, the theory goes, they send impulses back to the original hand area in the brain so that the brain is "fooled" into thinking the hand is still there: hence the phantom limb and the notion that the accompanying pain arises because the neuromas are painful.

On the basis of this tenuous reasoning, surgeons have devised various treatments for phantom limb pain in which they cut and remove neuromas. Some patients experience temporary relief, but surprisingly, both the phantom and the associated pain usually return with a vengeance. To alleviate this problem, sometimes surgeons perform a second or even a third amputation (making the stump shorter and shorter), but when you think about this, it's logically absurd. Why would a second amputation help? You'd simply expect a second phantom, and indeed that's usually what happens; it's an endless regress problem.

Surgeons even perform dorsal rhizotomies to treat phantom limb pain, cutting the sensory nerves going into the spinal cord. Sometimes it works; sometimes it doesn't. Others try the even more drastic procedure of cutting the back of the spinal cord itself—a cordotomy—to prevent impulses from reaching the brain, but that, too, is often ineffective. Or they will go all the way into the thalamus, a brain relay station that processes signals before they are sent to the cortex, and again find that they have not helped the patient. They can chase the phantom farther and farther into the brain, but of course they'll never find it.

Why? One reason, surely, is that the phantom doesn't exist in any one of these areas; it exists in more central parts of the brain, where the remapping has occurred. To put it crudely, the phantom emerges not from the stump but from the face and jaw, because every time Tom smiles or moves his face and lips, the impulses activate the "hand" area of his cortex, creating the illusion that his hand is still there. Stimulated by all these spurious signals, Tom's brain literally hallucinates his arm, and perhaps this is the essence of a phantom limb. If so, the only way to get rid of the phantom would be to remove his jaw. (And if you think about it, that wouldn't help either. He'd probably end up with a phantom jaw. It's that endless regress problem again.)

But remapping can't be the whole story. For one thing, it doesn't explain why Tom or other patients experience the feeling of being able to move their phantoms voluntarily or why the phantom can change its posture. Where do these movement sensations originate? Second, remapping doesn't account for what both doctor and patient are most seriously concerned about—the genesis of phantom pain. We'll explore these two subjects in the next chapter.

When we think of sensations arising from skin we usually only think of touch. But, in fact, distinct neural pathways that mediate sensations of warmth, cold and pain also originate on the skin surface. These sensations have their own target areas or maps in the brain, but the paths used by them may be interlaced with each other in complicated ways. If so, could such remapping also occur in these

evolutionarily older pathways quite independently of the remapping that occurs for touch? In other words, is the remapping seen in Tom and in Pons's monkeys peculiar to touch, or does it point to a very general principle—would it occur for sensations like warmth, cold, pain or vibration? And if such remapping were to occur would there be instances of accidental "cross-wiring" so that a touch sensation would evoke warmth or pain? Or would they remain segregated? The question of how millions of neural connections in the brain are hooked up so precisely during development—and the extent to which this precision is preserved when they are reorganized after injury—is of great interest to scientists who are trying to understand the development of pathways in the brain.

To investigate this, I placed a drop of warm water on Tom's face. He felt it there immediately but also said that his phantom hand felt distinctly warm. Once, when the water accidentally trickled down his face, he exclaimed with considerable surprise that he could actually feel the warm water trickling down the length of his phantom arm. He demonstrated this to me by using his normal hand to trace out the path of the water down his phantom. In all my years in neurology clinics, I had never seen anything quite so remarkable—a patient systematically mis-localizing a complex sensation such as a "trickle" from his face to his phantom hand.

These experiments imply that highly precise and organized new connections can be formed in the adult brain in a few days. But they don't tell us how these new pathways actually emerge, what the underlying mechanisms are at the cellular level.

I can think of two possibilities. First, the reorganization could involve sprouting—the actual growth of new branches from nerve fibers that normally innervate the face area toward cells in the hand area in the cortex. If this hypothesis were true, this would be quite remarkable since it is difficult to see how highly organized sprouting could take place over relatively long distances (in the brain several millimeters might as well be a mile) and in such a short period. Moreover, even if sprouting occurs, how would the new fibers "know" where to go? One can imagine a higgledy-piggledy jumble of connections, but not precisely organized pathways.

The second possibility is that there is in fact a tremendous redundancy of connections in the normal adult brain but that most of them are nonfunctional or have no obvious function. Like reserve troops, they may be called into action only when needed. Thus even in healthy normal adult brains there might be sensory inputs from the face to the brain's face map and to the hand map area as well. If so, we must assume that this occult or hidden input is ordinarily inhibited by the sensory fibers arriving from the real hand. But when the hand is removed, this silent input originating from the skin on the face is unmasked and allowed to express itself so that touching the face now activates the hand area and leads to sensations in the phantom hand. Thus every time Tom whistles, he might feel a tingling in his phantom arm.

We have no way at present of easily distinguishing between these two theories, although my hunch is that both mechanisms are at work. After all, we had seen the effect in Tom in less than four weeks and this seems too short a time for sprouting to take place. My colleague at the Massachusetts General Hospital Dr. David Borsook<sup>9</sup> has seen similar effects in a patient just twenty-four hours after amputation, and there is no question of sprouting's occurring in such a short period. The final answer to this will come from simultaneously tracking perceptual changes and brain changes (using imaging)

in a patient over a period of several days. If Borsook and I are right, the completely static picture of these maps that you get from looking at textbook diagrams is highly misleading and we need to rethink the meaning of brain maps completely. Far from signaling a specific location on the skin, each neuron in the map is in a state of dynamic equilibrium with other adjacent neurons; its significance depends strongly on what other neurons in the vicinity are doing (or not doing).

These findings raise an obvious question: What if some body part is lost other than the hand? Will the same kind of remapping occur? When my studies on Tom were first published, I got many letters and phone calls from amputees wanting to know more. Some of them had been told that phantom sensations are imaginary and were relieved to learn that that isn't true. (Patients always find it comforting to know that there is a logical explanation for their otherwise inexplicable symptoms; nothing is more insulting to a patient than to be told that his pain is "all in the mind.")

One day I got a call from a young woman in Boston. "Dr. Ramachandran," she said, "I'm a graduate student at Beth Israel Hospital and for several years I've been studying Parkinson's disease. But recently I decided to switch to the study of phantom limbs."

"Wonderful," I said. "The subject has been ignored far too long. Tell me what you are studying."

"Last year I had a terrible accident on my uncle's farm. I lost my left leg below the knee and I've had a phantom limb ever since. But I'm calling to thank you because your article made me understand what is going on." She cleared her throat. "Something really strange happened to me after the amputation that didn't make sense. Every time I have sex I experience these strange sensations in my phantom foot. I didn't dare tell anybody because it's so weird. But when I saw your diagrams, that in the brain the foot is next to the genitals, it became instantly clear to me."

She had experienced and understood, as few of us ever will, the remapping phenomenon. Recall that in the Penfield map the foot is beside the genitals. Therefore, if a person loses a leg and is then stimulated in the genitals, she will experience sensations in the phantom leg. This is what you'd expect if input from the genital area were to invade the territory vacated by the foot.

The next day the phone rang again. This time it was an engineer from Arkansas.

"Is this Dr. Ramachandran?"

"Yes."

"You know, I read about your work in the newspaper, and it's really exciting. I lost my leg below the knee about two months ago but there's still something I don't understand. I'd like your advice."

"What's that?"

"Well, I feel a little embarrassed to tell you this."

I knew what he was going to say, but unlike the graduate student, he didn't know about the Penfield map.

"Doctor, every time I have sexual intercourse, I experience sensations in my phantom foot. How do you explain that? My doctor said it doesn't make sense."

"Look," I said. "One possibility is that the genitals are right next to the foot in the body's brain maps. Don't worry about it."

He laughed nervously. "All that's fine, doctor. But you still don't understand. You see, I actually experience my orgasm in my foot. And therefore it's much bigger than it used to be because it's no

longer just confined to my genitals.”

Patients don't make up such stories. Ninety-nine percent of the time they're telling the truth, and if it seems incomprehensible, it's usually because we are not smart enough to figure out what's going on in their brains. This gentleman was telling me that he sometimes enjoyed sex more after his amputation. The curious implication is that it's not just the tactile sensation that transferred to his phantom but the erotic sensations of sexual pleasure as well. (A colleague suggested I title this book "The Man Who Mistook His Foot for a Penis.")

This makes me wonder about the basis of foot fetishes in normal people, a subject that—although not exactly central to our mental life—everyone is curious about. (Madonna's book, *Sex*, has a whole chapter devoted to the foot.) The traditional explanation for foot fetishes comes, not surprisingly, from Freud. The penis resembles the foot, he argues, hence the fetish. But if that's the case, why not some other elongated body part? Why not a hand fetish or a nose fetish? I suggest that the reason is quite simply that in the brain the foot lies right next to the genitalia. Maybe even many of us so-called normal people have a bit of cross-wiring which would explain why we like to have our toes sucked. The journeys of science are often tortuous with many unexpected twists and turns, but I never suspected that I would begin seeking an explanation for phantom limbs and end up explaining foot fetishes as well.

Given these assumptions, other predictions follow.<sup>10</sup> What happens when the penis is amputated? Carcinoma of the penis is sometimes treated with amputation, and many of these patients experience a phantom penis—sometimes even phantom erections! In such cases you would expect that stimulation of the feet would be felt in the phantom penis. Would such a patient find tap dancing especially enjoyable?

What about mastectomy? An Italian neurologist, Dr. Salvatore Aglioti, recently found that a certain proportion of women with radical mastectomies experience vivid phantom breasts. So, he asked himself, what body parts are mapped next to the breast? By stimulating adjacent regions on the chest he found that parts of the sternum and clavicle, when touched, produce sensations in the phantom nipple. Moreover, this remapping occurred just two days after surgery.

Aglioti also found to his surprise that one third of the women with radical mastectomies tested reported tingling, erotic sensations in their phantom nipples when their earlobes were stimulated. But this happened only in the phantom breast, not in the real one on the other side. He speculated that in one of the body maps (there are others besides the Penfield map) the nipple and ear are next to each other. This makes you wonder why many women report feeling erotic sensations when their ears are nibbled during sexual foreplay. Is it a coincidence, or does it have something to do with brain anatomy? (Even in the original Penfield map, the genital area of women is mapped right next to the nipples.)

A less titillating example of remapping also involving the ear came from Dr. A. T. Caccace, a neurologist who told me about an extraordinary phenomenon called gaze tinnitus.

People with this condition have a weird problem. When they look to the left (or right), they hear a ringing sound. When they look straight ahead, nothing happens. Physicians have known about this syndrome for a long time but were stymied by it. Why does it happen when the eyes deviate? Why

does it happen at all?

After reading about Tom, Dr. Caccace was struck by the similarity between phantom limbs and gaze tinnitus, for he knew that his patients had suffered damage to the auditory nerve—the major conduit connecting the inner ear to the brain stem. Once in the brain stem the auditory nerve hooks up with the auditory nucleus, which is right next to another structure called the oculomotor nerve nucleus. This second, adjacent structure sends commands to the eyes, instructing them to move. Eureka! The mystery is solved.<sup>11</sup> Because of the patient's damage, the auditory nucleus no longer gets input from one ear. Axons from the eye movement center in the cortex invade the auditory nucleus so that every time the person's brain sends a command to move the eyes, that command is sent inadvertently to the auditory nerve nucleus and translated into a ringing sound.

The study of phantom limbs offers fascinating glimpses of the architecture of the brain, its astonishing capacity for growth and renewal<sup>12</sup> and may even explain why playing footsie is so enjoyable. But about half the people with phantom limbs also experience the most unpleasant manifestation of the phenomenon—phantom limb pain. Real pain, such as the pain of cancer, is hard enough to treat; imagine the challenge of treating pain in a limb that isn't there! There is very little that can be done, at the moment, to alleviate such pain, but perhaps the remapping that we observed with Tom may help explain why it happens. We know, for instance, that intractable phantom pain may develop weeks or months after the limb is amputated. Perhaps as the brain adjusts and cells slowly make new connections, there is a slight error in the remapping so that some of the sensory input from touch receptors is accidentally connected to the pain areas of the brain. If this were to happen, then every time the patient smiled or accidentally brushed his cheek, the touch sensations would be experienced as excruciating pain. This is almost certainly not the whole explanation for phantom pain (as we shall see in the next chapter), but it's a good place to start.

As Tom left my office one day, I couldn't resist asking him an obvious question. During the last four weeks, had he ever noticed any of these peculiar referred sensations in his phantom hand when his face had been touched—when he shaved every morning, for example?

"No, I haven't," he replied, "but you know, my phantom hand sometimes itches like crazy and I never know what to do about it. But now," he said, tapping his cheek and winking at me, "I know exactly where to scratch!"

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### **Ramachandran's Footnotes** (pp. 266-269)

1. Throughout this book I use fictitious names for patients. The place, time and circumstances have also been altered substantially, but the clinical details are presented as accurately as possible. For more detailed clinical information, the reader should consult the original scientific articles.

In one or two instances when I describe a classic syndrome (such as the neglect syndrome in Chapter 6), I use several patients to create composites of the kind used in neurology textbooks in order to emphasize salient aspects of the disorder, even though no single patient may display all the symptoms and signs described.

2. Silas Weir Mitchell, 1872; Sunderland, 1972.

3. Aristotle was an astute observer of natural phenomena, but it never occurred to him that you could do experiments; that you could generate conjectures and proceed to test them systematically. For instance, he believed that women had fewer teeth than men; all he needed to do to verify or refute the theory was to ask a number of men and women to open their mouths so he could count their teeth. Modern experimental science really began with Galileo. It astonishes me when I sometimes hear developmental psychologists assert that babies are "born scientists," because it is perfectly clear to me that even adults are not. If the experimental method is completely natural to the human mind—as they assert—why did we have to wait so many thousands of years for Galileo and the birth of the experimental method? Everyone believed that big, heavy objects fall much faster than light ones, and all it took was a five-minute experiment to disprove it. (In fact, the experimental method is so alien to the human mind that many of Galileo's colleagues dismissed his experiments on falling bodies even after seeing them with their own eyes! ) And even to this day, three hundred years after the scientific revolution began, people have great difficulty in understanding the need for a "control experiment" or "double-blind" studies. (A common fallacy is, I got better after I took pill A, therefore I got better because I took pill A.)

4. Penfield and Rasmussen, 1950.

The reason for this peculiar arrangement is unclear and probably lost in our phylogenetic past. Martha Farah of the University of Pennsylvania has proposed a hypothesis that is consistent with my view (and Merzenich's) that brain maps are highly malleable. She points out that in the curled-up fetus, the arms are usually bent at the elbow with the hands touching the cheek and the legs are bent with the feet touching the genitals. The repeated coactivation of these body parts and the synchronous firing of corresponding neurons in the fetus may have resulted in their being laid down close to each other in the brain. Her idea is ingenious, but it doesn't explain why in other brain areas (S2 in the cortex) the foot (not just the hand) lies next to the face as well. My own bias is to think that even though the maps are modifiable by experience, the basic blueprint for them is genetic.

5. The first clear experimental demonstration of "plasticity" in the central nervous system was provided by Patrick Wall of the University College, London, 1977, and by Mike Merzenich, a distinguished neuroscientist at the University of California in San Francisco, 1984.

The demonstration that sensory input from the hand can activate the "face area" of the cortex in adult monkeys comes from Tim Pons and his colleagues 1991.

6. When people are pitched from a motorcycle at high speed, one arm is often partially wrenched from the shoulder, producing a kind of naturally occurring rhizotomy. As the arm is pulled, both the sensory (dorsal) and motor (ventral) nerve roots going from the arm into the spine are yanked off the spinal cord so that the arm becomes completely paralysed and devoid of sensation even though it remains attached to the body. The question is, How much function—if any—can people recover in the arm during rehabilitation? To explore this, physiologists cut the sensory nerves going from the arm into the spinal cord in a group of monkeys. Their goal was to try to re-educate the monkeys to use the arm, and a great deal of valuable information was obtained from studying these animals (Taub et al., 1993 ). Eleven years after this study was done these monkeys became a cause celebre when animal rights activists complained that the experiment was needlessly cruel. The so-called Silver Spring

monkeys were soon sent to the equivalent of an old age home for primates and, because they were said to be suffering, scheduled to be killed.

Dr. Pons and his collaborators agreed to the euthanasia but decided first to record from their brains to see whether anything had changed. The monkeys were anesthetized before the recordings were made, so that they would not feel any pain during the procedure.

7. Ramachandran et al., 1992a, b; 1993;1994;1996. Ramachandran, Hirstein and Rogers-Ramachandran, 1998.

8. It had been noticed by many previous researchers (Weir Mitchell, 1871) that stimulating certain trigger points on the stump often elicits sensations from missing fingers. William James (1887) once wrote, "A breeze on the stump is felt as a breeze on the phantom" (see also an important monograph by Cronholm, 1951). Unfortunately, neither Penfield's map nor the results of Pons and his collaborators were available at the time, and these early observations were therefore open to several interpretations. For example, the severed nerves in the stump would be expected to reinnervate the stump; if they did, that might explain why sensations from this region are referred to the fingers. Even when points remote from the stump elicited referred sensations, the effect was often attributed to diffuse connections in a "neuromatrix" (Melzack, 1990). What was novel about our observations is that we discovered an actual topographically organized map on the face and also found that relatively complex sensations such as "trickling," "metal" and "rubbing" (as well as warmth, cold and vibration) were referred from the face to the phantom hand in a modality-specific manner. Obviously, this cannot be attributed to accidental stimulation of nerve endings on the stump or to "diffuse" connections. Our observations imply instead that highly precise and organized new connections can be formed in the adult brain with extreme rapidity, at least in some patients.

Furthermore, we have tried to relate our findings in a systematic way to physiological results, especially the "remapping" experiments of Pons et al., 1991. We have suggested, for example, that the reason we often see two clusters of points—one on the lower face region and a second set near or around the amputation line—is that the map of the hand on the sensory homunculus in the cortex and the thalamus is flanked on one side by the face and the other side by the upper arm, shoulder and axilla. If the sensory input from the face and from the upper arm above the stump were to "invade" the cortical territory of the hand, one would expect precisely this sort of clustering of points. This principle allows one to dissociate proximity of points on the body surface from proximity of points in brain maps, an idea that we refer to as the remapping hypothesis of referred sensations. If the hypothesis is correct, then one would also expect to see referral from the genitals to the foot after leg amputation, since these two body parts are adjacent on the Penfield map. (See Ramachandran, 1993b; Aglioti et al., 1994.) But one would never see referral from the face to a phantom foot or from the genitals to a phantom arm. Also see note 10.

9. Recently David Borsook, Hans Breiter and their colleagues at the Massachusetts General Hospital (MGH) have shown that in some patients sensations such as touch, paintbrush, rubbing and pinpricks are referred (in a modality-specific manner) from the face to the phantom just a few hours after amputation (Borsook et al., 1998). This makes it clear that disinhibition or "masking" of pre-existing

connections must at least contribute to the effect, although some sprouting of new connections probably occurs as well.

10. If the remapping hypothesis is correct, then cutting the trigeminal nerve (supplying half the face) should result in the exact opposite of what we noticed in Tom. In such a patient, touching the hand should cause sensations to emerge in the face (Ramachandran, 1994). Stephanie Clark and her colleagues recently tested this prediction in an elegant and meticulous series of experiments. Their patient had the trigeminal nerve ganglion cut because a tumor had to be removed in its vicinity, and two weeks later they found that when the hand was touched, the patient felt the sensations emerging from the face—even though the nerves from the face were cut. In her brain, the sensory input from the skin of the hand had invaded territory vacated by the sensory input from her face.

Intriguingly, in this patient the sensations were felt only on the face—not on the hand—when the hand was touched. One possibility is that during the initial remapping there is a sort of "overshoot"—the new sensory input from hand skin to the face area of the cortex is actually stronger than the original connections and as a result the sensations are felt predominantly on the face, masking the weaker hand sensations.

11. Caccace et al., 1994.

12. Referred sensations provide an opportunity for studying changing cortical maps in the adult human brain, but the question remains, What is the *function* of remapping? Is it an epiphenomenon—residual plasticity left over from infancy— or does it continue to have a function in the adult brain? For example, would the larger cortical area devoted to the face after arm amputation lead to improved sensory discrimination—measured by two-point discrimination—or tactile hyperacuity on the face? Would such improvement, if it occurred at all, be seen only after the abnormal referred sensations have disappeared, or would it be seen immediately? Such experiments would settle, once and for all, the question of whether or not remapping is actually useful for the organism.