

## The Route of Phantom Pain Amputees lead scientists to a startling new view of how the brain works

By Shannon Brownlee and Karen Mitchell

James Peacock knew he should anticipate help with such simple tasks as taking a shower when his right arm was amputated last December. But what the former California security guard did not expect was pain so unbearable that it could not be controlled with a medicine cabinet full of drugs. "The pain was driving me batty," he says. And strangest of all, he felt it in the arm that no longer filled his sleeve.

Peacock suffers from phantom-limb pain, an agonizing condition that plagues at least 70 percent of the 4 million amputees in the United States and that has baffled doctors since it was first recognized more than a century ago. When a part of the body is amputated, most patients can still feel sensation there, as if the phantom breast still swelled a bra or the missing toe still hit the end of a shoe. But for many amputees, the phantom also throbs with intense pain.

This year, researchers have shown that the source of this pain is faulty signals in the brain. Tracing the roots of this bizarre affliction, says Edward Taub, a psychologist at the University of Alabama, "is one of the hottest areas of neuroscience"--and a focus of a conference held last week in Washington, D.C.

New treatments. Recent discoveries about the nature of phantom pain have overturned neurobiology's once central tenet: The brain is immutable. Taub and his peers used to believe that the myriad connections between nerve fibers forged soon after infancy never changed. Now they know these fibers can trace new routes. It is those new connections that cause phantom pain. Understanding that already has produced a way to help some amputees and could lead to treatments for other neurological conditions such as stroke, dyslexia and schizophrenia.

For many amputees, phantom pain could not be more agonizing if it were devised by the Marquis de Sade. A missing hand seems to clench so tightly that the fingernails dig into the palm, or an amputated leg feels as if it is being burned, squeezed, crushed or twisted. Sen.

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Bob Kerrey, who lost his right leg to a land mine in Vietnam, beat his phantom foot with a fungo bat to subdue its phantom spasms. Until now, doctors relegated phantom pain to the realm of psychologists, who told patients they were indulging in "wish fulfillment."

In 1984, researchers got their first inkling that the trouble starts in a part of the brain known as the sensory cortex, where all sensations, from the brush of a feather to the jab of a needle, are processed. The sensory cortex carries a rough map of the body, called a homunculus or "little man," that is a strangely distorted figure projected onto the pleated screen of the brain. Each "body part" in the homunculus is wired to its corresponding portion of the real anatomy.

A team led by neuroscientist Michael Merzenich of the University of California at San Francisco performed an experiment in which they cut off a monkey's finger to test how the homunculus functions. After a few weeks, they used electrodes to record nerve impulses from the sensory cortex. Neurobiologists once would have predicted that the bit of the monkey's homunculus corresponding to its lost finger would be as silent as a dead phone line. Instead, Merzenich's team found that neurons in this portion of the monkey's cortex fired every time they touched the two fingers adjacent to the one that was amputated. It was as if the sensory cortex could not accept the loss of the finger and had rewired its circuitry to make up for the signals it was no longer receiving from the missing digit.

It is now known that the human brain indulges in the same self-delusion, by undergoing a level of rewiring that was once considered impossible. Vilayanur Ramachandran, a neurologist at Scripps Research Institute and at the University of California at San Diego, blindfolded people who had lost an arm and gently brushed their faces with a cotton swab. His subjects reported that they felt the touch on the face--and on their missing limb. Last June, Taub and colleagues in Germany reported the results of measuring the magnetic output of the brains of 13 amputees: The more their subjects' sensory cortexes had been reorganized, the greater their phantom pain.

Rewired. Researchers are now scrambling to find out precisely how the rewiring occurs. They have two theories: Perhaps nerve impulses in the sensory cortex begin to course down previously untraveled pathways, like cars following a detour around a highway wreck. Or, as some researchers surmise, neurons in the cortex may actually invade the territory left fallow because sensations are no longer received from the missing limb.

Researchers do not yet know why this sensory reorganization leads to pain, but already they can envision ways to put the brain's newfound plasticity to good use. Taub and colleagues

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have found that for certain stroke victims, binding their good arm substantially increases their power over the arm that was paralyzed. Taub speculates that reorganization is responsible. Others envision using chemicals called neurotransmitters and growth factors to block the nerve growth of amputees or promote nerve growth in stroke victims to allow intact parts of the brain to shoulder the tasks once performed by the section that is damaged.

Until then, Ramachandran has devised a far simpler means of helping some amputees. James Peacock and others who have lost a limb are now testing Ramachandran's mirror box, which allows an amputee to "see" his phantom. When Peacock slips his intact left arm into the box, mirrors make it appear as if his missing right arm has slipped into the box as well. The box has provided the only relief Peacock knows from wrenching spasms in his phantom hand. "When I move my left hand," he says, "I can feel it moving my phantom hand."

WHAT CAUSES PHANTOM PAIN? Scientists are solving the mystery of why many amputees are tortured by pain that seems to come from their missing limbs.

Sensation's seat. All sensations are processed in the brain's sensory cortex. It carries a map of the body, called a homunculus, or "little man". Every body part is wired to its corresponding section of the cortex. More-sensitive body parts, such as the lips, command a larger proportion of the cortex than do less sensitive parts, like the upper torso.

Faulty wiring. When a limb is lost, the sensory cortex gets rewired and sensations from intact body parts seem to be coming from the missing limb. This rewiring often results in pain.

Nerves. Pathways cross to the left hemisphere of the brain, which controls the right side of the body.

[Labels]: Homunculus; Genitals; Foot; Leg; Torso; Head; Arm; Hand; Fingers; Thumb; Eye; Nose; Face; Lips; Mouth; Throat; Intra-abdominal; Sensory area of lost limb; Sensory cortex; Spinal cord; Phantom limb

USN&WR--Basic data: McGraw-Hill Encyclopedia of Science and Technology, Edward Taub

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