

STORIES of PERSONAL TRIUMPH from
the FRONTIERS OF BRAIN SCIENCE

The BRAIN That
CHANGES
ITSELF



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Chapter 3

Redesigning the Brain

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A Scientist Changes Brains to Sharpen Perception and Memory,
Increase Speed of Thought, and Heal Learning Problems

Michael Merzenich is a driving force behind scores of neuroplastic innovations and practical inventions, and I am on the road to Santa Rosa, California, to find him. His is the name most frequently praised by other neuroplasticians, and he's by far the hardest to track down. Only when I found out that he would be at a conference in Texas, went there, and sat myself down beside him, was I finally able to set up a meeting in San Francisco.

"Use *this* e-mail address," he says.

"And if you don't respond again?"

"Be persistent."

At the last minute, he switches our meeting to his villa in Santa Rosa.

Merzenich is worth the search.

The Irish neuroscientist Ian Robertson has described him as "the world's leading researcher on brain plasticity." Merzenich's specialty is improving people's ability to think and perceive by redesigning the brain by training specific processing areas, called brain maps, so that they do more mental work. He has also, perhaps more than any other scientist, shown in rich scientific detail *how* our brain-processing areas change.

This villa in the Santa Rosa hills is where Merzenich slows down and regenerates himself. This air, these trees, these vineyards, seem like a piece of Tuscany transplanted into North America. I spend the night here with him and his family, and then in the morning we are off to his lab in San Francisco.

Those who work with him call him "Merz," to rhyme with "whirs" and "stirs." As he drives his small convertible to meetings—he's been double-booked much of the afternoon—his gray hair flies in the wind, and he tells me that many of his most vivid memories, in this, the second half of his life—he's sixty-one—are of conversations about scientific ideas. I hear him pour them into his cell phone, in his crackling voice. As we pass over one of San Francisco's glorious bridges, he pays a toll he doesn't have to because he's so involved with the concepts we are discussing. He has dozens of collaborations and experiments all going on at once and has started several companies. He describes himself as "just this side of crazy." He is not, but he is an interesting mix of intensity and informality. He was born in Lebanon, Oregon, of German stock, and though his name is Teutonic and his work ethic unrelenting, his speech is West Coast, easygoing, down-to-earth.

Of neuroplasticians with solid hard-science credentials, it is Merzenich who has made the most ambitious claims for the field: that brain exercises may be as useful as drugs to treat diseases as severe as schizophrenia; that plasticity exists from the cradle to the grave; and that radical improvements in cognitive functioning—how we learn, think, perceive, and remember—are possible even in the elderly. His latest patents are for techniques that show promise in allowing adults to learn language skills, without effortful memorization. Merzenich argues that practicing a new skill, under the right conditions, can change hundreds of millions and possibly billions of the connections between the nerve cells in our brain maps.

If you are skeptical of such spectacular claims, keep in mind that they come from a man who has already helped cure some disorders that were once thought intractable. Early in his career Merzenich developed, along with his group, the most commonly used design for the cochlear implant, which allows congenitally deaf children

to hear. His current plasticity work helps learning-disabled students improve their cognition and perception. These techniques—his series of plasticity-based computer programs, *Fast ForWord*—have already helped hundreds of thousands. *Fast ForWord* is disguised as a children's game. What is amazing about it is how quickly the change occurs. In some cases people who have had a lifetime of cognitive difficulties get better after only thirty to sixty hours of treatment. Unexpectedly, the program has also helped a number of autistic children.

Merzenich claims that when learning occurs in a way consistent with the laws that govern brain plasticity, the mental “machinery” of the brain can be improved so that we learn and perceive with greater precision, speed, and retention.

Clearly when we learn, we increase what we know. But Merzenich's claim is that we can also change the very structure of the brain itself and increase its capacity to learn. Unlike a computer, the brain is constantly adapting itself.

“The cerebral cortex,” he says of the thin outer layer of the brain, “is actually selectively refining its processing capacities to fit each task at hand.” It doesn't simply learn; it is always “learning how to learn.” The brain Merzenich describes is not an inanimate vessel that we fill; rather it is more like a living creature with an appetite, one that can grow and change itself with proper nourishment and exercise. Before Merzenich's work, the brain was seen as a complex machine, having unalterable limits on memory, processing speed, and intelligence. Merzenich has shown that each of these assumptions is wrong.

Merzenich did not set out to understand how the brain changes. He only stumbled on the realization that the brain could reorganize its maps. And though he was not the first scientist to demonstrate neuroplasticity, it was through experiments he conducted early in his career that mainstream neuroscientists came to accept the plasticity of the brain.

To understand how brain maps can be changed, we need first to have a picture of them. They were first made vivid in human beings by the neurosurgeon Dr. Wilder Penfield at the Montreal Neurological Institute in the 1930s. For Penfield, “mapping” a patient's brain meant finding where in the brain different parts of the body were represented and their activities processed—a solid localizationist project. Localizationists had discovered that the frontal lobes were the seat of the brain's *motor* system, which initiates and coordinates the movement of our muscles. The three lobes behind the frontal lobe, the temporal, parietal, and occipital lobes, comprise the brain's *sensory* system, processing the signals sent to the brain from our sense receptors—eyes, ears, touch receptors, and so on.

Penfield spent years mapping the sensory and motor parts of the brain, while performing brain surgery on cancer and epilepsy patients who could be conscious during the operation, because there are no pain receptors in the brain. Both the sensory and motor maps are part of the cerebral cortex, which lies on the brain's surface and so is easily accessible with a probe. Penfield discovered that when he touched a patient's sensory brain map with an electric probe, it triggered sensations that the patient felt in his body. He used the electric probe to help him distinguish the healthy tissue he wanted to preserve from the unhealthy tumors or pathological tissue he needed to remove.

Normally, when one's hand is touched, an electrical signal passes to the spinal cord and up to the brain, where it turns on cells in the map that make the hand feel touched. Penfield found he could also make the patient feel his hand was touched by turning on the hand area of the brain map electrically. When he stimulated another part of the map, the patient might feel his arm being touched; another part, his face. Each time he stimulated an area, he asked his patients what they'd felt, to make sure he didn't cut away healthy tissue. After many such operations he was able to show where on the brain's sensory map all parts of the body's surface were represented.

He did the same for the motor map, the part of the brain that controls movement. By touching different parts of this map, he could trigger movements in a patient's leg, arm, face, and other muscles.

One of the great discoveries Penfield made was that sensory and motor brain maps, like geographical maps, are topographical, meaning that areas adjacent to each other on the body's surface are generally adjacent to each other on the brain maps. He also discovered that when he touched certain parts of the brain, he triggered long-lost childhood memories or dreamlike scenes—which implied that higher mental activities were also mapped in the brain.

The Penfield maps shaped several generations' view of the brain. But because scientists believed that the brain couldn't change, they assumed, and taught, that the maps were fixed, immutable, and universal—the same in each of us—though Penfield himself never made either claim.

Merzenich discovered that these maps are neither immutable within a single brain nor universal but vary in their borders and size from person to person. In a series of brilliant experiments he showed that the shape of our brain maps changes depending upon what we do over the course of our lives. But in order to prove this point he needed a tool far finer than Penfield's electrodes, one that would be able to detect changes in just a few neurons at a time.

While an undergraduate at the University of Portland, Merzenich and a friend used electronic lab equipment to demonstrate the storm of electrical activity in insects' neurons. These experiments came to the attention of a professor who admired Merzenich's talent and curiosity and recommended him for graduate school at both Harvard and Johns Hopkins. Both accepted him. Merzenich opted for Hopkins to do his Ph.D. in physiology under one of the great neuroscientists of the time, Vernon Mountcastle, who in the 1950s was demonstrating that the subtleties of brain architecture could be discovered by studying the electrical activity of neurons using a new technique: micromapping with pin-shaped microelectrodes.

Microelectrodes are so small and sensitive that they can be inserted inside or beside a single neuron and can detect when an *individual* neuron fires off its electrical signal to other neurons. The neuron's signal passes from the microelectrode to an amplifier and then to an oscilloscope screen, where it appears as a sharp spike. Merzenich would make most of his major discoveries with microelectrodes.

This momentous invention allowed neuroscientists to decode the communication of neurons, of which the adult human brain has approximately 100 billion. Using large electrodes as Penfield did, scientists could observe thousands of neurons firing at once. With microelectrodes, scientists could "listen in on" one or several neurons at a time as they communicated with one another. Micromapping is still about a thousand times more precise than the current generation of brain scans, which detect bursts of activity that last one second in thousands of neurons. But a neuron's electrical signal often lasts a thousandth of a second, so brain scans miss an extraordinary amount of information. Yet micromapping hasn't replaced brain scans because it requires an extremely tedious kind of surgery, conducted under a microscope with microsurgical instruments.

Merzenich took to this technology right away. To map the area of the brain that processes feeling from the hand, Merzenich would cut away a piece of a monkey's skull over the sensory cortex, exposing a 1- to 2-millimeter strip of brain, then insert a microelectrode beside a sensory neuron. Next, he would tap the monkey's hand until he touched a part—say, the tip of a finger—that caused that neuron to fire an electrical signal into the microelectrode. He would record the location of the neuron that represented the fingertip, establishing the first point on the map. Then he would remove the microelectrode, reinsert it near another neuron, and tap different parts of the hand, until he located the part that turned on that neuron. He did this until he'd mapped the entire hand. A single mapping might require five hundred insertions and take several days, and Merzenich and his colleagues did thousands of these laborious surgeries to make their discoveries.

At about this time, a crucial discovery was made that would forever affect Merzenich's work. In the 1960s, just as Merzenich was beginning to use microelectrodes on the brain, two other scientists, who had also worked at Johns Hopkins with Mountcastle, discovered that the brain in very young animals is plastic. David Hubel and Torsten Wiesel were micromapping the visual cortex to learn how vision is processed. They'd inserted microelectrodes into the visual cortex of kittens and discovered that different parts of the cortex processed the lines, orientations, and movements of visually perceived objects. They also discovered that there was a "critical period," from the third to the eighth week of life, when the newborn kitten's brain *had to* receive visual stimulation in order to develop normally. In the crucial experiment Hubel and Wiesel sewed shut one eyelid of a kitten during its critical period, so the eye got no visual stimulation. When they opened this shut eye, they found that the visual areas in the brain map that normally processed input from the shut eye had failed to develop, leaving the kitten blind in that eye for life. Clearly the brains of kittens during the critical period were plastic, their structure literally shaped by experience.

When Hubel and Wiesel examined the brain map for that blind eye, they made one more unexpected discovery about plasticity. The part of the kitten's brain that had been deprived of input from the shut eye did not remain idle. It had begun to process visual input from the open eye, as though the brain didn't want to waste any "cortical real estate" and had found a way to rewire itself—another indication that the brain is plastic in the critical period. For this work Hubel and Wiesel received the Nobel Prize. Yet even though they had discovered plasticity in infancy, they remained localizationists, defending the idea that the adult brain is hardwired by the end of infancy to perform functions in fixed locations.

The discovery of the critical period became one of the most famous in biology in the second half of the twentieth century. Scientists soon showed that other brain systems required environmental stimuli to develop. It also seemed that each neural system had a different critical period, or window of time, during which it was especially plastic and sensitive to the environment, and during which it had rapid, formative growth. Language development, for instance, has a critical period that begins in infancy and ends between eight years and puberty. After this critical period closes, a person's ability to learn a second language without an accent is limited. In fact, second languages learned after the critical period are not processed in the same part of the brain as is the native tongue.

The notion of critical periods also lent support to ethologist Konrad Lorenz's observation that goslings, if exposed to a human being for a brief period of time, between fifteen hours and three days after birth, bonded with that person, instead of with their mother, for life. To prove it, he got goslings to bond to him and follow him around. He called this process "imprinting." In fact, the psychological version of the critical period went back to Freud, who argued that we go through developmental stages that are brief windows of time, during which we must have certain experiences to be healthy; these periods are formative, he said, and shape us for the rest of our lives.

Critical-period plasticity changed medical practice. Because of Hubel and Wiesel's discovery, children born with cataracts no longer faced blindness. They were now sent for corrective surgery as infants, during their critical period, so their brains could get the light required to form crucial connections. Microelectrodes had shown that plasticity is an indisputable fact of childhood. And they also seemed to show that, like childhood, this period of cerebral suppleness is short-lived.

Merzenich's first glimpse of adult plasticity was accidental. In 1968, after completing his doctorate, he went to do a postdoc with Clinton Woolsey, a researcher in Madison, Wisconsin, and peer of Penfield's. Woolsey asked Merzenich to supervise two neurosurgeons, Drs. Ron Paul and Herbert Goodman. The three decided to observe what happens in the brain when one of the peripheral nerves in the hand is cut and then starts to regenerate.

It is important to understand that the nervous system is divided into two parts. The first part is the central nervous system (the brain and spinal cord), which is the command-and-control center of the system; it was thought to lack plasticity. The second part is the peripheral nervous system, which brings messages from the sense receptors to the spinal cord and brain and carries messages from the brain and spinal cord to the muscles and glands. The peripheral nervous system was long known to be plastic; if you cut a nerve in your hand, it can "regenerate" or heal itself.

Each neuron has three parts. The *dendrites* are treelike branches that receive input from other neurons. These dendrites lead into the *cell body*, which sustains the life of the cell and contains its DNA. Finally the *axon* is a living cable of varying lengths (from microscopic lengths in the brain, to some that can run down to the legs and reach up to six feet long). Axons are often compared to wires because they carry electrical impulses at very high speeds (from 2 to 200 miles per hour) toward the dendrites of neighboring neurons.

A neuron can receive two kinds of signals: those that excite it and those that inhibit it. If a neuron receives enough *excitatory* signals from other neurons, it will fire off its own signal. When it receives enough *inhibitory* signals, it becomes less likely to fire. Axons don't quite touch the neighboring dendrites. They are separated by a microscopic space called a *synapse*. Once an electrical signal gets to the end of the axon, it triggers the release of

a chemical messenger, called a neurotransmitter, into the synapse. The chemical messenger floats over to the dendrite of the adjacent neuron, exciting or inhibiting it. When we say that neurons “rewire” themselves, we mean that alterations occur at the synapse, strengthening and increasing, or weakening and decreasing, the number of connections between the neurons.

Merzenich, Paul, and Goodman wanted to investigate a well-known but mysterious interaction between the peripheral and central nervous systems. When a *large* peripheral nerve (which consists of many axons) is cut, sometimes in the process of regeneration the “wires get crossed.” When axons reattach to the axons of the wrong nerve, the person may experience “false localization,” so that a touch on the index finger is felt in the thumb. Scientists assumed that this false localization occurred because the regeneration process “shuffled” the nerves, sending the signal from the index finger to the brain map for the thumb.

The model scientists had of the brain and the nervous system was that each point on the body surface had a nerve that passed signals directly to a specific point on the brain map, anatomically hardwired at birth. Thus a nerve branch for the thumb always passed its signals directly to the spot on the sensory brain map for the thumb. Merzenich and the group accepted this “point-to-point” model of the brain map and innocently set out to document what was happening *in the brain* during this shuffling of nerves.

They micromapped the hand maps in the brains of several adolescent monkeys, cut a peripheral nerve to the hand, and immediately sewed the two severed ends close together but not quite touching, hoping the many axonal wires in the nerve would get crossed as the nerve regenerated itself. After seven months they remapped the brain. Merzenich assumed they would see a very disturbed, chaotic brain map. Thus, if the nerves for the thumb and the index finger had been crossed, he expected that touching the index finger would generate activity in the map area for the thumb. But he saw nothing of the kind. The map was almost normal.

“What we saw,” says Merzenich, “was absolutely astounding. I couldn’t understand it.” It was *topographically* arranged as though the brain had unshuffled the signals from the crossed nerves.

This breakthrough week changed Merzenich’s life. He realized that he, and mainstream neuroscience, had fundamentally misinterpreted how the human brain forms maps to represent the body and the world. If the brain map could normalize its structure in response to abnormal input, the prevailing view that we are born with a *hardwired* system had to be wrong. The brain had to be plastic.

How could the brain do it? Moreover, Merzenich also observed that the new topographical maps were forming in slightly different places than before. The localizationist view, that each mental function was always processed in the same location in the brain, had to be either wrong or radically incomplete. What was Merzenich to make of it?

He went back to the library to look for evidence that contradicted localizationism. He found that in 1912 Graham Brown and Charles Sherrington had shown that stimulating *one point* in the motor cortex might cause an animal to bend its leg at one time and straighten it at another. This experiment, lost in the scientific literature, implied that there was no point-to-point relationship between the brain’s motor map and a given movement. In 1923 Karl Lashley, using equipment far cruder than microelectrodes, exposed a monkey’s motor cortex, stimulated it in a particular place, and observed the resulting movement. He then sewed the monkey back up. After some time he repeated the experiment, stimulating the monkey in that same spot, only to find that the movement produced often changed. As Harvard’s great historian of psychology of the time, Edwin G. Boring, put it, “One day’s mapping would no longer be valid on the morrow.”

Maps were dynamic.

Merzenich immediately saw the revolutionary implications of these experiments. He discussed the Lashley experiment with Vernon Mountcastle, a localizationist, who, Merzenich told me, “had actually been bothered by the Lashley experiment. Mountcastle did not instinctively want to believe in plasticity. He wanted things to be in their place, forever. And Mountcastle knew that this experiment represented an important challenge to how you think about the brain. Mountcastle thought that Lashley was an extravagant exaggerator.”

Neuroscientists were willing to accept Hubel and Wiesel’s discovery that plasticity exists in infancy, because they accepted that the infant brain was in the midst of development. But they rejected Merzenich’s discovery that plasticity continues into adulthood.

Merzenich leans back with an almost mournful expression and remembers, “I had all of these reasons why I wanted to believe that the brain wasn’t plastic in this way, and they were thrown over in a week.”

Merzenich now had to find his mentors among the ghosts of dead scientists, like Sherrington and Lashley. He wrote a paper on the shuffled nerve experiment, and in the discussion section he argued for several pages that the adult brain is plastic—though he didn’t use the word.

But the discussion was never published. Clinton Woolsey, his supervisor, wrote a big X across it, saying that it was too conjectural and that Merzenich was going way beyond the data. When the paper was published, no mention was made of plasticity, and only minimal emphasis was given to explaining the new topographic organization. Merzenich backed down from the opposition, at least in print. He was still, after all, a postdoc working in another man’s lab.

But he was angry, and his mind was churning. He was beginning to think that plasticity might be a basic property of the brain that had evolved to give humans a competitive edge and that it might be “a fabulous thing.”

In 1971 Merzenich became a professor at the University of California at San Francisco, in the department of otolaryngology and physiology, which did research on diseases of the ear. Now his own boss, he began the series of experiments that would prove the existence of plasticity beyond a doubt. Because the area was still so controversial, he did his plasticity experiments in the guise of more acceptable research. Thus he spent much of the early 1970s mapping the auditory cortex of different species of animals, and he helped others invent and perfect the cochlear implant.

The cochlea is the microphone inside our ears. It sits beside the vestibular apparatus that deals with position sense and that was damaged in Cheryl, Bach-y-Rita’s patient. When the external world produces sound, different frequencies vibrate different little hair cells within the cochlea. There are three thousand such hair cells, which convert the sound into patterns of electrical signals that travel down the auditory nerve into the auditory cortex. The micromappers discovered that in the auditory cortex, sound frequencies are mapped “tonotopically.” That is, they are organized like a piano: the lower sound frequencies are at one end, the higher ones at the other.

A cochlear implant is not a hearing aid. A hearing aid amplifies sound for those who have partial hearing loss due to a partially functioning cochlea that works well enough to detect some sound. Cochlear implants are for those who are deaf because of a profoundly damaged cochlea. The implant replaces the cochlea, transforming speech sounds into bursts of electrical impulses, which it sends to the brain. Because Merzenich and his colleagues could not hope to match the complexity of a natural organ with three thousand hair cells, the question was, could the brain, which had evolved to decode complex signals coming from so many hair cells, decode impulses from a far simpler device? If it could, it would mean that the auditory cortex was plastic, capable of modifying itself and responding to artificial inputs. The implant consists of a sound receiver, a converter that translates sound into electrical impulses, and an electrode inserted by surgeons into the nerves that run from the ear to the brain.

In the mid-1960s some scientists were hostile to the very idea of cochlear implants. Some said the project was impossible. Others argued that they would put deaf patients at risk of further damage. Despite the risks, patients volunteered for implants. At first some heard only noise; others heard just a few tones, hisses, and sounds starting and stopping.

Merzenich’s contribution was to use what he had learned from mapping the auditory cortex to determine the kind of input patients needed from the implant to be able to decode speech, and where to implant the electrode. He worked with communication engineers to design a device that could transmit complex speech on a small number of bandwidth channels and still be intelligible. They developed a highly accurate, multichannel implant that allowed deaf people to hear, and the design became the basis for one of the two primary cochlear implant devices available today.

What Merzenich most wanted, of course, was to investigate plasticity directly. Finally, he decided to do a simple, radical experiment in which he would cut off all sensory input to a brain map and see how it responded. He went to his friend and fellow neuroscientist Jon Kaas, of Vanderbilt University in Nashville, who worked with

adult monkeys. A monkey's hand, like a human's, has three main nerves: the radial, the median, and the ulnar. The *median* nerve conveys sensation mostly from the *middle* of the hand, the other two from either side of the hand. Merzenich cut the median nerve in one of the monkeys to see how the median nerve brain map would respond when *all* input was cut off. He went back to San Francisco and waited.

Two months later he returned to Nashville. When he mapped the monkey, he saw, as he expected, that the portion of the brain map that serves the median nerve showed no activity when he touched the middle part of the hand. But he was shocked by something else.

When he stroked the *outsides* of the monkey's hand—the areas that send their signals through the radial and ulnar nerves—the median nerve map lit up! The brain maps for the radial and ulnar nerves had almost doubled in size and *invaded* what used to be the median nerve map. And these new maps were topographical. This time he and Kaas, writing up the findings, called the changes “spectacular” and used the word “plasticity” to explain the change, though they put it in quotes.

The experiment demonstrated that if the median nerve was cut, other nerves, still brimming with electrical input, would take over the unused map space to process their input. When it came to allocating brain-processing power, brain maps were governed by competition for precious resources and the principle of *use it or lose it*.

The competitive nature of plasticity affects us all. There is an endless war of nerves going on inside each of our brains. If we stop exercising our mental skills, we do not just forget them: the brain map space for those skills is turned over to the skills we practice instead. If you ever ask yourself, “How often must I practice French, or guitar, or math to keep on top of it?” you are asking a question about competitive plasticity. You are asking how frequently you must practice one activity to make sure its brain map space is not lost to another.

Competitive plasticity in adults even explains some of our limitations. Think of the difficulty most adults have in learning a second language. The conventional view now is that the difficulty arises because the critical period for language learning has ended, leaving us with a brain too *rigid* to change its structure on a large scale. But the discovery of competitive plasticity suggests there is more to it. As we age, the more we use our native language, the more it comes to dominate our linguistic map space. Thus it is also because our brain is *plastic*—and because plasticity is competitive—that it is so hard to learn a new language and end the tyranny of the mother tongue.

But why, if this is true, is it easier to learn a second language when we are young? Is there not competition then too? Not really. If two languages are learned at the same time, during the critical period, both get a foothold. Brain scans, says Merzenich, show that in a bilingual child all the sounds of its two languages share a single large map, a library of sounds from both languages.

Competitive plasticity also explains why our bad habits are so difficult to break or “unlearn.” Most of us think of the brain as a container and learning as putting something in it. When we try to break a bad habit, we think the solution is to put something new into the container. But when we learn a bad habit, it takes over a brain map, and each time we repeat it, it claims more control of that map and prevents the use of that space for “good” habits. That is why “unlearning” is often a lot harder than learning, and why early childhood education is so important—it's best to get it right early, before the “bad habit” gets a competitive advantage.

Merzenich's next experiment, ingeniously simple, made plasticity famous among neuroscientists and eventually did more to win over skeptics than any plasticity experiment before or since.

He mapped a monkey's hand map in the brain. Then he amputated the monkey's middle finger. After a number of months he remapped the monkey and found that the brain map for the amputated finger had disappeared and that the maps for the adjacent fingers had grown into the space that had originally mapped for the middle finger. Here was the clearest possible demonstration that brain maps are dynamic, that there is a competition for cortical real estate, and that brain resources are allocated according to the principle of *use it or lose it*.

Merzenich also noticed that animals of a particular species may have similar maps, but they are *never* identical. Micromapping allowed him to see differences that Penfield, with larger electrodes, could not. He also found that the maps of normal body parts change every few weeks. Every time he mapped a normal monkey's

face, it was unequivocally different. Plasticity doesn't require the provocation of cut nerves or amputations. Plasticity is a normal phenomenon, and brain maps are constantly changing. When he wrote up this new experiment, Merzenich finally took the word "plasticity" out of quotes. Yet despite the elegance of his experiment, opposition to Merzenich's ideas did not melt away overnight.

He laughs when he says it. "Let me tell you what happened when I began to declare that the brain was plastic. I received hostile treatment. I don't know how else to put it. I got people saying things in reviews such as, 'This would be really interesting if it could possibly be true, but it could not be.' It was as if I just made it up."

Because Merzenich was arguing that brain maps could alter their borders and location and change their functions well into adulthood, localizationists opposed him. "Almost everybody I knew in the mainstream of neuroscience," he says, "thought that this was sort of *semi*-serious stuff—that the experiments were sloppy, that the effects described were uncertain. But actually the experiment had been done enough times that I realized that the position of the majority was arrogant and indefensible."

One of the major figures who voiced doubts was Torsten Wiesel. Despite the fact that Wiesel had shown that plasticity exists in the critical period, he still opposed the idea that it existed in adults, and wrote that he and Hubel "firmly believed that once cortical connections were established in their mature form, they stayed in place permanently." He had indeed won the Nobel Prize for establishing where visual processing occurs, a finding considered one of localizationism's greatest triumphs. Wiesel now accepts adult plasticity and has gracefully acknowledged in print that for a long time he was wrong and that Merzenich's pioneering experiments ultimately led him and his colleagues to change their minds. Hardcore localizationists took notice when a man of Wiesel's stature changed his mind.

"The most frustrating thing," says Merzenich, "was that I saw that neuroplasticity had all kinds of potential implications for medical therapeutics—for the interpretation of human neuropathology and psychiatry. And nobody paid any attention."

Since plastic change is a process, Merzenich realized he would only really be able to understand it if he could see it unfolding in the brain over time. He cut a monkey's median nerve and then did multiple mappings over a number of months.

The first mapping, immediately after he cut the nerve, showed, as he expected, that the brain map for the median nerve was completely silent when the middle of the hand was stroked. But when he stroked the part of the hand served by the outside nerves, the silent median nerve portion of the map lit up immediately. Maps for the outside nerves, the radial and ulnar nerves, now appeared in the median map space. These maps sprang up so quickly, it was as though they had been hidden there all along, since early development, and now they were "unmasked."

On the twenty-second day Merzenich mapped the monkey again. The radial and ulnar maps, which had been lacking in detail when they first appeared, had grown more refined and detailed and had now expanded to occupy almost the entire median nerve map. (A primitive map lacks detail; a refined map has a lot and thus conveys more information.)

By the 144th day the whole map was every bit as detailed as a normal map.

By doing multiple mappings over time, Merzenich observed that the new maps were changing their borders, becoming more detailed, and even moving around the brain. In one case he even saw a map disappear altogether, like Atlantis.

It seemed reasonable to assume that if totally new maps were forming, then new connections must have been forming among neurons. To help understand this process, Merzenich invoked the ideas of Donald O. Hebb, a Canadian behavioral psychologist who had worked with Penfield. In 1949 Hebb proposed that learning linked neurons in new ways. He proposed that when two neurons fire at the same time repeatedly (or when one fires, causing another to fire), chemical changes occur in both, so that the two tend to connect more strongly. Hebb's concept—actually proposed by Freud sixty years before—was neatly summarized by neuroscientist Carla Shatz: *Neurons that fire together wire together.*

Hebb's theory thus argued that neuronal structure can be altered by experience. Following Hebb, Merzenich's new theory was that neurons in brain maps develop strong connections to one another when they are activated at

the same moment in time. And if maps could change, thought Merzenich, then there was reason to hope that people born with problems in brain map-processing areas—people with learning problems, psychological problems, strokes, or brain injuries—might be able to form new maps if he could help them form new neuronal connections, by getting their healthy neurons to fire together and wire together.

Starting in the late 1980s, Merzenich designed or participated in brilliant studies to test whether brain maps are time based and whether their borders and functioning can be manipulated by “playing” with the timing of input to them.

In one ingenious experiment, Merzenich mapped a normal monkey’s hand, then sewed together two of the monkey’s fingers, so that both fingers moved as one. After several months of allowing the monkey to use its sewn fingers, the monkey was remapped. The two maps of the originally separate fingers had now merged into a single map. If the experimenters touched any point on either finger, this new single map would light up. Because all the movements and sensations in those fingers always occurred simultaneously, they’d formed the same map. The experiment showed that timing of the input to the neurons in the map was the key to forming it—neurons that fired together *in time* wired together to make one map.

Other scientists tested Merzenich’s findings on human beings. Some people are born with their fingers fused, a condition called syndactyly or “webbed-finger syndrome.” When two such people were mapped, the brain scan found that they each had one large map for their fused fingers instead of two separate ones.

After surgeons separated the webbed fingers, the subjects’ brains were remapped, and two distinct maps emerged for the two separated digits. Because the fingers could move independently, the neurons no longer fired simultaneously, illustrating another principle of plasticity: if you separate the signals to neurons in time, you create separate brain maps. In neuroscience this finding is now summarized as *Neurons that fire apart wire apart*—or *Neurons out of sync fail to link*.

In the next experiment in the sequence, Merzenich created a map for what might be called a nonexistent finger that ran perpendicular to the other fingers. The team stimulated all five fingertips of a monkey simultaneously, five hundred times a day for over a month, preventing the monkey from using its fingers one at a time. Soon the monkey’s brain map had a new, elongated finger map, in which the five fingertips were merged. This new map ran perpendicular to the other fingers, and all the fingertips were part of it, instead of part of their individual finger maps, which had started to melt away from disuse.

In the final and most brilliant demonstration, Merzenich and his team proved that maps cannot be anatomically based. They took a small patch of skin from one finger, and—this is the key point—with the nerve to its brain map still attached, surgically grafted the skin onto an adjacent finger. Now that piece of skin and its nerve were stimulated whenever the finger it was attached to was moved or touched in the course of daily use. According to the anatomical-hardwiring model, the signals should *still* have been sent from the skin along its nerve to the brain map for the finger that the skin and nerve originally came from. Instead, when the team stimulated the patch of skin, the map of its *new* finger responded. The map for the patch of skin migrated from the brain map of the original finger to its new one, because both the patch and the new finger were stimulated simultaneously.

In a few short years Merzenich had discovered that adult brains are plastic, persuaded skeptics in the scientific community this was the case, and shown that experience changes the brain. But he still hadn’t explained a crucial enigma: how the maps organize themselves to become topographical and function in a way that is useful to us.

When we say a brain map is organized topographically, we mean that the map is ordered as the body itself is ordered. For instance, our middle finger sits between our index finger and our ring finger. The same is true for our brain map: the map for the middle finger sits between the map for our index finger and that of our ring finger. Topographical organization is efficient, because it means that parts of the brain that often work together are close together in the brain map, so signals don’t have to travel far in the brain itself.

The question for Merzenich was, how does this topographic order emerge in the brain map? The answer he and his group came to was ingenious. A topographic order emerges because many of our everyday activities involve repeating sequences in a fixed order. When we pick up an object the size of an apple or baseball, we

usually grip it first with our thumb and index finger, then wrap the rest of our fingers around it one by one. Since the thumb and index finger often touch at almost the same time, sending their signals to the brain almost simultaneously, the thumb map and the index finger map tend to form close together in the brain. (Neurons that fire together wire together.) As we continue to wrap our hand around the object, our middle finger will touch it next, so its brain map will tend to be beside the index finger and farther away from the thumb. As this common grasping sequence—thumb first, index finger second, middle finger third—is repeated thousands of times, it leads to a brain map where the thumb map is next to the index finger map, which is next to the middle finger map, and so on. Signals that tend to arrive at separate times, like thumbs and pinkies, have more distant brain maps, because neurons that fire apart wire apart.

Many if not all brain maps work by spatially grouping together events that happen together. As we have seen, the auditory map is arranged like a piano, with mapping regions for low notes at one end and for high notes at the other. Why is it so orderly? Because the low frequencies of sounds tend to come together with one another in nature. When we hear a person with a low voice, most of the frequencies are low, so they get grouped together.

The arrival of Bill Jenkins at Merzenich's lab ushered in a new phase of research that would help Merzenich develop practical applications of his discoveries. Jenkins, trained as a behavioral psychologist, was especially interested in understanding how we learn. He suggested they teach animals to learn new skills, to observe how learning affected their neurons and maps.

In one basic experiment they mapped a monkey's sensory cortex. Then they trained it to touch a spinning disk with its fingertip, with just the right amount of pressure for ten seconds to get a banana-pellet reward. This required the monkey to pay close attention, learning to touch the disk very lightly and judge time accurately. After thousands of trials, Merzenich and Jenkins remapped the monkey's brain and saw that the area mapping the monkey's fingertip had enlarged as the monkey had learned how to touch the disk with the right amount of pressure. The experiment showed that when an animal is motivated to learn, the brain responds plastically.

The experiment also showed that as brain maps get bigger, the individual neurons get more efficient in two stages. At first, as the monkey trained, the map for the fingertip grew to take up more space. But after a while individual neurons within the map became more efficient, and eventually fewer neurons were required to perform the task.

When a child learns to play piano scales for the first time, he tends to use his whole upper body—wrist, arm, shoulder—to play each note. Even the facial muscles tighten into a grimace. With practice the budding pianist stops using irrelevant muscles and soon uses only the correct finger to play the note. He develops a "lighter touch," and if he becomes skillful, he develops "grace" and relaxes when he plays. This is because the child goes from using a massive number of neurons to an appropriate few, well matched to the task. This more efficient use of neurons occurs whenever we become proficient at a skill, and it explains why we don't quickly run out of map space as we practice or add skills to our repertoire.

Merzenich and Jenkins also showed that individual neurons got more selective with training. Each neuron in a brain map for the sense of touch has a "receptive field," a segment on the skin's surface that "reports" to it. As the monkeys were trained to feel the disk, the receptive fields of individual neurons got smaller, firing only when small parts of the fingertip touched the disk. Thus, despite the fact that the size of the brain map increased, each neuron in the map became responsible for a smaller part of the skin surface, allowing the animal to have finer touch discrimination. Overall, the map became more precise.

Merzenich and Jenkins also found that as neurons are trained and become more efficient, they can process *faster*. This means that the speed at which we think is itself plastic. Speed of thought is essential to our survival. Events often happen quickly, and if the brain is slow, it can miss important information. In one experiment Merzenich and Jenkins successfully trained monkeys to distinguish sounds in shorter and shorter spans of time. The trained neurons fired more quickly in response to the sounds, processed them in a shorter time, and needed less time to "rest" between firings. Faster neurons ultimately lead to faster thought—no minor matter—because speed of thought is a crucial component of intelligence. IQ tests, like life, measure not only whether you can get the right answer but how long it takes you to get it.

They also discovered that as they trained an animal at a skill, not only did its neurons fire faster, but because they were faster their signals were clearer. Faster neurons were more likely to fire in sync with each other—becoming better team players—wiring together more and forming groups of neurons that gave off clearer and more powerful signals. This is a crucial point, because a powerful signal has greater impact on the brain. When we want to remember something we have heard we must hear it clearly, because a memory can be only as clear as its original signal.

Finally, Merzenich discovered that paying close attention is essential to long-term plastic change. In numerous experiments he found that lasting changes occurred *only* when his monkeys paid close attention. When the animals performed tasks automatically, without paying attention, they changed their brain maps, but the changes did not last. We often praise “the ability to multitask.” While you can learn when you divide your attention, divided attention doesn’t lead to abiding change in your brain maps.

When Merzenich was a boy, his mother’s first cousin, a grade-school teacher in Wisconsin, was chosen teacher of the year for the entire United States. After the ceremony at the White House, she visited the Merzenich family in Oregon.

“My mother,” he recalls, “asked the inane question that you’d ask in conversation: ‘What are your most important principles in teaching?’ And her cousin answered, ‘Well, you test them when they come into school, and you figure out whether they are worthwhile. And if they are worthwhile, you really pay attention to them, and you don’t waste time on the ones that aren’t.’ That’s what she said. And you know, in one way or another, that’s reflected in how people have treated children who are different, forever. It’s just so destructive to imagine that your neurological resources are permanent and enduring and cannot be substantially improved and altered.”

Merzenich now became aware of the work of Paula Tallal at Rutgers, who had begun to analyze why children have trouble learning to read. Somewhere between 5 and 10 percent of preschool children have a language disability that makes it difficult for them to read, write, or even follow instructions. Sometimes these children are called dyslexic.

Babies begin talking by practicing consonant-vowel combinations, cooing “da, da, da” and “ba, ba, ba.” In many languages their first words consist of such combinations. In English their first words are often “mama” and “dada,” “pee pee,” and so on. Tallal’s research showed that children with language disabilities have auditory processing problems with common consonant-vowel combinations that are spoken quickly and are called “the fast parts of speech.” The children have trouble hearing them accurately and, as a result, reproducing them accurately.

Merzenich believed that these children’s auditory cortex neurons were firing too slowly, so they couldn’t distinguish between two very similar sounds or be certain, if two sounds occurred close together, which was first and which was second. Often they didn’t hear the beginnings of syllables or the sound changes within syllables. Normally neurons, after they have processed a sound, are ready to fire again after about a 30-millisecond rest. Eighty percent of language-impaired children took at least three times that long, so that they lost large amounts of language information. When their neuron-firing patterns were examined, the signals weren’t clear.

“They were muddy in, muddy out,” says Merzenich. Improper hearing led to weaknesses in *all* the language tasks, so they were weak in vocabulary, comprehension, speech, reading, and writing. Because they spent so much energy decoding words, they tended to use shorter sentences and failed to exercise their memory for longer sentences. Their language processing was more childlike, or “delayed,” and they still needed practice distinguishing “da, da, da” and “ba, ba, ba.”

When Tallal originally discovered their problems, she feared that “these kids were ‘broken’ and there was nothing you could do” to fix their basic brain defect. But that was before she and Merzenich combined forces.

In 1996 Merzenich, Paula Tallal, Bill Jenkins, and one of Tallal’s colleagues, psychologist Steve Miller, formed the nucleus of a company, Scientific Learning, that is wholly devoted to using neuroplastic research to help people rewire their brains.

Their head office is in the Rotunda, a Beaux Arts masterpiece with an elliptical glass dome, 120 feet high, its edges painted in 24-karat gold leaf, in the middle of downtown Oakland, California. When you enter, you enter

another world. The Scientific Learning staff includes child psychologists, plasticity researchers, experts in human motivation, speech pathologists, engineers, programmers, and animators. From their desks these researchers, bathed in natural light, can look up into the gorgeous dome.

Fast ForWord is the name of the training program they developed for language-impaired and learning-disabled children. The program exercises every basic brain function involved in language from decoding sounds up to comprehension—a kind of cerebral cross-training.

The program offers seven brain exercises. One teaches the children to improve their ability to distinguish short sounds from long. A cow flies across the computer screen, making a series of mooing sounds. The child has to catch the cow with the computer cursor and hold it by depressing the mouse button. Then suddenly the length of the moo sound changes subtly. At this point the child must release the cow and let it fly away. A child who releases it just after the sound changes scores points. In another game children learn to identify easily confused consonant-vowel combinations, such as “ba” and “da,” first at slower speeds than they occur in normal language, and then at increasingly faster speeds. Another game teaches the children to hear faster and faster frequency glides (sounds like “whoooooop” that sweep up). Another teaches them to remember and match sounds. The “fast parts of speech” are used throughout the exercises but have been slowed down with the help of computers, so the language-disabled children can hear them and develop clear maps for them; then gradually, over the course of the exercises, they are sped up. Whenever a goal is achieved, something funny happens: the character in the animation eats the answer, gets indigestion, gets a funny look on its face, or makes some slapstick move that is unexpected enough to keep the child attentive. This “reward” is a crucial feature of the program, because each time the child is rewarded, his brain secretes such neurotransmitters as dopamine and acetylcholine, which help consolidate the map changes he has just made. (Dopamine reinforces the reward, and acetylcholine helps the brain “tune in” and sharpen memories.)

Children with milder difficulties typically work at *Fast ForWord* for an hour and forty minutes a day, five days a week for several weeks, and those with more severe difficulties work for eight to twelve weeks.

The first study results, reported in the journal *Science* in January 1996, were remarkable. Children with language impairments were divided into two groups, one that did *Fast ForWord* and a control group that did a computer game that was similar but didn’t train temporal processing or use modified speech. The two groups were matched for age, IQ, and language-processing skills. The children who did *Fast ForWord* made significant progress on standard speech, language, and auditory-processing tests, ended up with normal or better-than-normal language scores, and kept their gains when retested six weeks after training. They improved far more than children in the control group.

Further study followed five hundred children at thirty-five sites—hospitals, homes, and clinics. All were given standardized language tests before and after *Fast ForWord* training. The study showed that most children’s ability to understand language normalized after *Fast ForWord*. In many cases, their comprehension rose above normal. The average child who took the program moved ahead 1.8 years of language development in six weeks, remarkably fast progress. A Stanford group did brain scans of twenty dyslexic children, before and after *Fast ForWord*. The opening scans showed that the children used different parts of their brains for reading than normal children do. After *Fast ForWord* new scans showed that their brains had begun to normalize. (For instance, they developed increased activity, on average, in the left temporo-parietal cortex, and their scans began to show patterns that were similar to those of children who have no reading problems.)

Willy Arbor is a seven-year-old from West Virginia. He’s got red hair and freckles, belongs to Cub Scouts, likes going to the mall, and, though barely over four feet tall, loves wrestling. He’s just gone through *Fast ForWord* and has been transformed.

“Willy’s main problem was hearing the speech of others clearly,” his mother explains. “I might say the word ‘copy,’ and he would think I said ‘coffee.’ If there was any background noise, it was especially hard for him to hear. Kindergarten was depressing. You could *see* his insecurity. He got into nervous habits like chewing on his clothes, or his sleeve, because everybody else was getting the answer right, and he wasn’t. The teacher had actually talked about holding him back in first grade.” Willy had trouble reading, both to himself and aloud.

“Willy,” his mother continues, “couldn’t hear change in pitch properly. So he couldn’t tell when a person was making an exclamation or just a general statement, and he didn’t grasp inflections in speech, which made it hard for him to read people’s emotions. Without the high and low pitch he wasn’t hearing that *wow* when people are excited. It was like everything was the same.”

Willy was taken to a hearing specialist, who diagnosed his “hearing problem” as caused by an auditory-processing disorder that originated in his brain. He had difficulty remembering strings of words because his auditory system was so easily overloaded. “If you gave him more than three instructions, such as ‘please put your shoes upstairs—put them in the closet—then come down for dinner,’ he’d forget them. He’d take his shoes off, go up the steps, and ask ‘Mom what did you want me to do?’ Teachers had to repeat instructions all the time.” Though he appeared to be a gifted child—he was good at math—his problems held him back in that area too.

His mother protested making Willy repeat first grade and over the summer sent him to *Fast ForWord* for eight weeks.

“Before he did *Fast ForWord*,” his mother recalls, “you’d put him at the computer, and he got very stressed out. With this program, though, he spent a hundred minutes a day for a solid eight weeks at the computer. He loved doing it and loved the scoring system because he could see himself going up, up, up,” says his mother. As he improved, he became able to perceive inflections in speech, got better at reading the emotions of others, and became a less anxious child. “So much changed for him. When he brought his midterms home, he said, ‘It is better than last year, Mommy.’ He began bringing home A and B marks on his papers most of the time—a noticeable difference...Now it’s ‘I can do this. This is my grade. I can make it better.’ I feel like I had my prayer answered, it’s done so much for him. It’s amazing.” A year later he continues to improve.

Merzenich’s team started hearing that *Fast ForWord* was having a number of spillover effects. Children’s handwriting improved. Parents reported that many of the students were starting to show sustained attention and focus. Merzenich thought these surprising benefits were occurring because *Fast ForWord* led to some general improvements in mental processing.

One of the most important brain activities—one we don’t often think about—is the determination of how long things go on, or temporal processing. You can’t move properly, perceive properly, or predict properly if you can’t determine how long events last. Merzenich discovered that when you train people to distinguish very fast vibrations on their skin, lasting only 75 milliseconds, these same people could detect 75-millisecond *sounds* as well. It seemed that *Fast ForWord* was improving the brain’s general ability to keep time. Sometimes these improvements spilled over into visual processing as well. Before *Fast ForWord*, when Willy was given a game that asked which items are out of place—a boot up in the tree, or a tin can on the roof—his eyes jumped all over the page. He was trying to see the whole page instead of taking in a little section at a time. At school he skipped lines when he read. After *Fast ForWord* his eyes no longer jumped around the page, and he was able to focus his visual attention.

A number of children who took standardized tests shortly after completing *Fast ForWord* showed improvements not only in language, speaking, and reading, but in math, science, and social studies as well. Perhaps these children were hearing what was going on in class better or were better able to read—but Merzenich thought it might be more complicated.

“You know,” he says, “IQ goes up. We used the matrix test, which is a *visual*-based measurement of IQ—and IQ goes up.”

The fact that a *visual* component of the IQ went up meant that the IQ improvements were not caused simply because *Fast ForWord* improved the children’s ability to read verbal test questions. Their mental processing was being improved in a general way, possibly because their temporal processing was improving. And there were other unexpected benefits. Some children with autism began to make some general progress.

The mystery of autism—a human mind that cannot conceive of other minds—is one of the most baffling and poignant in psychiatry and one of the most severe developmental disorders of childhood. It is called a “pervasive

developmental disorder,” because so many aspects of development are disturbed: intelligence, perception, socializing skills, language, and emotion.

Most autistic children have an IQ of less than 70. They have major problems connecting socially to others and may, in severe cases, treat people like inanimate objects, neither greeting them nor acknowledging them as human beings. At times it seems that autistics don’t have a sense that “other minds” exist in the world. They also have perceptual processing difficulties and are thus often hypersensitive to sound and touch, easily overloaded by stimulation. (That may be one reason autistic children often avoid eye contact: the stimulation from people, especially when coming from many senses at once, is too intense.) Their neural networks appear to be overactive, and many of these children have epilepsy.

Because so many autistic children have language impairments, clinicians began to suggest the *Fast ForWord* program for them. They never anticipated what might happen. Parents of autistic children who did *Fast ForWord* told Merzenich that their children became more connected socially. He began asking, were the children simply being trained to be more attentive listeners? And he was fascinated by the fact that with *Fast ForWord* both the language symptoms and the autistic symptoms seemed to be fading together. Could this mean that the language and autistic problems were different expressions of a common problem?

Two studies of autistic children confirmed what Merzenich had been hearing. One, a language study, showed that *Fast ForWord* quickly moved autistic children from severe language impairment to the normal range. But another pilot study of one hundred autistic children showed that *Fast ForWord* had a significant impact on their autistic symptoms as well. Their attention spans improved. Their sense of humor improved. They became more connected to people. They developed better eye contact, began greeting people and addressing them by name, spoke with them, and said good-bye at the end of their encounters. It seemed the children were beginning to experience the world as filled with other human minds.

Lauralee, an eight-year-old autistic girl, was diagnosed with moderate autism when she was three. Even as an eight-year-old she rarely used language. She didn’t answer to her name, and to her parents, it seemed she was not hearing it. Sometimes she would speak, but when she did, “she had her own language,” says her mother, “which was often unintelligible.” If she wanted juice, she didn’t ask for it. She would make gestures and pull her parents over to the cabinets to get things for her.

She had other autistic symptoms, among them the repetitive movements that autistic children use to try to contain their sense of being overwhelmed. According to her mother, Lauralee had “the whole works—the flapping of the hands, toe-walking, a lot of energy, biting. And she couldn’t tell me what she was feeling.”

She was very attached to trees. When her parents took her walking in the evening to burn off energy, she’d often stop, touch a tree, hug it, and speak to it.

Lauralee was unusually sensitive to sounds. “She had bionic ears,” says her mother. “When she was little, she would often cover her ears. She couldn’t tolerate certain music on the radio, like classical and slow music.” At her pediatrician’s office she heard sounds from the floor upstairs that others didn’t. At home she would go over to the sinks, fill them with water, then wrap herself around the pipes, hugging them, listening to the water drain through them.

Lauralee’s father is in the navy and served in the Iraq war in 2003. When the family was transferred to California, Lauralee was enrolled in a public school with a special-ed class that used *Fast ForWord*. The program took her about two hours a day for eight weeks to complete.

When she finished it, “she had an explosion in language,” says her mother, “and began to speak more and use complete sentences. She could tell me about her days at school. Before I would just say, ‘Did you have a good day or a bad day?’ Now she was able to say what she did, and she remembered details. If she got into a bad situation, she would be able to tell me, and I wouldn’t have to prompt her to get it out of her. She also found it easier to remember things.” Lauralee has always loved to read, but now she is reading longer books, nonfiction and the encyclopedia. “She is listening to quieter sounds now and can tolerate different sounds from the radio,” says her mother. “It was an awakening for her. And with the better communication, there was an awakening for all of us. It was a big blessing.”

Merzenich decided that to deepen his understanding of autism and its many developmental delays, he would have to go back to the lab. He thought the best way to go about it was first to produce an “autistic animal”—one that had multiple developmental delays, as autistic children do. Then he could study it and try to treat it.

As Merzenich began to think through what he calls the “infantile catastrophe” of autism, he had a hunch that something might be going wrong in infancy, when most critical periods occur, plasticity is at its height, and a massive amount of development should be occurring. But autism is largely an inherited condition. If one identical twin is autistic, there is an 80 to 90 percent chance the other twin will be as well. In cases of *nonidentical* twins, where one is autistic, the nonautistic twin will often have some language and social problems.

Yet the incidence of autism has been climbing at a staggering rate that can’t be explained by genetics alone. When the condition was first recognized over forty years ago, about one in 5,000 people had it. Now it is fifteen in 5,000. That number has risen partly because autism is more often diagnosed, and because some children are labeled mildly autistic to get public funding for treatment. “But,” says Merzenich, “even when all of the corrections are made by very hard-assed epidemiologists, it looks like it’s about a threefold increase over the last fifteen years. There is a world emergency that relates to risk factors for autism.”

He has come to think it likely that an environmental factor affects the neural circuits in these children, forcing the critical periods to shut down early, before the brain maps are fully differentiated. When we are born, our brain maps are often “rough drafts,” or sketches, lacking detail, *undifferentiated*. In the critical period, when the structure of our brain maps is literally getting shaped by our first worldly experiences, the rough draft normally becomes detailed and differentiated.

Merzenich and his team used micromapping to show how maps in newborn rats are formed in the critical period. Right after birth, at the beginning of the critical period, auditory maps were undifferentiated, with only two broad regions in the cortex. Half of the map responded to *any* high-frequency sound. The other half responded to *any* low-frequency sound.

When the animal was exposed to a particular frequency during the critical period, that simple organization changed. If the animal was repeatedly exposed to a high C, after a while only a few neurons would turn on, becoming *selective* for high C. The same would happen when the animal was exposed to a D, E, F, and so on. Now the map, instead of having two broad areas, had many different areas, each responding to different notes. It was now differentiated.

What is remarkable about the cortex in the critical period is that it is so plastic that its structure can be changed just by exposing it to new stimuli. That sensitivity allows babies and very young children in the critical period of language development to pick up new sounds and words effortlessly, simply by hearing their parents speak; mere exposure causes their brain maps to wire in the changes. After the critical period older children and adults can, of course, learn languages, but they really have to *work* to pay attention. For Merzenich, the difference between critical-period plasticity and adult plasticity is that in the critical period the brain maps can be changed just by being exposed to the world because “the learning machinery is continuously on.”

It makes good biological sense for this “machinery” always to be on because babies can’t possibly know what will be important in life, so they pay attention to everything. Only a brain that is already somewhat organized can sort out what is worth paying attention to.

The next clue Merzenich needed in order to understand autism came from a line of research that was originated during the Second World War, in Fascist Italy, by a young Jewish woman, Rita Levi-Montalcini, while in hiding. Levi-Montalcini was born in Turin in 1909 and attended medical school there. In 1938, when Mussolini barred Jews from practicing medicine and doing scientific research, she fled to Brussels to continue her studies; when the Nazis threatened Belgium, she went back to Turin and built a secret laboratory in her bedroom, to study how nerves form, forging microsurgical equipment from sewing needles. When the Allies bombed Turin in 1940, she fled to Piedmont. One day in 1940, traveling to a small northern Italian village in a cattle car that had been converted into a passenger train, she sat down on the floor and read a scientific paper by Viktor Hamburger, who had been doing pioneering work on the development of neurons by studying chick embryos. She decided to repeat and extend his experiments, working on a table in a mountain house with eggs from a local farmer. When she

finished each experiment, she ate the eggs. After the war Hamburger invited Levi-Montalcini to join him and his researchers in St. Louis to work on their discovery that the nerve fibers of chicks grew faster in the presence of tumors from mice. Levi-Montalcini speculated that the tumor might be releasing a substance to promote nerve growth. With biochemist Stanley Cohen she isolated the protein responsible and called it nerve growth factor, or NGF. Levi-Montalcini and Cohen were awarded the Nobel Prize in 1986.

Levi-Montalcini's work led to the discovery of a number of such nerve growth factors, one of which, brain-derived neurotrophic factor, or BDNF, caught Merzenich's attention.

BDNF plays a crucial role in reinforcing plastic changes made in the brain in the critical period. According to Merzenich, it does this in four different ways.

When we perform an activity that requires specific neurons to fire together, they release BDNF. This growth factor consolidates the connections between those neurons and helps to wire them together so they fire together reliably in the future. BDNF also promotes the growth of the thin fatty coat around every neuron that speeds up the transmission of electrical signals.

During the critical period BDNF turns on the nucleus basalis, the part of our brain that allows us to focus our attention—and *keeps it on, throughout the entire critical period*. Once turned on, the nucleus basalis helps us not only pay attention but remember what we are experiencing. It allows map differentiation and change to take place effortlessly. Merzenich told me, "It is like a teacher in the brain saying, 'Now *this* is really important—this you have to know for the exam of life.'" Merzenich calls the nucleus basalis and the attention system the "modulatory control system of plasticity"—the neurochemical system that, when turned on, puts the brain in an extremely plastic state.

The fourth and final service that BDNF performs—when it has completed strengthening key connections—is to help close down the critical period. Once the main neuronal connections are laid down, there is a need for stability and hence less plasticity in the system. When BDNF is released in sufficient quantities, it turns off the nucleus basalis and ends that magical epoch of effortless learning. Henceforth the nucleus can be activated only when something important, surprising, or novel occurs, or if we make the effort to pay close attention.

Merzenich's work on the critical period and BDNF helped him develop a theory that explains how so many different problems could be part of a single autistic whole. During the critical period, he argues, some situations overexcite the neurons in children who have genes that predispose them to autism, leading to *the massive, premature release of BDNF*. Instead of *important* connections being reinforced, *all* connections are. So much BDNF is released that it turns off the critical period prematurely, sealing all these connections in place, and the child is left with scores of undifferentiated brain maps and hence pervasive developmental disorders. Their brains are hyperexcitable and hypersensitive. If they hear one frequency, the whole auditory cortex starts firing. This is what seemed to be happening in Lauralee, who had to cover her "bionic" ears when she heard music. Other autistic children are hypersensitive to touch and feel tormented when the labels in their clothes touch their skin. Merzenich's theory also explains the high rates of epilepsy in autism: because of BDNF release, the brain maps are poorly differentiated, and because so many connections in the brain have been indiscriminately reinforced, once a few neurons start firing, the whole brain can be set off. It also explains why autistic children have bigger brains—the substance increases the fatty coating around the neurons.

If BDNF release was contributing to autism and language problems, Merzenich needed to understand what might cause young neurons to get "overexcited" and release massive amounts of the chemical.

Several studies alerted him to how an environmental factor might contribute. One disturbing study showed that the closer children lived to the noisy airport in Frankfurt, Germany, the lower their intelligence was. A similar study, on children in public housing high-rises above the Dan Ryan Expressway in Chicago, found that the closer their floor was to the highway, the lower their intelligence. So Merzenich began wondering about the role of a new environmental risk factor that might affect everyone but have a more damaging effect on genetically predisposed children: the continuous background noise from machines, sometimes called white noise. White noise consists of many frequencies and is very stimulating to the auditory cortex.

“Infants are reared in continuously more noisy environments. There is always a din,” he says. White noise is everywhere now, coming from fans in our electronics, air conditioners, heaters, and car engines. How would such noise affect the developing brain? Merzenich wondered.

To test this hypothesis, his group exposed rat pups to pulses of white noise throughout their critical period and found that the pups’ cortices were devastated.

“Every time you have a pulse,” Merzenich says, “you are exciting everything in the auditory cortex—every neuron.” So many neurons firing results in a massive BDNF release. And as his model predicted, this exposure brings the critical period to a premature close. The animals are left with undifferentiated brain maps and utterly indiscriminate neurons that get turned on by any frequency.

Merzenich found that these rat pups, like autistic children, were predisposed to epilepsy, and exposing them to normal speech caused them to have epileptic fits. (Human epileptics find that strobe lights at rock concerts set off their seizures. Strobes are pulsed emissions of white light and consist of many frequencies as well.) Merzenich now had his animal model for autism.

Recent brain scan studies now confirm that autistic children do indeed process sound in an abnormal way. Merzenich thinks that the undifferentiated cortex helps to explain why they have trouble learning, because a child with an undifferentiated cortex has a very difficult time paying attention. When asked to focus on one thing, these children experience booming, buzzing confusion—one reason autistic children often withdraw from the world and develop a shell. Merzenich thinks this same problem, in a milder form, may contribute to more common attention disorders.

Now the question for Merzenich was, could anything be done to normalize undifferentiated brain maps after the critical period? If he and his team could do so, they could offer hope for autistic children.

Using white noise, they first dedifferentiated the auditory maps of rats. Then, after the damage was done, they normalized and redifferentiated the maps using very simple tones, one at a time. With training, in fact, they brought the maps to an above-normal range. “And that,” says Merzenich, “is exactly what we are trying to do in these autistic children.” He is currently developing a modification of *Fast ForWord* that is designed for autism, a refinement of the program that helped Lauralee.

What if it were possible to reopen critical-period plasticity, so that adults could pick up languages the way children do, just by being exposed to them? Merzenich had already shown that plasticity extends into adulthood, and that with work—by paying close attention—we can rewire our brains. But now he was asking, could the critical period of effortless learning be extended?

Learning in the critical period is effortless because during that period the nucleus basalis is always on. So Merzenich and his young colleague Michael Kilgard set up an experiment in which they artificially turned on the nucleus basalis in adult rats and gave them learning tasks where they wouldn’t have to pay attention and wouldn’t receive a reward for learning.

They inserted microelectrodes into the nucleus basalis and used an electric current to keep it turned on. Then they exposed the rats to a 9 Hz sound frequency to see if they could effortlessly develop a brain map location for it, the way pups do during the critical period. After a week Kilgard and Merzenich found they could *massively* expand the brain map for that particular sound frequency. They had found an artificial way to reopen the critical period in adults.

They then used the same technique to get the brain to speed up its processing time. Normally an adult rat’s auditory neurons can only respond to tones at a maximum of 12 pulses per second. By stimulating the nucleus basalis, it was possible to “educate” the neurons to respond to ever more rapid inputs.

This work opens up the possibility of high-speed learning later in life. The nucleus basalis could be turned on by an electrode, by microinjections of certain chemicals, or by drugs. It is hard to imagine that people will not—for better or for worse—be drawn to a technology that would make it relatively effortless to master the facts of

science, history, or a profession, merely by being exposed to them briefly. Imagine immigrants coming to a new country, now able to pick up their new language, with ease and without an accent, in a matter of months. Imagine how the lives of older people who have been laid off from a job might be transformed, if they were able to learn a new skill with the alacrity they had in early childhood. Such techniques would no doubt be used by high school and university students in their studies and in competitive entrance exams. (Already many students who do not have attention deficit disorder use stimulants to study.) Of course, such aggressive interventions might have unanticipated, adverse effects on the brain—not to mention our ability to discipline ourselves—but they would likely be pioneered in cases of dire medical need, where people are willing to take the risk. Turning on the nucleus basalis might help brain-injured patients, so many of whom cannot relearn the lost functions of reading, writing, speaking, or walking because they can't pay close enough attention.

Merzenich has started a new company, Posit Science, devoted to helping people preserve the plasticity of their brains as they age and extend their mental lifespans. He's sixty-one but is not reluctant about calling himself old. "I love old people. I've always loved old people. Probably my favorite person was my paternal grandfather, one of the three or four most intelligent and interesting people I've met in life." Grandpa Merzenich came from Germany at nine on one of the last clipper ships. He was self-educated, an architect and a building contractor. He lived to be seventy-nine, at a time when life expectancy was closer to forty.

"It's estimated that by the time someone who is sixty-five now dies, the life expectancy will be in the late eighties. Well, when you are eighty-five, there is a forty-seven percent chance that you will have Alzheimer's disease." He laughs. "So we've created this bizarre situation in which we are keeping people alive long enough so that on the average, half of them get the black rock before they die. We've got to do something about the mental lifespan, to extend it out and into the body's lifespan."

Merzenich thinks our neglect of intensive learning as we age leads the systems in the brain that modulate, regulate, and control plasticity to waste away. In response he has developed brain exercises for age-related cognitive decline—the common decline of memory, thinking, and processing speed.

Merzenich's way of attacking mental decline is at odds with mainstream neuroscience. Tens of thousands of papers, written about the physical and chemical changes that occur in the aging brain, describe processes that occur as neurons die. There are many drugs on the market and scores of drugs in the pipeline designed to block these processes and raise levels of falling chemicals in the brain. Yet, Merzenich believes that such drugs, worth billions in sales, provide only about four to six months of improvement.

"And there is something really wrong about all this," he says. "It all neglects the role of what is required to *sustain* normal skills and abilities...It is as if your skills and abilities, acquired in the brain at some young age, are just destined to deteriorate as the physical brain deteriorates." The mainstream approach, he argues, is based on no real understanding of what it takes to develop a new skill in the brain, never mind to sustain it. "It is imagined," he says, "that if you manipulate the levels of the right neurotransmitter...that memory will be recovered, and cognition will be useful, and that you will start moving like a gazelle again."

The mainstream approach doesn't take into account what is required to maintain a sharp memory. A major reason memory loss occurs as we age is that we have trouble *registering* new events in our nervous systems, because processing speed slows down, so that the accuracy, strength, and sharpness with which we perceive declines. If you can't register something clearly, you won't be able to remember it well.

Take one of the most common problems of aging, trouble finding words. Merzenich thinks this problem often occurs because of the gradual neglect and atrophy of the brain's attentional system and nucleus basalis, which have to be engaged for plastic change to occur. This atrophy leads to our representing oral speech with "fuzzy engrams," meaning that the representation of sounds or words is not sharp because the neurons that encode these fuzzy engrams are not firing in the coordinated, quick way needed to send a powerful sharp signal. Because the neurons that represent speech pass on fuzzy signals to all the neurons downstream from them ("muddy in, muddy out") we also have trouble remembering, finding, and using words. It is similar to the problem we saw occurring in the brains of language-impaired children, who also have "noisy brains."

When our brains are “noisy,” the signal for a new memory can’t compete against the background electrical activity of the brain, causing a “signal-noise problem.”

Merzenich says the system gets noisier for two reasons. First because as everyone knows, “everything is progressively going to hell.” But “the main reason it is getting noisier is that it is not being appropriately exercised.” The nucleus basalis, which works by secreting acetylcholine—which, as we said, helps the brain “tune in” and form sharp memories—has been totally neglected. In a person with mild cognitive impairment the acetylcholine produced in the nucleus basalis is not even measurable.

“We have an intense period of learning in childhood. Every day is a day of new stuff. And then, in our early employment, we are intensely engaged in learning and acquiring new skills and abilities. And more and more as we progress in life we are operating as users of mastered skills and abilities.”

Psychologically, middle age is often an appealing time because, all else being equal, it can be a relatively placid period compared with what has come before. Our bodies aren’t changing as they did in adolescence; we’re more likely to have a solid sense of who we are and be skilled at a career. We still regard ourselves as active, but we have a tendency to deceive ourselves into thinking that we are learning as we were before. We rarely engage in tasks in which we must focus our attention as closely as we did when we were younger, trying to learn a new vocabulary or master new skills. Such activities as reading the newspaper, practicing a profession of many years, and speaking our own language are mostly the replay of mastered skills, not learning. By the time we hit our seventies, we may not have systematically engaged the systems in the brain that regulate plasticity for fifty years.

That’s why learning a new language in old age is so good for improving and maintaining the memory generally. Because it requires intense focus, studying a new language turns on the control system for plasticity and keeps it in good shape for laying down sharp memories of all kinds. No doubt *Fast ForWord* is responsible for so many general improvements in thinking, in part because it stimulates the control system for plasticity to keep up its production of acetylcholine and dopamine. Anything that requires highly focused attention will help that system—learning new physical activities that require concentration, solving challenging puzzles, or making a career change that requires that you master new skills and material. Merzenich himself is an advocate of learning a new language in old age. “You will gradually sharpen *everything* up again, and that will be very highly beneficial to you.”

The same applies to mobility. Just doing the dances you learned years ago won’t help your brain’s motor cortex stay in shape. To keep the mind alive requires learning something truly *new* with intense focus. That is what will allow you to both lay down new memories and have a system that can easily access and preserve the older ones.

The thirty-six scientists at Posit Science are working on five areas that tend to fall apart as we age. The key in developing exercises is to give the brain the right stimuli, in the right order, with the right timing to drive plastic change. Part of the scientific challenge is to find the most efficient way to train the brain, by finding mental functions to train that apply to real life.

Merzenich told me, “Everything that you can see happen in a young brain can happen in an older brain.” The only requirement is that the person must have enough of a reward, or punishment, to keep paying attention through what might otherwise be a boring training session. If so, he says, “the changes can be every bit as great as the changes in a newborn.”

Posit Science has exercises for memory of words and language, using *Fast ForWord*-like listening exercises and computer games for auditory memory designed for adults. Instead of giving people with fading memories lists of words to memorize, as many self-help books recommend, these exercises rebuild the brain’s basic ability to process sound, by getting people to listen to slowed, refined speech sounds. Merzenich doesn’t believe you can improve a fading memory by asking people to do what they can’t. “We don’t want to kick a dead horse with training,” he says. Adults do exercises that refine their ability to hear in a way they haven’t since they were in the crib trying to separate out Mother’s voice from background noise. The exercises increase processing speed and make basic signals stronger, sharper, and more accurate, while stimulating the brain to produce the dopamine and acetylcholine.

Various universities are now testing the memory exercises, using standardized tests of memory, and Posit Science has published its first control study in the *Proceedings of the National Academy of Sciences, USA*. Adults

between the ages of sixty and eighty-seven trained on the auditory memory program an hour a day, five days a week, for eight to ten weeks—a total of forty to fifty hours of exercises. Before the training, the subjects functioned on average like typical seventy-year-olds on standard memory tests. After, they functioned like people in the broad forty-to-sixty-year-old range. Thus, many turned back their memory clock ten or more years, and some individuals turned it back about twenty-five years. These improvements held at a three-month follow-up. A group at the University of California at Berkeley, led by William Jagust, did “before” and “after” PET (positron emission tomography) scans of people who underwent the training, and found that their brains did not show the signs of “metabolic decline”—neurons gradually becoming less active—typically seen in people of their age. The study also compared seventy-one-year-old subjects who used the auditory memory program with those of the same age who spent the same amount of time reading newspapers, listening to audiobooks, or playing computer games. Those who didn’t use the program showed signs of continuing metabolic decline in their frontal lobes, while those who used it didn’t. Rather, program users showed increased metabolic activity in their right parietal lobes and in a number of other brain areas, which correlated with their better performance on memory and attention tests. These studies show that brain exercises not only slow age-related cognitive decline but can lead to improved functioning. And keep in mind that these changes were seen with only forty to fifty hours of brain exercise; it may be that with more work, greater change is possible.

Merzenich says they have been able to turn back the clock on people’s cognitive functioning so that their memories, problem-solving abilities, and language skills are more youthful again. “We’ve driven people to abilities that apply to a much more youthful person—twenty or thirty years of reversal. An eighty-year-old is acting, operationally, like they are fifty or sixty years old.” These exercises are now available in thirty independent-living communities and for individuals through the Posit Science Web site.

Posit Science is also working on visual processing. As we age, we stop seeing clearly, not just because our eyes fail but because the vision processors in the brain weaken. The elderly are more easily distracted and more prone to lose control of their “visual attention.” Posit Science is developing computer exercises to keep people on task and speed up visual processing by asking subjects to search for various objects on a computer screen.

There are exercises for the frontal lobes that support our “executive functions” such as focusing on goals, extracting themes from what we perceive, and making decisions. These exercises are also designed to help people categorize things, follow complex instructions, and strengthen associative memory, which helps put people, places, and things into context.

Posit Science is also working on fine motor control. As we age, many of us give up on tasks such as drawing, knitting, playing musical instruments, or woodworking because we can’t control the fine movements in our hands. These exercises, now being developed, will make fading hand maps in the brain more precise.

Finally, they are working on “gross motor control,” a function that declines as we age, leading to loss of balance, the tendency to fall, and difficulties with mobility. Aside from the failure of vestibular processing, this decline is caused by the decrease in sensory feedback from our feet. According to Merzenich, shoes, worn for decades, limit the sensory feedback from our feet to our brain. If we went barefoot, our brains would receive many different kinds of input as we went over uneven surfaces. Shoes are a relatively flat platform that spreads out the stimuli, and the surfaces we walk on are increasingly artificial and perfectly flat. This leads us to dedifferentiate the maps for the soles of our feet and limit how touch guides our foot control. Then we may start to use canes, walkers, or crutches or rely on other senses to steady ourselves. By resorting to these compensations instead of exercising our failing brain systems, we hasten their decline.

As we age, we want to look down at our feet while walking down stairs or on slightly challenging terrain, because we’re not getting much information from our feet. As Merzenich escorted his mother-in-law down the stairs of the villa, he urged her to stop looking down and start feeling her way, so that she would maintain, and develop, the sensory map for her foot, rather than letting it waste away.

Having devoted years to enlarging brain maps, Merzenich now believes there are times you want to shrink them. He has been working on developing a mental eraser that can eliminate a problematic brain map. This

technique could be of great use for people who have post-traumatic flashbacks, recurring obsessional thoughts, phobias, or problematic mental associations. Of course, its potential for abuse is chilling.

Merzenich continues to challenge the view that we are stuck with the brain we have at birth. The Merzenich brain is structured by its constant collaboration with the world, and it is not only the parts of the brain most exposed to the world, such as our senses, that are shaped by experience. Plastic change, caused by our experience, travels deep into the brain and ultimately even into our genes, molding them as well—a topic to which we shall return.

This Mediterranean-style villa where he spends so much time sits among low mountains. He has just planted his own vineyard, and we walk through it. At night we talk about his early years studying philosophy, while four generations of his spirited family tease each other, breaking into peals of laughter. On the couch sits Merzenich's latest grandchild, just a few months old and in the midst of many critical periods. She makes everyone around her happy because she is such a good audience. You can coo at her, and she listens, thrilled. You tickle her toes, and she is completely attentive. As she looks around the room she takes in everything.

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