The Mind and the Brain: Neuroplasticity and the Power of Mental Force - Jeffrey M. Schwartz, Sharon Begley (2003)

Chapter 7. NETWORK REMODELING

The mind is its own place, and in itself Can make a heaven of hell.

—*John Milton*, Paradise Lost

In the previous two chapters, we examined the brain's talent for rewriting its zoning laws—or, to be more formal about it, the expression of neuroplasticity that neuroscientists call cortical remapping. We've seen how a region of somatosensory cortex that once processed feelings from an arm can be rezoned to handle input from the face; how the visual cortex can stop "seeing" and begin to "feel" how the motor cortex can reassign its neuronal real estate so that regions controlling much-used digits expand, much as a town might expand a playground when it enjoys a baby boom. In all these cases, brain plasticity follows an increase or decrease in sensory input: an increase, as in the case of violin players' giving their fingering digits a workout, leads to an expansion of the cortical space devoted to finger movement, whereas a decrease in sensory input, as in the case of amputation, leads to a shrinkage. But there is another aspect of neuroplasticity. Rather than a brute force expansion or shrinkage of brain regions zoned for particular functions, this form of neuroplasticity alters circuitry within a given region. And it results not from a change in the amount of sensory input, but from a change in its quality.

By the mid-1990s, Michael Merzenich and his UCSF team had two decades of animal research behind them. In addition to all the studies they had made of how changing levels of sensory stimulation altered the somatosensory cortex, they had shown that auditory inputs have the power to change the brain, too: altering sound input, they found, can physically change the auditory cortex of a monkey's brain and thus change the rate at which the brain processes sounds. The researchers began to suspect that the flip side of this held, too: a brain unable to process rapid-fire sounds, and thus to recognize the differences between sounds like *gee* and *key*, or *zip* and *sip*, may be different—physically different—from a brain that can. Across the country, at Rutgers University in New Jersey, Paula Tallal and Steve Miller had been studying children who had specific language impairment (SLI). In this condition, the kids have normal intelligence but great difficulty in reading and writing, and even in comprehending spoken language. Perhaps the best-known form of specific language impairment is dyslexia, which affects an estimated 5 to 17 percent of the U.S. population. When Tallal began studying dyslexia in the early 1970s, most educators ascribed it to deficits of visual processing. As the old (and now disproved) stereotype had it, a dyslexic confuses *p* with *q*, and *b* with *d*. Tallal didn't buy it. She suspected that dyslexia might reflect a problem not with recognizing the appearance of letters and words but, instead, with processing certain speech sounds—fast ones.

Her hunch was counterintuitive—most dyslexics, after all, have no detectable speech impediments—but it turned out to be right. Dyslexia often does arise from deficits in phonological processing. Dyslexics therefore struggle to decompose words into their constituent sounds and have the greatest trouble with *phonemes* (the smallest units of oral speech) like the sounds of *b, p, d*, and *g*, all of which burst from the lips and vanish in just a few thousandths of a second. In these dyslexics the auditory cortex, it seems, can no more resolve closely spaced sounds than a thirty-five-millimeter camera on Earth can resolve the craters and highlands of the Moon. They literally cannot hear these staccato sounds. How might this happen? Pat Kuhl's work, discussed in Chapter 3, shows how infants normally become attuned to the sounds of their native language: particular clumps of neurons in the auditory cortex come to represent the phonemes they hear every day. But consider what would happen if this input were somehow messed up, if the brain never correctly detected the phoneme. One likely result would be a failure to assign neurons to particular phonemes. As a result, dyslexics would be no more able to distinguish some phonemes than most native Japanese speakers are to distinguish *l* from *r*. Since learning to read involves matching written words to the heard language—learning that *C A T* has a one-to-one correspondence with the sound *cat*, for instance—a failure to form clear cortical representations of spoken language leads to impaired reading ability.

Merzenich knew about Tallal's hypothesis. So at a science meeting in Santa Fe, they discussed her suspicion that some children have problems hearing fast sounds, and her hunch that this deficit underlies their language impairment and reading problems. You could almost see the light bulb go off over Merzenich's head: his plasticity experiments on monkeys, he told Tallal, had implications for her ideas about dyslexia. Might reading be improved in dyslexics, he wondered, if their ability to process rapid phonemes were improved? And could that be done by harnessing the power of neuroplasticity? Just as his monkeys' digits became more sensitive through repeated manipulation of little tokens, Merzenich thought, so dyslexics might become more sensitive to phonemes through repeated exposure to auditory stimuli. But they would have to be acoustically modified stimuli: if the basis of dyslexia is that the auditory cortex failed to form dedicated circuits for explosive, staccato phonemes, then the missing circuits would have to be created. They would have to be coaxed into being by exposing a child over and over to phonemes that had been artificially drawn out, so that instead of being so staccato they remained in the hearing system a fraction of a second longer—just enough to induce a cortical response.

Tallal, in the meantime, had received a visit from officials of the Charles A. Dana Foundation, which the industrialist David Mahoney was leading away from its original mission of education and into neuroscience. But not just any neuroscience. Incremental science was all well and good, Mahoney told Tallal, but what he was interested in was discovery science, risk-taking science—research that broke paradigms and made us see the world, and ourselves, in a new light. "Put your

hand in the fire!" he encouraged her. The upshot was the launch of a research program on the neurological mechanisms that underlie reading and on how glitches in those mechanisms might explain reading difficulties. Rutgers and UCSF would collaborate in a study aimed at determining whether carefully manipulated sounds could drive changes in the human auditory cortex.

In January 1994, Merzenich, Bill Jenkins, Christoph Schreiner (a postdoc in Merzenich's lab), and Xiaoqin Wang trekked east, and over two days Tallal and her collaborators told the Californians "everything they knew about kids with Specific Language Impairment," recalls Jenkins. "We sat there and listened, and about halfway through I blurted out, 'It sounds like these kids have a backwards masking problem'—a brain deficit in auditory processing. That gave us the insight into how we might develop a way to train the brain to process sounds correctly." Two months later, the Dana Foundation awarded them a three-year grant of $2.3 million.

The UCSF and Rutgers teams set to work, trying to nail down whether a phonological processing deficit truly underlies dyslexia and whether auditory plasticity might provide the basis for fixing it. They started with the hypothesis that children with specific language impairment construct their auditory cortex from faulty inputs. The kids take in speech sounds in chunks of one-third to one-fifth of a second—a period so long that it's the length of syllables, not phonemes—with the result that they do not make sharp distinctions between syllables. It's much like trying to see the weapons carried by troops when your spy camera can't resolve anything smaller than a tank. So it is with this abnormal "signal chunking": the brains of these children literally do not hear short phonemes. *Ba*, for instance, starts with a *b* and segues explosively into *aaaah* in a mere 40 milliseconds. For brains unable to process transitions shorter than 200 milliseconds, that's a problem. The transition from *mmm* to *all* in *mall*, in contrast, takes about 300 milliseconds. Children with specific language impairment can hear *mall* perfectly well, but *ba* is often confused with *da* because all they actually hear is the vowel sound. There are undoubtedly multiple causes of this processing abnormality, including developmental delays, but middle ear infections that muffle sounds are a prime suspect. These deficits in acoustic signal reception seem to emerge in the first year of life and have profound consequences. By age two or three, children with these deficits lag behind their peers in language production and understanding. Later, they often fail to connect the letters of written speech with the sounds that go with those letters. When *ba* sounds like *da*, it's tough to learn to read phonetically.

If language deficits are the result of abnormal learning by the auditory cortex, then the next question was obvious: can the deficits be remedied by learning, too? To find out, Rutgers recruited almost a dozen kids with SLI and set up experimental protocols; UCSF developed the acoustic input, in the form of stretched-out speech, that they hoped would rewire the children's auditory cortex. But from the beginning Mike Merzenich was concerned. The auditory map forms early in life, so that by the time children are two they have heard spoken something like 10 million to 20

million words—words that, if the hypothesis about phonemic processing deficits was correct, sounded wrong. He knew that cortical representations are maintained through experience, and experience was what these kids had every time they misheard speech. "How are we going to undo that?" he worried. And worse, although the kids would hear modified speech in the lab, they would be hearing, and mishearing, the regular speech of their family and friends the rest of the time. That, Merzenich fretted, would reinforce all of the faulty phonemic mapping that was causing these kids' problems. Short of isolating the children, there was no way around it: the researchers would simply have to take their best shot at rebuilding a correct phonemic representation in the children's brains, competing input be damned.

As luck would have it, Xiaoqin Wang had joined Merzenich's lab in the early 1990s after finishing his Ph.D. at Johns Hopkins, where he had studied the auditory system. Although reading a book on the brain had lured him into neuroscience, Wang's first love had been information processing: he had earned a master's degree in computer science and electrical engineering. That experience had given him just the signal-processing knowledge that Paula Tallal and Merzenich needed to produce modified speech tapes that would, they hoped, repair the faulty phonemic representations in the brains of SLI children. Wang was reluctant to enlist in the project, because he was so busy with the experiments on cortical remapping of monkeys' hand representations. "But Mike is someone you just can't say no to," he recalls. "So we took this idea of Tallal's that if you slow down rapid phonemes the kids will hear them. What I managed to do was slow down speech without changing its pitch or other characteristics. It still sounded like spoken English, but the rapid phonemes were drawn out." The software stretched out the time between *b* and *aaah*, for example, and also changed which syllables were emphasized. To people with normal auditory processing, the sound was like an underwater shout. But to children with SLI, the scientists hoped, it would sound like *baa*—a sound they had never before heard clearly. When Tallal listened to what Wang had come up with, she was so concerned that the kids would be bored out of their minds, listening to endless repetitions of words and phonemes, that she dashed out to pick up a supply of Cheetos. She figured her team would really have to bribe—er, motivate—the kids to stick with the program.

And so began Camp Rutgers, in the summer of 1994. It was a small study with a grand goal: to see whether chronic exposure to acoustically modified phonemes would alter the cortical representation of language of an SLI child and help him overcome his impairment. The scientists' audacious hope was that they could retrain neurons in the auditory cortex to recognize lightning-fast phonemes. The school-age kids would show up every weekday morning at eight and stay until eleven. While their parents watched behind a one-way mirror, the children donned headphones. Using tapes of speech processed with Wang's software, they were coached in listening, grammar, and following directions (a novelty for some, since they'd never understood many instructions in the first place). For example, "Point

to the boy who's chasing the girl who's wearing red," intoned the program over and over, the better to create the cortical representations of phonemes. To break up the monotony, the scientists offered the kids snacks and puppets, frequent breaks—and in one case, even handstand demonstrations. Steve Miller recalls, "All we did for three hours every day was listen. We couldn't even talk to the kids: they got enough normal [misheard] speech outside the lab. It was so boring that Paula had to give us pep talks and tell us to stop whining. She would give us a thumbs-up for a good job—and we'd give her a different finger back." In addition to the three hours listening to modified speech in the lab, every day at home the children played computer games that used processed speech.

As the children progressed, the program moved them from ultra-drawn-out phonemes through progressively less drawn-out ones, until the modified speech was almost identical to normal speech. The results startled even the scientists. After only a month, all the children had advanced two years in language comprehension. For the first time in their life, they understood speech as well as other kids their age.

"So we had these great results from a small group of kids," Steve Miller says. "But when Paula went to a conference in Hawaii, people jumped all over her, screaming that we couldn't make these results public. They pointed out that we had no controls: how did we know that the language improvement didn't reflect simply the one-on-one attention the kids got, rather than something specific to the modified speech?" Merzenich was hugely offended. He was itching to get the results to people who would benefit from them. But he agreed to keep quiet. "Sure, we had these great results with seven kids," says Bill Jenkins. "But we knew no one would believe it. We knew we had to go back," to get better data on more children.

So they did. The following summer, they held Camp Rutgers II. For twenty days, twenty-two SLI kids aged five to nine played CD-ROM games structured to coax the brain into building those absent phonological representations. One game, for instance, asked the child to "point to rake" when pictures of a lake as well as a rake were presented, or to click a mouse when a series of spoken *g*'s was interrupted by a *k*. At first, the computer voice stretched out the target sounds: *rrrrrake*. The usual 0.03-second (30-millisecond) difference between *day* and *bay*, for instance, lasted several times that long. The modified speech seemed to be recruiting neurons to make progressively faster and more accurate distinctions between sounds. When a child mastered the difference between *ba* and *pa* when the initial phoneme was stretched to 300 milliseconds, the software shortened the transition to, say, 280 milliseconds. The goal was to push the auditory cortex to process faster and faster phonemes. The kids also took home books like *The Cat in the Hat* on tape, recorded in processed speech. Again the results were striking: a few months after receiving twenty to forty hours of training, all the children tested at normal or above in their ability to distinguish phonemes. Their language ability rose by two years. Although the research did not include brain scans, it seemed for all the world that Fast ForWord (as the program was now called) was doing something

a bit more revolutionary than your run-of-the-mill educational CD: it was rewiring brains.

In January 1996, the Rutgers and UCSF teams reported their results in the journal *Science*. Modified speech, they concluded, had altered the children's brains in such a way that they could now distinguish phonemes and map them correctly onto written words. Just as Greg Recanzone showed that when monkeys pay attention to a frequency-discrimination task their auditory cortex changes and their ability to hear tiny differences in tone improves, so SLI children who had received intensive training in discriminating acoustically modified phonemes seemed to have undergone cortical reorganization in the region of the brain that carries out auditory processing. "You create your brain from the input you get," says Paula Tallal.

"We realized we had a tiger by the tail," says Jenkins. Merzenich fretted that once the results were out, everyone with a language-impaired child would want it. He was right. The work was covered in newspapers and magazines, and in just ten days some 17,000 people had jammed the Rutgers switchboard, blowing out the e-mail and phone systems, in an effort to get hold of the miraculous CD-ROM that seemed to conquer dyslexia. Desperate parents awakened Merzenich at 2 A.M. (his phone number was listed), imploring him to help their children. Representatives from the venture capital firm E. M. Warburg, Pincus & Co. descended on Tallal's lab to figure out whether she had the basis for a profit-making business. Fellow scientists were appalled. Some even suspected that the Rutgers/UCSF team had manufactured all the media interest, as if in a replay of the cold fusion claims of the 1980s.

A Rutgers regent offered advice on how they might license the CD-ROM, but Merzenich, who had been on the team that developed the cochlear implant for hearing loss, was convinced that if you license a scientific discovery, "you lose all control over it." He and Bill Jenkins discussed the dilemma endlessly. "We were afraid that if we just licensed the software to Broderbund or the Learning Company or something they wouldn't understand the scientific complexity of it, and wouldn't implement it right," says Jenkins. "And if that happened, the opportunity would be lost. We wanted to make sure the science got properly translated." So the month after the *Science*publication, Merzenich, Paula Tallal, Bill Jenkins, Steve Miller, and recruits from the business world raised enough private financing to form Scientific Learning Corp., the first company dedicated to making money from neuroplasticity.

Merzenich told colleagues that forming a business was the only way to get the benefits of neuroplasticity out of the lab and into the hands—or brains, actually—of the people it could help. When Ed Taub once expressed frustration about how slow the rehabilitation community was to embrace constraint-induced movement therapy for stroke, Merzenich responded that only the profit motive was strong enough to overcome entrenched professional interests and the prejudice that the brain has lost plasticity after infancy. By October 1996 Merzenich and his partners had secured venture capital funding from E.M. Warburg, and the next month Scientific

Learning conducted its first public demonstration of Fast ForWord, at the annual meeting of the American Speech-Language-Hearing Association. "No one would be using Fast ForWord if there were not a commercial force driving it into the world," Merzenich said four years later. "The nonprofit motive is simply too slow."

By unleashing the force of commercialism, Merzenich is convinced, Fast ForWord reached more children than it would have if he and Tallal had simply sung its praises from the offices of their ivy-walled universities. In October 1997 19 schools in nine districts across the country participated in a pilot program using Fast ForWord, enrolling more than 450 students with specific language impairment. Within four years some 500 school systems had learning specialists trained to use Fast ForWord (soon renamed Fast ForWord Language), and by the year 2000 25,000 SLI children had practiced on it for at least 100 minutes a day, five days a week. Once the children master recognition of the stretched-out phonemes, the program speeds them up until eventually the children are hearing ordinary speech. After about four weeks, the kids can process phonemes pronounced at normal speed. After six to eight weeks, "90 percent of the kids who complete the program have made 1.5 to two years of progress in reading skills," says Tallal. Scientific Learning itself graduated, too, financially speaking: in July 1999 it announced its initial public offering. Anyone who believed in neuroplasticity, and its power to turn a profit, could now ante up.

Scientific Learning has hardly won universal acceptance. Critics say it is too expensive for most schools. Some also say the system is being rushed to market before its stunning claims have been proved in independent tests. The claim that Fast ForWord reshapes the brain has been the target of the most vituperation. In one representative comment, Dr. Michael Studdert-Kennedy, past president of the Haskins Laboratories, a center for the study of speech and language at Yale University, told the *New York Times* in 1999 that inducing neuroplasticity was "an absurd stunt" that would not help anyone learn to read.

Yet only a year later, researchers reported compelling evidence that Fast ForWord changes the brain no less than Taub's constraint-induced movement therapy or Merzenich's monkey training does. Merzenich, Tallal, and colleagues had teamed up with John Gabrieli of Stanford University to perform brain imaging on dyslexic and normal adults. For the first time, brain scans would be used to look for changes that accompanied the use of their learning program. Using functional magnetic resonance imaging (fMRI), the researchers first ascertained that their eight adult dyslexics and ten matched controls differed in their processing of rapid acoustic stimuli. When they heard rapid, computer-generated nonsense syllables (designed to mimic the consonant-vowel-consonant pattern of English, but without being real words), the brains of nine of ten normal readers showed greater activation (compared to that triggered by slower sounds) in the left prefrontal region of what are called Brodmann's areas 46/10/9. Only two of eight dyslexics showed such left prefrontal activity when they heard rapid acoustic signals. The highly significant difference between the groups strongly suggests that the response in that region

had been disrupted in the dyslexics. Since this area is thought to be responsible for the processing of staccato sounds, its lack of activity could explain dyslexics' inability to hear those sounds.

The researchers next performed fMRIs on the three dyslexics who had undergone Fast ForWord training for 100 minutes a day, five days a week, for about thirty-three sessions. Two of the three showed significantly greater activation in this left prefrontal region. These were also the subjects who showed the greatest improvements, after Fast ForWord, in their processing of rapid auditory signals and language comprehension. (The dyslexic whose brain showed no such change also did not improve on auditory processing.) Training in rapid acoustic discrimination can apparently induce the left prefrontal cortex, which is normally attuned to fast-changing acoustic stimuli but is disrupted in dyslexics, to do its job. The region, even in adults, remains "plastic enough…to develop such differential sensitivity after intensive training," the scientists concluded.

The discovery that modified speech can drive neuroplasticity in the mature brain is just the most dramatic example (so far) of how sensory stimuli can rewire neuronal circuits. In fact, soon after Merzenich and Tallal published their results, other scientists began collecting data showing that, as in my own studies of OCD patients, brain changes do not require changes in either the quantity or the quality of sensory input. To the contrary: the brain could change even if all patients did was use mindfulness to respond to their thoughts differently. Applied mindfulness could change neuronal circuitry.

It seemed to me that if the mindfulness-based Four Steps had any chance of finding applicability beyond obsessive-compulsive disorder, its best hope lay in Tourette's syndrome. Recent evidence indicates that this disease strikes about 5 people per 1,000. Although its precise cause remains to be worked out, Tourette's has a strong genetic component. Drs. James Leckman and David Pauls of Yale University had shown in 1986 that there is a biological link between OCD and Tourette's, such that the presence of Tourette's in a family puts relatives at risk of OCD. But I was interested in a different common characteristic of the two diseases. The defining symptoms of Tourette's are sudden stereotypical outbursts, called tics. They include vocalizations such as grunting or barking or spouting profanities, as well as muscle movements such as twitches and jerks of the face, head, or shoulders. These echo the compulsions of OCD, but there is more: the motor and vocal tics that characterize Tourette's usually have a harbinger, a vague discomfort that patients often describe as an irresistible urge to perform the head jerk, to utter the profanity. The more the patient suppresses the tic, the more insistent the urge becomes, until the inevitable surrender brings immediate (albeit temporary) relief. The similarities to OCD are obvious: Tourette's patients suffer a bothersome urge to twitch their face, blink their eyes, purse their lips, sniffle, grunt, or clear their throat in much the same way as OCD patients feel compelled to count, organize, wash, or check.

The two diseases also seem to share a neural component. The symptoms of Tourette's apparently arise from impaired inhibition in the circuit linking the cortex and the basal ganglia—a circuit that is also impaired in OCD. The basal ganglia, you'll recall from Chapter 2, play a central role in switching from one behavior to another. Impairment there could account for the perseveration of obsessions and compulsions, as well as the tics characteristic of Tourette's.

The first case study of this disease appeared in 1825, with a description of one Marquise de Dampierre. "In the midst of a conversation that interests her extremely, all of a sudden, without being able to prevent it, she interrupts what she is saying or what she is listening to with bizarre shouts and with words that are more extraordinary and which make a deplorable contrast with her intellect and her distinguished manners," reads the translation of the account in *Archives Générales de Médecine*. "The words are for the most part gross swear words and obscene epithets and, something that is no less embarrassing for her than for the listeners, an extremely crude expression of a judgment or of an unfavorable opinion of someone in the group." Sixty years later, Georges Gilles de la Tourette took up "the case of the cursing marquise," identifying it as the prototypical example of what he called *maladie des tics*. The disease was given its current name in 1968 by the psychiatrist Arthur Shapiro and his wife, the psychologist Elaine Shapiro. In the search for a cause, physicians suspected patients' families of inflicting early psychological trauma, and patients themselves were blamed for a failure of will.

The disease's mysterious cause inspired a wide range of treatments, from leeches to hypnosis and even lobotomies. More recently, physicians, suspecting that dopamine transmission in the basal ganglia circuit causes the disease, have tried to treat Tourette's with haloperidol and pimozide, drugs that block the neurotransmitter dopamine. (Uncertainty remains, however, over whether an excess of dopamine, sensitivity of dopamine receptors, basal ganglia malfunction, or some combination of these is at fault. In any case, it is likely that the genetic basis of the disease manifests itself somewhere in the dopamine system.) Drugs typically reduce tic symptoms 50 to 60 percent in the 80 percent of patients who respond at all. But dopamine blockers do not work for every patient. Worse, the drugs have big drawbacks, often producing serious side effects, even leaving some patients in a zombielike state. In fact, side effects lead up to 90 percent of patients to discontinue the drugs. Of those who stick with the regimen, inconsistent compliance is common. Many parents, concerned about the lack of information on the long-term effects of the medications on children, are understandably reluctant to keep their kids drugged. No wonder drugs have fallen from their perch as the treatment of choice.

That leaves behavioral treatment. But behavioral approaches have been hampered by—and there is no way to put this politely—lousy science. Over several decades, almost a hundred studies have investigated half a dozen behavioral therapies. They looked into *massed practice*, in which the patient performs his worst tic for perhaps five minutes at a time, with a minute of rest, before repeating the process for a

total of about thirty minutes. Other studies investigated *operant conditioning*, in which parents and others are taught to praise and encourage a child when he is not performing a tic, and punish the performance of a tic. Others tried *anxiety management* (since tics seem to get worse with stress) and *relaxation training*, with deep breathing and imagery; although many patients managed to control tics during the therapy session, the improvement seldom carried over into the real world. Some studies explored awareness training, using videotapes and mirrors to make the patient realize how bad his tics were. But few of the studies included more than nine subjects, few included children, most failed to use standard measures of tics, and many piled so many behavioral interventions on top of one another that it was impossible to tease out which therapy was responsible for any observed effects. Follow-up was poor (a real problem since tics wax and wane naturally). In other words, the scientific underpinnings of this generation of behavioral therapies were so seriously flawed as to compromise their credibility.

Suspecting that Tourette's might be amenable to a mindfulness-based approach like the one that was succeeding with OCD, I began (in a nice way) jawboning researchers who might be sympathetic. In 1989, at the annual meeting of the American College of Neuropsychopharmacology (ACNP), I struck up a conversation with Jim Leckman. Jim is arguably the country's leading expert on the cause of Tourette's. On top of that, he is trained as a psychoanalyst and so is keenly interested in the mind-brain interface. After 1989 we became good friends, but it was not until the mid-1990s, at another ACNP meeting, that I began telling Jim about the broader implications of the PET data we had collected on OCD patients—implications about the power of the mind to shape the brain. Although he kept an open mind, he was decidedly skeptical. Because Jim is perhaps the most polite member of the baby boom generation, it took me almost a decade to realize just how much he had been graciously humoring me. Eventually, he became convinced that there might be clinical advantages to giving patients an active role in therapy—in the case of Tourette's, by using mindfulness to modulate the physical expression of the tics. Only then did he start to believe that my arguments were more than a lot of hot air.

Even after Jim started to come around, his boss at the Yale Child Study Center remained less than a true believer in this idea. When I visited Jim's lab in July 1998, he and his department chair, Donald Cohen, arranged for me to meet with an adolescent boy with OCD in what's called an observed interview. As Jim, Cohen, and a group of the clinical staff looked on, I did a brief, interactive, and animated overview of the Four Steps with this bright kid. Afterward, as we reviewed the clinical interaction, Cohen looked at me with an amused expression and said, "So, it seems like you managed to sell that young man on your shtick." "Well, it's not really a shtick…" I began. "It sounds like a shtick to me," he shot back. I tried to point out that it's not a gimmick to teach patients suffering with OCD that their intrusive thoughts and urges are caused by brain imbalances, and that we now know they can physically alter those imbalances through mindfulness and self-

directed behavioral therapy techniques. Although to psychiatry professors the Four Steps of Relabel, Reattribute, Refocus, Revalue may initially seem like a shtick, we had strong scientific evidence that this approach can bring about changes in brain function. (Of course Cohen already knew all this, or I wouldn't have been at Yale in the first place.)

This seemed to calm matters down a bit. In any event, we all went out for a nice dinner. And besides, the Yale Child Study group had already done a major brain imaging study relevant to this point. Just three months before, in April 1998, in a study based on reasoning quite similar to the Four Steps approach to changing the brain circuits underlying OCD, Brad Peterson, Jim Leckman, and their Yale colleagues published important data on what happens when Tourette's patients use willful effort to suppress tic expression. The Yale group had patients undergo fMRIs while they alternated forty seconds of letting their tics be expressed with forty seconds of volitionally suppressing them. Hearing the word *now* told the volunteers when to switch—particularly, when to call up whatever reserves of will they could muster to prevent the tics from causing bodily movements. The investigators noted how brain activity changed during tic suppression compared to when tics are given free rein. The most relevant regions seemed to house the circuit involving our old friends the prefrontal cortex, anterior cingulate gyrus, basal ganglia, and thalamus. Activity in this circuit—the very one involved in OCD and in the formation of habits—was noticeably altered (activity in the caudate increased and activity in the putamen decreased) when patients willfully prevented themselves from moving in response to the intrusive bothersome urges of Tourette's. The study also found that the worse the tics, the less the basal ganglia and thalamus activity change when the tics are suppressed.

This finding is quite consistent with the notion of a "brain lock" in Tourette's, which may be similar to that in OCD patients. You'll remember from Chapter 2 that prior to cognitive-behavioral treatment the brain structures of the OCD circuit—the orbital frontal cortex, anterior cingulate gyrus, caudate, and thalamus—showed such high correlations in their activity they seemed to be functioning in lockstep. This same circuit also seems to be "locked up" in patients with Tourette's. As the Yale researchers put it, "A failure to inhibit tics may result from an impaired ability to alter subcortical neuronal activity." Thus in Tourette's, as in OCD, the gearshift of the basal ganglia seems to be locked. As it happened, my UCLA colleague John Piacentini was in the middle of a study designed to gauge whether mindful awareness and directed mental force could help unfreeze this jammed transmission.

In August 2000 Jim Leckman was in Los Angeles attending to family matters, so he, John Piacentini, and I got together. Piacentini had just put together the data from his ongoing study using a cognitive-behavioral approach incorporating mindfulness to treat children with Tourette's. This new approach had been designed with an eye toward combining classical behavioral techniques for treating tics with the mindfulness component of the Four Steps. The key was to make patients understand that tics are an expression of a biological brain malfunction, much as

the Four Steps makes OCD patients aware that their obsessions and compulsions originate in an overactive brain circuit. This new treatment aims to teach the patient that the behavioral response to the tic urge can be modified so that both the functional impairments (social and otherwise) and the physical damage to joints and muscles are reduced. After all, tics can be painful.

As Piacentini explained it to Jim Leckman and me, he asks each child to describe his or her tic occurrences in detail and reenact them in front of a mirror. Piacentini points out a tic if one occurs during a session. He also teaches the patient to identify the situations when a tic is most likely to recur, to recognize the very first glimmerings of the urge to tic, and to enhance that awareness by labeling it with the verbal or mental note *t:* as soon as the child feels a tic coming on, he says *t* to himself.

But the distinctive ingredient is training patients to develop what are called *competing responses*. Then, every time the urge to tic arises, that urge is paired with a behavior designed to modify the expression of the urge in order to control it better. If it is a verbal tic, John teaches the patient to breathe through the nose, slowly; that makes it physically impossible to bark out a curse. If it is a motor tic, John coaches him to hold his arm close to his body, tense the neck muscles, or slowly open and close his eyes—activities that preclude wild arm swings, head jerks, or fast blinking, respectively. In the really creative part of the therapy John teaches the patient attenuated behavior, such as moving the arm slowly and wiping his brow to make the movement more volitional and controlled. The strategy has a good deal in common with directing OCD patients to Refocus attention away from a pathological compulsion and onto a healthy behavior. "What you want to do is substitute voluntary, controlled movement for the involuntary tic," says Piacentini. "You need to be able to recognize the onset of the urge to tic, pay attention, and be motivated. It's similar to the Four Steps approach to OCD. Patients are trained to recognize and label tic urges consciously and then either try to resist these urges, or else respond in a controlled and attenuated way. Most youngsters are eventually able to significantly diminish and/or eliminate targeted tics."

When Leckman, Piacentini, and I sat down to look at John's preliminary data, it was clear he had something. Twenty-four Tourette's children, aged seven to seventeen, had enrolled in the study. Piacentini had divided the kids into two groups. In one, the children practiced recognizing when an urge to tic arose. In this stage, analogous to the Relabel and Reattribute parts of the Four Steps, they would realize that the urge to tic had arisen and give it that label *t*. "This is the urge to tic." This is called *awareness training*. In the other group, Piacentini combined awareness training with habit modulation, in which the child is taught to respond to the urge to tic in a safe way by, for instance, executing a less intense movement. This is analogous to the Refocus step. Seventeen of the children completed the eight-week program. The assessors, gauging the children's tic severity, were blind to which treatment group each child had been assigned to.

The results were striking. Patients receiving awareness training alone had an approximately 10 percent improvement in tic severity. But those also receiving habit modulation training had a 30 percent reduction in tic severity and a 56 percent improvement in tic-related impairment. "Now it is being accepted that you can use behavioral intervention to treat a biologically-mediated disease," Piacentini says. Although John has not yet done before-and-after brain scans to ascertain whether the children's clinical improvement is accompanied by brain changes of the kind we detected in OCD patients, it is quite likely that brain changes analogous to those we found in OCD were occuring.

Innumerable studies have now shown that the mind can affect the body: mere thoughts can set hearts racing and hormones surging. Although mind-body medicine is usually understood as the mind's effect on the body from the neck down, the power of the Four Steps to remodel neuronal connections—strengthening those underlying healthy habits and inhibiting those between the frontal cortex and basal ganglia (the OCD circuit) underlying pathological ones—strongly suggests that the mind can also affect the brain. In 1997, colleagues who knew of my interest in mindfulness told me about the work of John Teasdale at the Medical Research Council Cognition and Brain Sciences Unit in Cambridge, England. They said that Teasdale, working with Mark Williams and Zindel Segal, seemed to be harnessing exactly this power of the mind, but to treat depression: he proposed that patients would lower their risk of falling back into clinical depression if they learned to experience their depressive thoughts "simply as events in the mind." That, of course, is a hallmark of the Impartial Spectator and mindful awareness. Teasdale and colleagues suspected that this perspective would diminish the power of so-called triggering cues to tip someone into a depressive episode. Just as my OCD patients learned to recognize intrusive thoughts as the manifestation of their brain's misbehavior, so Teasdale's depressives, the researchers thought, could learn to prevent a relapse by processing emotional material in a new way. By 1995, they were was boldly using *mindfulness* in the titles of their research papers, and in 2000 Teasdale named his approach *mindfulness-based cognitive therapy*.

Depression is often a chronic disorder, characterized by frequent relapses. Over a lifetime, a patient has an 80 percent chance of suffering a recurrence and, on average, experiences four major depressive episodes lasting twenty weeks each. Antidepressants are the most widely used treatment. But in the 1990s, studies had begun to suggest that cognitive therapy, too, had the power to prevent relapses. In one study of 158 patients who had been treated with only partial success by antidepressants, some received cognitive therapy as well as drugs for their remaining symptoms. The rest received only the medication. The difference in relapse rates over the sixty-eight-week period of the study was significant: patients undergoing cognitive therapy experienced a 40 percent reduction in their rate of relapse compared to the drugs-only group.

Clearly, cognitive therapy helps prevent depressive relapse, and Teasdale thought he knew why. Other studies were showing that people are at greatest risk for

becoming depressed when a sad, dysphoric, or "blue" mood produces patterns of negative, hopeless thinking. What distinguishes people who get depressed from those who don't, Teasdale suspected, may be this: in the first group, dysphoria, that down-in-the-dumps feeling that most of us experience at least once in a while, triggers "patterns of depressogenic thinking" powerful enough to trigger full-blown depression. In these patients, dysphoria that may make a healthy person feel kind of blue plunges depression-prone patients into a well of despair. They ruminate on their perceived deficiencies and on the hopelessness of life. Although in a healthy person a bad day at work or a disastrous date may induce some passing sadness, in someone susceptible to depression it can readily escalate to "I'm completely incompetent and life is pointless." In these vulnerable people, a dysphoric thought or experience seems to trigger the onslaught of depression much as a burning ember kindles a brushfire: the sad thought ignites a conviction that one is pathetic and worthless, or that one's current problems are irreparable and eternal. In relapsing depressives, this connection becomes so habitual and automatic that they "keep the system 'stuck' in repetitively generating [depressogenic thoughts]." It follows, then, that the risk of relapse can depend on how easily sadness tips someone into the self-perpetuating biological imbalances that characterize major depression.

To Teasdale, the corollary to this hypothesis was clear. To prevent the recurrence of depression, it may be sufficient for a patient to process her emotions in a new way, a way that does not trigger the thoughts and mood states characteristic of a depressive episode. That is, it may be enough to find a way to disrupt the automatic segue from sadness to sickness—and the pathological brain states associated with it. With the right therapy, thoughts and feelings that once tipped the person into full-blown depression would instead become "short-lived and self-limiting," Teasdale suggested. His proposed therapy would change the very way patients think about their thoughts.

If Teasdale's hunch seems reminiscent of my work with OCD patients—in which the urge to perform some compulsive act still intrudes but is thwarted when patients think about their thoughts and feelings differently—well, so it seemed to me, too. Studies at a handful of labs were already demonstrating the power of cognitive therapy over depression. When patients were presented with a scenario such as "You go out with someone and it goes badly" and were then asked how much they agreed or disagreed with such statements as "My value as a person depends greatly on what others think of me," patients receiving only drugs were more likely to sink into dysfunctional thinking than those who also received cognitive-behavioral therapy. (The extent to which dysfunctional thinking follows dysphoria predicts the likelihood that a patient will suffer a relapse of depression.) That patients receiving cognitive-behavioral therapy are better able to resist being plunged into despair by sad thoughts suggests that this therapy changes emotional processing—the way people think about their feelings—in ways that prevent dysphoria from triggering full-blown depression. Such research, Teasdale

concludes, "suggests that emotional processing should focus primarily on changing emotional responses to internal affective events and thoughts, so that these responses are short-lived and self-limiting, rather than the first stages of an escalating process."

Teasdale then began to construct a therapy to achieve this. Through mindfulness-based cognitive therapy, he wanted to make patients more aware of their thoughts. In particular, he wanted them to recognize that sadness can (through a brain-based biological mechanism) escalate into depression. To prevent it from doing so, they would learn to meet the onset of dysphoria with such responses as "Thoughts are not facts" and "I am not my thoughts." Or as Teasdale puts it, they would learn to prevent what he calls *depressive interlock* (again, reminiscent of my "brain lock") : the strong, physical connection between unhappy thoughts and the memories, associations, and modes of thought that inflate sadness into depression. To do that, the therapist needs to help patients encode in memory alternative thought patterns that can be activated by the very same cues that otherwise tap into the despairing ones.

When I read this, in 1999, I was thrilled. Finally, I thought, I've found a kindred spirit in this profession. This guy is actually using mindfulness to help patients to see the passing, ephemeral nature of their depressive thoughts. Teasdale's proposed treatment also gave me a sense of déjà vu. Healthy emotional processing prevents the dysphoria from triggering global thoughts of hopelessness and self-worthlessness. It instead activates alternative memories and associations, so that the next time the patient encounters something that makes her sad she reacts not with despair but by calling up other, healthier associations. To me, this was reminiscent of OCD patients learning to respond to the compulsive urge to wash by deciding instead to crochet or garden—that is, by Refocusing. As Teasdale put it, "The new schematic models rather than the old will be accessed and these new models will determine emotional response." Much as I had, he was proposing that patients could learn to weaken the physical connections to the old, pathological schema—habitual way of thinking—and strengthen those to a new, healthier one. And as with the Four Steps approach, mindfulness was to be the key.

How, then, to apply mindfulness to depression? Teasdale identified three ways that depressives can process emotion-laden thoughts. They can mindlessly emote, or allow themselves to be engulfed by their feelings with little self-awareness or reflection. Patients who respond this way typically have poor outcomes to psychotherapy. Alternatively, patients can engage in "conceptualizing/doing." By this, Teasdale means having impersonal, even detached thoughts about the self, about depression, and about its causes and consequences. Conceptualizing/doing lacks the introspection inherent in mindfulness. Depressed patients who think this way also tend not to do well in therapy.

The third option is what Teasdale named "mindful experiencing/being." In this way of thinking about your emotions, you sense feelings, sensations, and thoughts from

the perspective of the Impartial Spectator. You regard your thoughts and feelings as passing, ephemeral "mental events" rather than as accurate reflections of reality. Instead of reacting to negative thoughts and feelings as "these are me," you come to regard them as "events in the mind that can be considered and examined." You recognize that thoughts are not facts (just as my OCD patients learned that their obsessions are only their brain's causing their mind to misbehave) but are instead "events that come and go through the mind," as Teasdale explains it. Mindfulness gives patients the attentional skills that allow them to disengage from, and focus instead on alternatives to, the dysfunctional ways of thinking that trigger a relapse of their depression. Teasdale had independently constructed, and taken the first steps toward proving, a model of depression much like my model of OCD. In a landmark paper in August 2000, Teasdale and his colleagues reported the results of his yearlong study on using mindfulness to prevent the relapse of depression, offering strong support for the findings in OCD patients that mindfulness can alter brain circuits. Using an approach pioneered by the American psychologist Jon Kabat-Zinn, Teasdale had his patients participate in two-hour group sessions once a week for eight weeks, receiving mindfulness training through tape-recorded instructions that taught them to direct their attention to specific regions of the body in succession. The goal was to become acutely aware of whatever sensations an arm, a cheek, a knee was experiencing at the moment. The patients then learned to focus on their breathing. If the mind wandered, patients acknowledged the distractions with "friendly awareness"—that is, not with frustration or anger—and learned to return calmly to a focus on the breath. Repeating this process over and over, patients learned to use their inhalations and exhalations as an anchor to pull them back to a mindful awareness of the present moment. The patients also had homework, including exercises designed to increase their moment-by-moment awareness of feelings, thoughts, and sensations and to allow them to view thoughts and feelings (particularly negative ones) as merely passing events in the mind and brain.

The results were impressive. Of the 145 patients from ages eighteen to sixty-five, who had suffered at least two episodes of major depression within the last five years, about half were randomly assigned to receive the standard treatment and half to receive the mindfulness training, too. All had been off antidepressants for at least the previous twelve weeks, long enough to clear the drugs from their system. Over the sixty-week study period (eight weeks of treatment then fifty-two weeks of follow-up), among patients who had suffered at least three episodes of major depression there was a 44 percent reduction in the rate of relapse among those who received mindfulness therapy compared to those receiving standard therapy. Adding mindfulness, then, cut the rate of relapse by almost half. This was the first demonstration that a mindfulness-based psychological intervention can reduce the rate of relapse in depression.

The will, it was becoming clear, has the power to change the brain—in OCD, in stroke, in Tourette's, and now in depression—by activating adaptive circuitry. That

a mental process alters circuits involved in these disorders offers dramatic examples of how the ways someone thinks about thoughts can effect plastic changes in the brain. Jordan Grafman, chief of cognitive neuroscience at the National Institute of Neurological Disorders and Stroke, calls this top-down plasticity, because it originates in the brain's higher-order functions. "Bottom-up" plasticity, in contrast, is induced by changes in sensory stimuli such as the loss of input after amputation. Merzenich's and Tallal's work shows the power of this bottom-up plasticity to resculpt the brain. The OCD work hints at the power of top-down plasticity, the power of the mind to alter brain circuitry. I suspect that when the requisite brain imaging is done with Teasdale's depressives, that research will also show the power of mind to change the brain. In fact, recent studies using a somewhat different form of psychotherapy called interpersonal therapy already have.

Sitting somewhere between purely mental events and purely sensory ones is this vast sea of life called experience. Research into how experience affects the brain is only in its infancy, but one of my favorite examples suggests where we may be heading.

One wag called the study "taxicology." When researchers at University College London decided to study how navigation expertise might change the brain, they didn't have to look far for subjects. London cabbies are renowned for their detailed knowledge of the capital's streets: to get their license, they have to pass a stringent police test assessing how well they know the fastest way from point A to point B and what streets are where. Drivers call it "being on The Knowledge," and it takes them an average of two years to learn it.

Earlier studies in small mammals, monkeys, birds, and humans had established that the right half of an unassuming little structure near the center of the brain called the hippocampus is involved in the formation of directional memories; in fact, the back of the right hippocampus seems to store a mental map of the environment. Eleanor Maguire and her colleagues at the university therefore decided to examine the hippocampi of London taxi drivers, using magnetic resonance imaging, and compare them to the hippocampi of Londoners who hadn't the faintest notion of the best way to get from Fleet and Chancery to Gresham and Noble.

Maguire scanned the brains of sixteen cabbies, aged thirty-two to sixty-two, and fifty ordinary right-handed men of the same age. Everyone's brain structures looked about the same, in both size and shape—except the hippocampus. In the taxi drivers, the back was significantly larger than it was in the other men, and the front was smaller. That might simply reflect the fact that if you're born with a big rear hippocampus, you are a navigational ace, and hence are more likely to take up hacking than if you can't tell east even at sunrise. So to see if the brain differences reflected experience, Maguire plotted the differences in the volume of the hippocampus against how experienced a driver was. There it was: the more years a

man had been a taxi driver, the smaller the front of his hippocampus and the larger the posterior. "Length of time spent as a taxi driver correlated positively with volume in…the right posterior hippocampus," found the scientists. Acquiring navigational skills causes a "redistribution of gray matter in the hippocampus" as a driver's mental map of London grows larger and more detailed with experience.

What cabbies might be sacrificing in the front part of their hippocampus for an enlarged posterior part remains unknown, as does the mechanism for the volume changes. Although neurogenesis might explain the enlargement of the rear of the hippocampus, the London scientists have their money on an overall reorganization of the hippocampus's circuitry "in response to a need to store an increasingly detailed spatial representation." One thing, however, is clear: a key brain structure can change in response to your experience as an adult. Published in 2000, this was the first demonstration that the basic anatomy of the adult brain, not just the details of its wiring, can be altered by the demands its owner places on it.

The study of neuroplasticity began with scientists' cataloguing the changes in sensory input that induce cortical remapping and rewiring. Now, even as they add to the list of examples of neuroplasticity, researchers are also exploring the cellular and molecular mechanisms that underlie it. We know that the formation of new synapses, as a result of the growth of existing axons or dendrites, is involved in both the remodeling of circuits and cortical remapping. A change in the quantity of available neurotransmitters, or the enzymes that regulate them, can also foster plasticity. But now researchers are examining a mechanism that had long been dismissed as an avenue to plasticity: the actual creation of new neurons. Although a slew of animal experiments had demonstrated that new synapses can form when the animal is exposed to an "enriched" environment, that was one step short of showing that new neurons, as opposed to new connections between neurons, were being born.

That changed in 1997. Fred Gage and colleagues at the Salk Institute in La Jolla, California, placed adult mice in an "enriched" environment (one that resembles the complex surroundings of the wild more than the near-empty cages of the rats in the "nonen-riched" environment do). By the end of the experiment, the formation and survival of new neurons had increased 15 percent in a part of the hippocampus called the dentate gyrus. These animals also learned to navigate a maze better. In 1999 Elizabeth Gould of Princeton University used similar techniques in adult rats to demonstrate that the creation of new neurons, called neurogenesis, was not a talent lost in infancy: the increased neurogenesis, she found, is directly related to learning tasks that involve the hippocampus. Also in 1999, Gage showed again that new neurons grow in the hippocampus of adult mice as a result of exercising on a wheel, and in 2001 Gould and colleagues demonstrated that newly generated neurons are "associated with the ability to acquire…memories."

"Neurogenesis was a hard thing for scientists to come to grips with," said Gage. But by the new millennium it was clear that new neurons arise from stem cells,

immature cells capable of differentiating into virtually any type of cell. There is now abundant evidence that neural stem cells persist in the adult brain and support ongoing neurogenesis. And the evidence is no longer confined to mice. In 1998, Peter Eriksson of Goteborg, Sweden, working with Gage, demonstrated that neurogenesis occurs in the adult human hippocampus. Thus Gage's and Gould's discoveries suggest that the possibilities for neuroplasticity are greater than even diehard believers thought: the brain may not be limited to working with existing neurons, fitting them together in new networks. It may, in addition, add fresh neurons to the mix. The neural electrician is not restricted to working with existing wiring, we now know: he can run whole new cables through the brain.

Neuroplasticity has come a long way since Nobel laureates ridiculed Mike Merzenich for his audacity in claiming to have shown that the mature central nervous system has the capacity to change. Even in the early 1990s neuroplasticity was viewed as, at best, an interesting little field. By the middle of the decade, however, it had become one of the hottest topics in neuroscience, and as the decade ended, hundreds of researchers had made it the focus of their studies. "If you had taken a poll of neuroscientists in the early 1990s, I bet only 10 to 15 percent would have said that neuroplasticity exists in the adult," Merzenich says. "Even by the middle of the decade the split would have been 50–50. What changed that was the human experiments" like Taub's. Now there is no question that the brain remodels itself throughout life, and that it retains the capacity to change itself as the result not only of passively experienced factors such as enriched environments, but also of changes in the ways we behave (taking up the violin) and the ways we think ("That's just my OCD acting up"). Nor is there any question that every treatment that exploits the power of the mind to change the brain involves an arduous effort—by patients afflicted by stroke or depression, by Tourette or OCD—to improve both their functional capacity and their brain function.

We began our discussion of neuroplasticity by quoting from the Spanish neuroanatomist Santiago Ramón y Cajal's description of the "nerve paths" in the adult brain as "fixed" and "immutable." It seems only right, then, to close with another passage from Cajal, who despite his pessimism about the seeming lack of malleability in the adult brain nevertheless saw a glimmer of hope: "It is for the science of the future to change, if possible, this harsh decree. Inspired with high ideals, it must work to impede or moderate the gradual decay of the neurones, to overcome the almost inevitable rigidity of their connections." The science of the future has arrived. And in what may be the most remarkable form of neuroplasticity, scientists are seeing glimpses that internal mental states can shape the structure and hence the function of the brain. Faced with examples of how the brain can be changed—from Taub's stroke patients and Piacentini's Tourette's patients to Teasdale's depressives and Merzenich's dyslexics—I had become more convinced than ever that such self-directed neuroplasticity is real. It was time to explore how attention in general, and wise attention—mindfulness—in particular, wields its power.