Five

Days to Months Before

Our act has occurred—the pulling of a trigger or the touching of an arm that can mean such different things in different contexts. Why did that just happen? We've seen how, seconds before, that behavior was the product of the nervous system, whose actions were shaped by sensory cues minutes to hours before, and how the brain's sensitivity to those cues was shaped by hormonal exposure in the preceding hours to days. What events in the prior days to months shaped that outcome?

Chapter 2 introduced the plasticity of neurons, the fact that things alter in them. The strength of a dendritic input, the axon hillock's set point for initiating an action potential, the duration of the refractory period. The previous chapter showed that, for example, testosterone increases the excitability of amygdaloid neurons, and glucocorticoids decrease excitability of prefrontal cortical neurons. We even saw how progesterone boosts the efficacy with which GABA-ergic neurons decrease the excitability of other neurons.

Those versions of neural plasticity occur over hours. We now examine more dramatic plasticity occurring over days to months. A few months is enough time for an Arab Spring, for a discontented winter, or for STDs to spread a lot during a Summer of Love. As we'll see, this is also sufficient time for enormous changes in the brain's structure.

NONLINEAR EXCITATION

We start small. How can events from months ago produce a synapse with altered excitability today? How do synapses "remember"?

When neuroscientists first approached the mystery of memory at the start of the twentieth century, they asked that question on a more macro level—how does a brain remember? Obviously, a memory was stored in a single neuron, and a new memory required a new neuron.

The discovery that adult brains don't make new neurons trashed that idea. Better microscopes revealed neuronal arborization, the breathtaking complexity of branches of dendrites and axon terminals. Maybe a new memory requires a neuron to grow a new axonal or dendritic branch.

Knowledge emerged about synapses, neurotransmitter-ology was born, and this idea was modified—a new memory requires the formation of a new synapse, a new connection between an axon terminal and a dendritic spine.

These speculations were tossed on the ash heap of history in 1949, because of the work of the Canadian neurobiologist Donald Hebb, a man so visionary that even now, nearly seventy years later, neuroscientists still own bobblehead dolls of him. In his seminal book, *The Organization of Behaviour*, Hebb proposed what became the dominant paradigm. Forming memories doesn't require new synapses (let alone new branches or neurons); it requires the strengthening of *preexisting* synapses.[1]

What does "strengthening" mean? In circuitry terms, if neuron A synapses onto neuron B, it means that an action potential in neuron A more readily triggers one in neuron B. They are more tightly coupled; they "remember." Translated into cellular terms, "strengthening" means that the wave of excitation in a dendritic spine spreads farther, getting closer to the distant axon hillock.

Extensive research shows that experience that causes repeated firing across a synapse "strengthens" it, with a key role played by the neurotransmitter glutamate.

Recall from chapter 2 how an excitatory neurotransmitter binds to its receptor in the postsynaptic dendritic spine, causing a sodium channel to open; some sodium flows in, causing a blip of excitation, which then spreads.

Glutamate signaling works in a fancier way that is essential to learning.[2] To simplify considerably, while dendritic spines typically contain only one type of receptor, those responsive to glutamate contain two. The first (the "non-NMDA") works in a conventional way—for every little smidgen of glutamate binding to these receptors, a smidgen of sodium flows in, causing a smidgen of excitation. The second (the "NMDA") works in a nonlinear, threshold manner. It is usually unresponsive to glutamate. It's not until the non-NMDA has been stimulated over and over by a long train of glutamate release, allowing enough sodium to flow in, that this activates the NMDA receptor. It suddenly responds to all that glutamate, opening its channels, allowing an explosion of excitation.

This is the essence of learning. The lecturer says something, and it goes in one ear and out the other. The factoid is repeated; same thing. It's repeated enough times and—aha!—the lightbulb goes on and suddenly you get it. At a synaptic level, the axon terminal having to repeatedly release glutamate is the lecturer droning on repetitively; the moment when the postsynaptic threshold is passed and the NMDA receptors first activate is the dendritic spine finally getting it.

“AHA” VERSUS ACTUALLY REMEMBERING

But this has only gotten us to first base. The lightbulb going on in the middle of the lecture doesn’t mean it’ll still be on in an hour, let alone during the final exam. How can we make that burst of excitation persist, so that NMDA receptors “remember,” are more easily activated in the future? How does the potentiated excitation become long term?

This is our cue to introduce the iconic concept of LTP—“long-term potentiation.” LTP, first demonstrated in 1966 by Terje Lømo at the University of Oslo, is the process by which the first burst of NMDA receptor activation causes a prolonged increase in excitability of the synapse.* Hundreds of productive careers have been spent figuring out how LTP works, and the key is that when NMDA receptors finally activate and open their channels, it is calcium, rather than sodium, that flows in. This causes an array of changes; here are a few:

- The calcium tidal wave causes more copies of glutamate receptors to be inserted into the dendritic spine’s membrane, making the neuron more responsive to glutamate thereafter.*
- The calcium also alters glutamate receptors that are already on the front lines of that dendritic spine; each will now be more sensitive to glutamate signals.*
- The calcium also causes the synthesis of peculiar neurotransmitters in the dendritic spine, which are released and travel *backward* across the synapse; there they increase the amount of glutamate released from the axon terminal after future action potentials.

In other words, LTP arises from a combination of the presynaptic axon terminal yelling “glutamate” more loudly and the postsynaptic dendritic spine listening more attentively.

As I said, additional mechanisms underlie LTP, and neuroscientists debate *which* is most important (the one they study, naturally) in neurons in organisms

when they are actually learning. In general, the debate has been whether pre- or the postsynaptic changes are more crucial.

After LTP came a discovery that suggests a universe in balance. This is LTD—long-term "depression"—experience-dependent, long-term decreases in synaptic excitability (and, interestingly, the mechanisms underlying LTD are not merely the opposite of LTP). LTD is not the functional opposite of LTP either—rather than being the basis of generic forgetting, it sharpens a signal by erasing what's extraneous.

A final point about LTP. There's long term and there's *long* term. As noted, one mechanism underlying LTP is an alteration in glutamate receptors so that they are more responsive to glutamate. That change might persist for the lifetime of the copies of that receptor that were in that synapse at the time of the LTPing. But that's typically only a few *days*, until those copies accumulate bits of oxygen-radical damage and are degraded and replaced with new copies (similar updating of all proteins constantly occurs). Somehow LTP-induced changes in the receptor are transferred to the next generation of copies. How else can octogenarians remember kindergarten? The mechanism is elegant but beyond the scope of this chapter.

All this is cool, but LTP and LDP are what happens in the hippocampus when you learn explicit facts, like someone's phone number. But we're interested in other types of learning—how we learn to be afraid, to control our impulses, to feel empathy, or to feel nothing for someone else.

Synapses utilizing glutamate occur throughout the nervous system, and LTP isn't exclusive to the hippocampus. This was a traumatic discovery for many LTP/hippocampus researchers—after all, LTP is what occurred in Schopenhauer's hippocampus when he read Hegel, not what the spinal cord does to make you more coordinated at twerking.*

Nonetheless, LTP occurs throughout the nervous system.*[3] For example, fear conditioning involves synapses LTPing in the basolateral amygdala. LTP underlies the frontal cortex learning to control the amygdala. It's how dopaminergic systems learn to associate a stimulus with a reward—for example, how addicts come to associate a location with a drug, feeling cravings when in that setting.

Let's add hormones to this, translating some of our stress concepts into the language of neural plasticity. Moderate, transient stress (i.e., the good, stimulatory stress) promotes hippocampal LTP, while prolonged stress disrupts it

and promotes LTD—one reason why cognition tanks at such times. This is the inverted-*U* concept of stress writ synaptic.[4]

Moreover, sustained stress and glucocorticoid exposure enhance LTP and suppress LTD in the amygdala, boosting fear conditioning, and suppress LTP in the frontal cortex. Combining these effects—more excitable synapses in the amygdala, fewer ones in the frontal cortex—helps explain stress-induced impulsivity and poor emotional regulation.[5]

Rescued from the Trash

The notion of memory resting on the strengthening of preexisting synapses dominates the field. But ironically, the discarded idea that memory requires the formation of new synapses has been resuscitated. Techniques for counting all of a neuron's synapses show that housing rats in a rich, stimulatory environment increases their number of hippocampal synapses.

Profoundly fancy techniques let you follow one dendritic branch of a neuron over time as a rat learns something. Astonishingly, over minutes to hours a new dendritic spine emerges, followed by an axon terminal hovering nearby; over the next weeks, they form a functioning synapse that stabilizes the new memory (and in other circumstances, dendritic spines retract, eliminating synapses).

Such "activity-dependent synaptogenesis" is coupled to LTP—when a synapse undergoes LTP, the tsunami of calcium rushing into the spine can diffuse and trigger the formation of a new spine in the adjacent stretch of the dendritic branch.

New synapses form throughout the brain—in motor-cortex neurons when you learn a motoric task, or in the visual cortex after lots of visual stimulation. Stimulate a rat's whiskers a lot, and ditto in the "whisker cortex."[6]

Moreover, when enough new synapses form in a neuron, the length and number of branches in its dendritic "tree" often expand as well, increasing the strength and number of the neurons that can talk to it.

Stress and glucocorticoids have inverted-*U* effects here as well. Moderate, transient stress (or exposure to the equivalent glucocorticoid levels) increases spine number in the hippocampus; sustained stress or glucocorticoid exposure does the opposite.[7] Moreover, major depression or anxiety—two disorders associated with elevated glucocorticoid levels—can reduce hippocampal

dendrite and spine number. This arises from decreased levels of that key growth factor mentioned earlier this chapter, BDNF.

Sustained stress and glucocorticoids also cause dendritic retraction and synapse loss, lower levels of NCAM (a "neural cell adhesion molecule" that stabilizes synapses), and less glutamate release in the frontal cortex. The more of these changes, the more attentional and decision-making impairments.[8]

Recall from chapter 4 how acute stress strengthens connectivity between the frontal cortex and motoric areas, while weakening frontal-hippocampal connections; the result is decision making that is habitual, rather than incorporating new information. Similarly, chronic stress increases spine number in frontal-motor connections and decreases it in frontal-hippocampal ones.[9]

Continuing the theme of the amygdala differing from the frontal cortex and hippocampus, sustained stress increases BDNF levels and expands dendrites in the BLA, persistently increasing anxiety and fear conditioning.[10] The same occurs in that way station by which the amygdala talks to the rest of the brain (the BNST—bed nucleus of the stria terminalis). Recall that while the BLA mediates fear conditioning, the central amygdala is more involved in innate phobias. Interestingly, stress seems not to increase the force of phobias or spine number in the central amygdala.

There's wonderful context dependency to these effects. When a rat secretes tons of glucocorticoids because it's terrified, dendrites atrophy in the hippocampus. However, if it secretes the same amount by voluntarily running on a running wheel, dendrites expand. Whether the amygdala is also activated seems to determine whether the hippocampus interprets the glucocorticoids as good or bad stress.[11]

Spine number and branch length in the hippocampus and frontal cortex are also increased by estrogen.[12] Remarkably, the size of neurons' dendritic trees in the hippocampus expands and contracts like an accordion throughout a female rat's ovulatory cycle, with the size (and her cognitive skills) peaking when estrogen peaks.*

Thus, neurons can form new dendritic branches and spines, increasing the size of their dendritic tree or, in other circumstances, do the opposite; hormones frequently mediate these effects.

Axonal Plasticity

Meanwhile, there's plasticity at the other end of the neuron, where axons can sprout offshoots that head off in novel directions. As a spectacular example, when a blind person adept at Braille reads in it, there's the same activation of the tactile cortex as in anyone else; but amazingly, uniquely, there is also activation of the *visual* cortex.[13] In other words, neurons that normally send axons to the fingertip-processing part of the cortex instead have gone miles off course, growing projections to the visual cortex. One extraordinary case concerned a congenitally blind woman, adept at Braille, who had a stroke in her visual cortex. And as a result, she lost the ability to read Braille—the bumps on the page felt flattened, imprecise—while other tactile functions remained. In another study, blind subjects were trained to associate letters with distinctive tones, to the point where they could hear a sequence of tones as letters and words. When these individuals would "read with sound," they'd activate the part of the visual cortex activated in sighted individuals when reading. Similarly, when a person who is deaf and adept at American Sign Language watches someone signing, there is activation of the part of their auditory cortex normally activated by speech.

The injured nervous system can "remap" in similar ways. Suppose there is stroke damage to the part of your cortex that receives tactile information from your hand. The tactile receptors in your hand work fine but have no neurons to talk to; thus you lose sensation in your hand. In the subsequent months to years, axons from those receptors can sprout off in new directions, shoehorning their way into neighboring parts of the cortex, forming new synapses there. An imprecise sense of touch may slowly return to the hand (along with a less precise sense of touch in the part of the body projecting to the cortical region that accommodated those refugee axon terminals).

Suppose, instead, that tactile receptors in the hand are destroyed, no longer projecting to those sensory cortical neurons. Neurons abhor a vacuum, and tactile neurons in the wrist may sprout collateral axonal branches and expand their territory into that neglected cortical region. Consider blindness due to retinal degeneration, where the projections to the visual cortex are silenced. As described, fingertip tactile neurons involved in reading Braille sprout projections into the visual cortex, setting up camp there. Or suppose there is a pseudoinjury: after merely five days of subjects being blindfolded, auditory projections start to remap into the visual cortex (and retract once the blindfolds come off).[14]

Consider how fingertip tactile neurons carrying information about Braille remap to the visual cortex in someone blind. The sensory cortex and visual

cortex are far away from each other. How do those tactile neurons “know” (a) that there’s vacant property in the visual cortex; (b) that hooking up with those unoccupied neurons helps turn fingertip information into “reading”; and (c) how to send axonal projections to this new cortical continent? All are matters of ongoing research.

What happens in a blind person when auditory projection neurons expand their target range into the inactive visual cortex? More acute hearing—the brain can respond to deficits in one realm with compensations in another.

So sensory projection neurons can remap. And once, say, visual cortex neurons are processing Braille in a blind person, *those* neurons need to remap where they project to, triggering further downstream remapping. Waves of plasticity.

Remapping occurs regularly throughout the brain in the absence of injury. My favorite examples concern musicians, who have larger auditory cortical representation of musical sounds than do nonmusicians, particularly for the sound of their own instrument, as well as for detecting pitch in speech; the younger the person begins being a musician, the stronger the remapping.[15]

Such remapping does not require decades of practice, as shown in beautiful work by Alvaro Pascual-Leone at Harvard.[16] Nonmusician volunteers learned a five-finger exercise on the piano, which they practiced for two hours a day. Within a few days the amount of motor cortex devoted to the movement of that hand expanded, but the expansion lasted less than a day without further practice. This expansion was probably “Hebbian” in nature, meaning preexisting connections transiently strengthened after repeated use. However, if subjects did the daily exercise for a crazed four weeks, the remapping persisted for many days afterward. This expansion probably involved axonal sprouting and the formation of new connections. Remarkably, remapping also occurred in volunteers who spent two hours a day *imagining* playing the finger exercise.

As another example of remapping, after female rats give birth, there is expansion of the tactile map representing the skin around the nipples. As a rather different example, spend three months learning how to juggle, and there is expansion of the cortical map for visual processing of movement.*[17]

Thus, experience alters the number and strength of synapses, the extent of dendritic arbor, and the projection targets of axons. Time for the biggest revolution in neuroscience in years.

DIGGING DEEPER IN THE ASH HEAP OF HISTORY

Recall the crude, Neanderthal-ish notion that new memories require new neurons, an idea discarded when Hebb was in diapers. The adult brain does not make new neurons. You've got your maximal number of neurons around birth, and it's downhill from there, thanks to aging and imprudence.

You see where we're heading—adult brains, including aged human brains, do make new neurons. The finding is truly revolutionary, its discovery epic.

In 1965 an untenured associate professor at MIT named Joseph Altman (along with a longtime collaborator, Gopal Das) found the first evidence for adult neurogenesis, using a then-novel technique. A newly made cell contains newly made DNA. So, find a molecule unique to DNA. Get a test tube full of the stuff and attach a miniscule radioactive tag to each molecule. Inject it into an adult rat, wait awhile, and examine its brain. If any neurons contain that radioactive tag, it means they were born during the waiting period, with the radioactive marker incorporated into the new DNA.

This is what Altman saw in a series of studies.[18] As even he notes, the work was initially well received, being published in good journals, generating excitement. But within a few years something shifted, and Altman and his findings were rejected by leaders in the field—it couldn't be true. He failed to get tenure, spent his career at Purdue University, lost funding for his adult neurogenesis work.

Silence reigned for a decade until an assistant professor at the University of New Mexico named Michael Kaplan extended Altman's findings with some new techniques. Again this caused mostly crushing rejection by senior figures in the field, including one of the most established men in neuroscience, Pasko Rakic of Yale.[19]

Rakic publicly rejected Kaplan's (and tacitly Altman's) work, saying he had looked for new neurons himself, they weren't there, and Kaplan was mistaking other cell types for neurons. At a conference he notoriously told Kaplan, "Those may look like neurons in New Mexico, but they don't in New Haven." Kaplan soon left research (and a quarter century later, amid the excitement of the

rediscovery of adult neurogenesis, wrote a short memoir entitled “Environmental Complexity Stimulates Visual Cortex Neurogenesis: Death of a Dogma and a Research Career”).

The field lay dormant for another decade until unexpected evidence of adult neurogenesis emerged from the lab of Fernando Nottebohm of Rockefeller University. Nottebohm, a highly accomplished and esteemed neuroscientist, as good an old boy as you get, studied the neuroethology of birdsong. He demonstrated something remarkable, using new, more sensitive techniques: new neurons are made in the brains of birds that learn a new territorial song each year.

The quality of the science and Nottebohm’s prestige silenced those who doubted that neurogenesis occurred. Instead they questioned its relevance—oh, that’s nice for Fernando and his birdies, but what about in real species, in mammals?

But this was soon convincingly shown in rats, using newer, fancier techniques. Much of this was the work of two young scientists, Elizabeth Gould of Princeton, and Fred “Rusty” Gage of the Salk Institute.

Soon lots of other people were finding adult neurogenesis with these new techniques, including, lo and behold, Rakic.[20] A new flavor of skepticism emerged, led by Rakic. Yes, the adult brain makes new neurons, but only a few, they don’t live long, and it doesn’t happen where it really counts (i.e., the cortex); moreover, this has been shown only in rodents, not in primates. Soon it was shown in monkeys.*[21] Yeah, said the skeptics, but not humans, and besides, there’s no evidence that these new neurons are integrated into preexisting circuits and actually function.

All of that was eventually shown—there’s considerable adult neurogenesis in the hippocampus (where roughly 3 percent of neurons are replaced each month) and lesser amounts in the cortex.[22] It happens in humans throughout adult life. Hippocampal neurogenesis, for example, is enhanced by learning, exercise, estrogen, antidepressants, environmental enrichment, and brain injury* and inhibited by various stressors.*[23] Moreover, the new hippocampal neurons integrate into preexisting circuits, with the perky excitability of young neurons in the perinatal brain. Most important, new neurons are essential for integrating new information into preexisting schemas, something called “pattern separation.” This is when you learn that two things you previously thought were the same are, in fact, different—dolphins and porpoises, baking soda and baking powder, Zooey Deschanel and Katy Perry.

Adult neurogenesis is the trendiest topic in neuroscience. In the five years after Altman's 1965 paper was published, it was cited (a respectable) twenty-nine times in the literature; in the last five, more than a thousand. Current work examines how exercise stimulates the process (probably by increasing levels of certain growth factors in the brain), how new neurons know where to migrate, whether depression is caused by a failure of hippocampal neurogenesis, and whether the neurogenesis stimulated by antidepressants is required for such medications to work.[24]

Why did it take so long for adult neurogenesis to be accepted? I've interacted with many of the principals and am struck by their differing takes. At one extreme is the view that while skeptics like Rakic were ham-handed, they provided quality control and that, counter to how path-of-the-hero epics go, some early work in the field was not all that solid. At the other extreme is the view that Rakic et al., having failed to find adult neurogenesis, couldn't accept that it existed. This psychohistorical view, of the old guard clinging to dogma in the face of changing winds, is weakened a bit by Altman's not having been a young anarchist running amok in the archives; in fact, he is a bit older than Rakic and other principal skeptics. All of this needs to be adjudicated by historians, screenwriters, and soon, I hope, by the folks in Stockholm.

Altman, who at the time of this writing is eighty-nine, published a 2011 memoir chapter.[25] Parts of it have a plaintive, confused tone—everyone was so excited at first; what happened? Maybe he spent too much time in the lab and too little marketing the discovery, he suggests. There's the ambivalence of someone who spent a long time as a scorned prophet who at least got to be completely vindicated. He's philosophical about it—hey, I'm a Hungarian Jew who escaped from a Nazi camp; you take things in stride after that.

SOME OTHER DOMAINS OF NEUROPLASTICITY

We've seen how in adults experience can alter the number of synapses and dendritic branches, remap circuitry, and stimulate neurogenesis.[26] Collectively, these effects can be big enough to actually change the size of brain regions. For example, postmenopausal estrogen treatment increases the size of the hippocampus (probably through a combination of more dendritic branches and more neurons). Conversely, the hippocampus atrophies (producing cognitive problems) in prolonged depression, probably reflecting its stressfulness and the typically elevated glucocorticoid levels of the disease. Memory problems and loss of hippocampal volume also occur in individuals with severe chronic pain syndromes, or with Cushing's syndrome (an array of disorders where a tumor causes extremely elevated glucocorticoid levels). Moreover, post-traumatic stress disorder is associated with increased volume (and, as we know, hyperreactivity) of the amygdala. In all of these instances it is unclear how much the stress/glucocorticoid effects are due to changes in neuron number or to changes in amounts of dendritic processes.*

One cool example of the size of a brain region changing with experience concerns the back part of the hippocampus, which plays a role in memory of spatial maps. Cab drivers use spatial maps for a living, and one renowned study showed enlargement of that part of the hippocampus in London taxi drivers. Moreover, a follow-up study imaged the hippocampus in people before and after the grueling multiyear process of working and studying for the London cabbie license test (called the toughest test in the world by the *New York Times*). The hippocampus enlarged over the course of the process—in those who passed the test.[27]

Thus, experience, health, and hormone fluctuations can change the size of parts of the brain in a matter of months. Experience can also cause long-lasting changes in the numbers of receptors for neurotransmitters and hormones, in levels of ion channels, and in the state of on/off switches on genes in the brain (to be covered in chapter 8).[28]

With chronic stress the nucleus accumbens is depleted of dopamine, biasing rats toward social subordination and biasing humans toward depression. As we saw in the last chapter, if a rodent wins a fight on his home territory, there are long-lasting increases in levels of testosterone receptors in the nucleus accumbens and ventral tegmentum, enhancing testosterone's pleasurable effects. There's even a parasite called *Toxoplasma gondii* that can infect the brain; over the course of weeks to months, it makes rats less fearful of the smell of cats and makes humans less fearful and more impulsive in subtle ways. Basically, most anything you can measure in the nervous system can change in response to a sustained stimulus. And importantly, these changes are often reversible in a different environment.*

SOME CONCLUSIONS

The discovery of adult neurogenesis is revolutionary, and the general topic of neuroplasticity, in all its guises, is immensely important—as is often the case when something the experts said couldn't be turns out to be.[29] The subject is also fascinating because of the nature of the revisionism—neuroplasticity radiates optimism. Books on the topic are entitled *The Brain That Changes Itself*, *Train Your Mind, Change Your Brain*, and *Rewire Your Brain: Think Your Way to a Better Life*, hinting at the "new neurology" (i.e., no more need for neurology once we can fully harness neuroplasticity). There's can-do Horatio Alger spirit every which way you look.

Amid that, some cautionary points:

- One recalls caveats aired in other chapters—the ability of the brain to change in response to experience is value free. Axonal remapping in blind or deaf individuals is great, exciting, and moving. It's cool that your hippocampus expands if you drive a London cab. Ditto about the size and specialization of the auditory cortex in the triangle player in the orchestra. But at the other end, it's disastrous that trauma enlarges the amygdala and atrophies the hippocampus, crippling those with PTSD. Similarly, expanding the amount of motor cortex devoted to finger dexterity is great in neurosurgeons but probably not a societal plus in safe crackers.
- The extent of neuroplasticity is most definitely finite. Otherwise, grievously injured brains and severed spinal cords would ultimately heal. Moreover, the limits of neuroplasticity are quotidian. Malcolm Gladwell has explored how vastly skilled individuals have put in vast amounts of practice—ten thousand hours is his magic number. Nevertheless, the reverse doesn't hold: ten thousand hours of practice does not guarantee the neuroplasticity needed to make any of us a Yo-Yo Ma or LeBron James.

Manipulating neuroplasticity for recovery of function does have enormous, exciting potential in neurology. But this domain is far from the concerns of this book. Despite neuroplasticity's potential, it's unlikely that we'll ever be able to, say, spritz neuronal growth factors up people's noses to make them more open-minded or empathic, or to target neuroplasticity with gene therapy to blunt some jerk's tendency to displace aggression.

So what's the subject good for in the realm of this book? I think the benefits are mostly psychological. This recalls a point from chapter 2, in the discussion of the neuroimaging studies demonstrating loss of volume in the hippocampus of people with PTSD (certainly an example of the adverse effects of neuroplasticity). I sniped that it was ridiculous that many legislators needed pictures of the brain to believe that there was something desperately, organically wrong with veterans with PTSD.

Similarly, neuroplasticity makes the functional malleability of the brain tangible, makes it "scientifically demonstrated" that brains change. That people change. In the time span considered in this chapter, people throughout the Arab world went from being voiceless to toppling tyrants; Rosa Parks went from victim to catalyst, Sadat and Begin from enemies to architects of peace, Mandela from prisoner to statesman. And you'd better bet that changes along the lines of those presented in this chapter occurred in the brains of anyone transformed by these transformations. A different world makes for a different worldview, which means a different brain. And the more tangible and real the neurobiology underlying such change seems, the easier it is to imagine that it can happen again.