CHAPTER ONE

Your Changeable Brain

Neurogenesis, Neuroplasticity, and Epigenetics

IN BRIEF

When you woke up today, you were a new person—literally. Many of the cells in your body had replaced themselves with younger versions, and your brain has been busy as well. Scientists have discovered your brain is a work in process. Every day, it seems, your brain makes new neurons in at least some sections, and almost every second, your brain is changing its networking in response to what you experience, think, feel, and need. In fact, your brain can even direct changes to some of your genes, turning them off or on.

Then: Your brain is hardwired and unchangeable, and you're born with all the brain cells you'll ever have. Good luck, because when they're gone, they're gone.

NOW: Who knew? Your brain creates new neurons in some areas and new networks, even into old age, and it changes physically in response to your actions, thoughts, and emotions. Your genes are not your destiny—or at least not all of it.

Tomorrow: We'll be able to direct changes: stimulate new brain cells and networks where and when we need them; turn genes off and on at will to repair brain damage, restore function, and optimize performance; and rewire our brains to manipulate memory and even reverse dementia and mental retardation.

The revolutionary findings about your brain's remarkable ability to change itself are barely a decade old. Biologists had long believed that the creation of brain cells was completed at or shortly after birth, and that the rest of your life was a slow slide into brain cell loss. In the 1990s, scientists rocked the field of neurobiology with the startling news that the mature mammalian brain is capable of sprouting new neurons in the hippocampus and the olefactory bulbs, and that it continues to do so even into old age. This process is called *neurogenesis.*

Scientists also confirmed what was long suspected: your brain is not hardwired. It can reinvent itself, as it were, by creating new pathways to reroute, readjust, and otherwise change the networking and connections, sometimes even substituting one area for another. When one part of your brain goes south—from a stroke or trauma, for example—other sections can sometimes take over some of those functions. Your brain also changes to reflect what you learn, do, and think. In fact, your brain is physically rearranging its networks just about every minute of every day. That's *neuroplasticity*.

Then they discovered that your actions, thoughts, feelings, or environment can change your genes—more specifically, whether certain genes are expressed—altering brain function; character traits; and risk of some diseases, from cancer to schizophrenia. That's *epigenetics.*

YOUR BRAIN IS A COMPUTER. NO, IT'S A SWISS ARMY KNIFE. NO, WAIT—IT'S THE INTERNET!

Scientists for centuries have focused on the brain in terms of its bits and parts—its components, in tech speak. Some time ago, they saw it as a machine; then, in the century just ended, it was popular to think of the brain as a kind of computer. More recently the Swiss army knife analogy appeared, which seemed to fit with what was being learned as we mapped the brain.

Neuroanatomists figured out that the visual cortex, for example, processes what we see; that Broca's area is the center for language; and that various other areas deal with specific functions and concepts, such as facial recognition, risk taking, romantic love, and even God.

But now it seems that's a bit simplistic too. As we learn more, it has become clear that how well the brain works depends on how these modules are linked together to perform as circuits. The brain is, in fact, more like the Internet.

True, there are areas that specialize. Roughly speaking, reason and rationality happen in the cortical areas, emotion and irrationality are experienced in the limbic system, and a number of interconnected neural networks may be bundled into module-like units. But in most ways, the working of the brain is described today as being splayed out over, under, or through the brain's crevasses—a "distributed intelligence" that more closely matches the World Wide Web.

These extraordinary findings, coupled with new imaging techniques that show the brain in action in real time, opened entire new ways of studying the brain and the tremendous impact of cognition. They showed how neglect, abuse, and bullying in childhood can stunt brain development, and they gave some credibility to age-old concepts of positive personal transformation through religious experiences, meditation, self-help programs, and even positive thinking and your own will. They also explain how and why talking cures such as psychotherapy and cognitive behavior therapy can change lives.

Researchers are working now on ways to both understand and facilitate those changes in beneficial ways. The methods range from some startlingly effective and simple solutions (such as binding back the good limb on a person who has had a stroke so the person is forced to use the affected limb, and the brain is forced to make new pathways) to the most technologically and scientifically complex (such as deep brain implants to block depression, tremors, and convulsions) to brain-machine interfaces and thought-driven prosthetics.

The Birth of Brain Cells: Neurogenesis

We've all heard the warnings: *If you* _____ (fill in the blank) *you'll kill brain cells.* And because scientists believed until very recently that you were born with all the brain cells you'd ever have, that was a fairly dire warning. You broke it, and you were stuck with the results.

Recently we've been able to relax a bit, because we know that our brain makes new cells in at least two sections: the dentate gyrus of the hippocampus, a structure involved in learning and memory, and the olefactory bulbs. And it may in fact create new neurons elsewhere in the brain; we don't know for certain yet.

Most of this research has been done on animals, but some human studies have confirmed the finding. Studies were done on terminal cancer patients who generously agreed to be injected with a marker for new cell production and to offer their brains for study after their death. The autopsies showed that even in the face of aging and death, their brains continued to produce new neurons to the very end.

Chemotherapy could give us an idea of what happens when we don't make new neurons. Chemotherapy impairs the cell division needed for making new cells, and people who have had chemotherapy treatment for cancer and some other serious diseases often complain about a syndrome sometimes referred to as *chemobrain.* They have trouble with the kinds of learning and remembering that everyone finds challenging, such as juggling multiple projects while trying to process new information.

Because having a ready supply of new neurons on tap could help to keep your brain intellectually limber, scientists are looking for ways to exploit this to prevent or treat disorders that bring about cognitive decline. Meanwhile, they've found that these new brain cells disappear if you don't use them.

Changes in Your Brain: Neuroplasticity

Scientists have long known that the brain can change itself. In fact, your brain is probably changing every microsecond in response to experiences, both external and internal. Those changes come mainly from the growth of new connections and networks among neurons, particularly among newborn neurons.

We've known that different kinds of experiences lead to changes in brain structure, with more activity in the networks used most. In musicians, for example, the parts of the brain dedicated to playing their instruments are disproportionately larger than in nonmusicians or in musicians who play a different instrument. A decade-old study of London taxi drivers skilled at navigation in the city center showed the same effect: they had larger hippocampi than nondrivers, reflecting the huge amount of data they needed to have at hand. Moreover, the longer they drove complicated routes around the city, the larger their hippocampi grew.

Also, brains apparently riddled with blank areas or plaque and other signs of Alzheimer's disease have come from people functioning very well into late old age. Indeed, some brains lacking a hemisphere—the entire half of a brain—can function quite well.

We also know the brain can sometimes repair itself after devastating injury, bypassing dead areas to create new connections. ABC news correspondent Bob Woodruff, critically injured by a roadside bomb in 2006 while covering the war in Iraq, suffered a brain injury so severe that part of his skull was permanently removed, and he was kept in a medically induced coma for more than a month. Few believed he would walk again, let alone work as a reporter. After more than a year of intensive therapy, which included relearning speech to

CENTENARIANS RULE: MORE REASONS TO TAKE CARE OF YOUR BRAIN

Centenarians—individuals one hundred years or older—are the fastest growing age group in the United States, and experts predict there may be as many as 1 million by 2050.

If you're sixty years old (or younger) today, you could be in that group. And if you want your mind to be there along with you, take good care of your brain.

You'll have plenty of company near your age: people aged eighty and older are the fastest-growing portion of the total population in many countries. By 2040, the number of people sixty-five or older worldwide will hit 1.3 billion, according to the National Institute on Aging, which announced the figures. And within ten years, there will be more people aged sixty-five and older than children under five in the world for the first time in human history.

The most rapid increase will be in developing countries. By 2040, they will be home to more than 1 billion people aged sixty-five and over—76 percent of the projected world total.

If you reach one hundred years, you are sure to live in interesting times, an old blessing (or curse) of the Chinese (who, incidentally, will have the world's largest population of elders by 2040). This global aging will change the social and economic nature of the planet and present some difficult challenges.

Interesting times, indeed.

overcome aphasia, he made a hard-hitting documentary about the plight of injured soldiers and the deficits in government care. And then he went back to work as a reporter—in Iraq.

Certainly Woodruff benefited from the kind of very expensive and intense treatment not available to all of us. Nevertheless, his recovery shows how remarkably able the brain is, especially because his was not a young brain: he was forty-four at the time of his injury.

What we did not know for certain until recently is that what you think and feel also physically change your brain, such as intellectual

challenges, deliberate brain training, anxiety, and joy. So it seems there is a biological basis to mind training: you can learn skills aimed at changing your brain just as you learn repeated activities to change your body. Meditation is a brain-changing example. Studies show that regular practice of meditation results in physical as well as mental and emotional changes. In long-time practitioners of meditation, the two hemispheres become more balanced, the trigger-happy amygdala shows less reaction to emotional sounds, and the many brain regions involved in focused attention show greater activity (see "Boosting Your Brain with Meditation," p. 31).

Changes in Your Genes: Epigenetics

Scientists are finding one of the ways your brain changes itself is by actually changing your genes—or more correctly, by the acting out (or not) of certain genes—in the process of epigenesis.

We know that your genome is the total deoxyribonucleic acid (DNA) that you inherit from your ancestors and contains the instructions for making your unique body and brain. Another layer of information, called the epigenome, is stored in the proteins and chemicals that surround and stick to the DNA. It's a kind of chemical switch that determines which genes are activated (or not): it tells your genes what to do and where and when.

Researchers have discovered that the epigenome can be affected by many things, from aging and diet to environmental toxins to even what you think and feel. This means that even your experiences can literally change your mind by chemically coating the DNA that controls a function. The coating doesn't alter the underlying genetic code; rather, it alters specific gene expression, shutting down or revving up the production of proteins that affect your mental state.

Epigenetics helps explain the gap between nature and nurture that has long puzzled scientists: why some illnesses and traits pop up in one but not both identical twins who have the same DNA, or why these traits skip a generation. It also helps explain neuroplasticity.

One researcher describes DNA as a computer hard disk, with certain areas that are password protected and others that are open. Epigenetics is the programming that accesses that material, writes Jörn Walter of Saarland, Germany, on the Web site Epigenome.

Epigenetics can profoundly affect your health and, it seems, your happiness, changing not only your vulnerability to some diseases such as cancer but also your mental health. Scientists have found, for example, that a mother rat's nurturing, through licking and loving behavior that boosts the expression of a gene that eases anxiety and stress, bolsters emotional resilience in her newborn pups. They've also found that distressing events can turn off the expression of genes for brain cell growth protein and thereby trigger depression, and that epigenetic changes may also underlie the pathology of schizophrenia, suicide, depression, and drug addiction.

The acting-out process of changeable genes—gene expression—is quite complicated and a new area of intense research. Just recently biologists have found that epigenetic changes may be heritable—passed on to your descendants—just as your DNA is. They have also found that altering gene expression with drugs or environments that provide more intellectual stimulation can improve learning and memory in cognitively impaired animals. Future therapies for memory disorders in humans might work in a similar way. It's a promising area with much to be learned. In 2008, the National Institutes of Health invested $190 million in the five-year Roadmap Epigenomics Program to pursue some of these promising fields of research.

Keeping Your New Brain Cells

So it turns out that your brain is a nursery: every day, it seems, new brain cells are born. But it seems that your brain doesn't always keep these newborn neurons. Just like all other babies, they need special care to survive. And it's not pampering: your newborn neurons, scientists are finding, need to be challenged, exercised, and run hard.

If you don't use those new cells, they will disappear. Animal research shows that most of these cells die within a couple of weeks unless that brain is challenged to learn something new and, preferably, something hard that involves a great deal of effort. And *new* is key here as well: just repeating old activities won't support new brain cells.

Scientists still don't really know why or what the heck the new neurons are doing or even why we make them. Are they made to replace dying cells? One theory is that they are backup, produced just in case they are needed. This idea suggests that your brain calls for reinforcements when new brain cells are available to aid in situations that tax the mind, and that a mental workout can buff up the brain much as physical exercise builds up the body.

In animal studies, scientists found that between five thousand and ten thousand new neurons arise in the rat hippocampus every day (it's not known how many we humans make, or how often). The birth rate depends on some environmental factors. Heavy alcohol consumption slows the production, for example, whereas exercise increases it. Rats and mice that log time on a running wheel kick out twice as many new cells as do mice that lead a more sedentary life. Even eating antioxidant-rich blueberries seems to goose the generation of new neurons in the rat hippocampus, as do exciting changes in their cages or new toys to pique their interest.

Elizabeth Gould (a discoverer of neurogenesis in adults), Tracy Stors, and colleagues have been examining the connection between learning and neurogenesis by studying the brains of rats and the importance of hard learning. In their experiments, they first injected the animals with BrdU (bromodeoxyuridine), a drug that marks only brand-new cells. A week later, they recruited half of the treated rats for a training program and let the rest lounge around their home cages.

The rats enrolled in Rodent University were given an eyeblink course: an animal hears a tone and then, some fixed time later (usually 500 milliseconds, or half a second), gets hit in the eye with a puff of air or a mild stimulation of the eyelid, which causes the animal to blink. After several hundred trials, the animal learns to connect the tone with the stimulus, anticipate when the stimulus will arrive, and

blink just before that happens: an anticipatory learning based on the ability to predict the future based on what has happened in the past.

After four or five days of training, the scientists found that the rats that had learned to time their blink had also retained more BrdU-labeled neurons (the newborn neurons) in the hippocampus than did rats who were just hanging out in their cages. The animals that got no mental workout held on to only a few of the newborn cells, and animals that failed to learn—or that learned poorly—didn't keep new neurons in spite of the training. Rats that went through some eight hundred trials but never learned to anticipate the eyelid stimulation ended up with just as few new neurons as the slacker animals that never left their cages.

The better the animal learned, the more new neurons it retained, convincing researchers that it was the process of learning—and not simply the exercise of training or exposure to a different cage or a different routine—that rescued new neurons from death.

No Pain, No Gain

Sorry to say, the research also showed that all types of learning are not equal. It seems that learning or practicing easy tasks won't cut it. Keeping new brain cells is like keeping your muscles. You've go to work them hard.

Research, mostly in rats, shows that new neurons that get a workout stay. For example, when rats were put in a pool of water to find and swim to a visible, submerged platform for a safe landing, they didn't keep new brain cells. Scientists speculated that that's because the task didn't require much thought. But when rats had to learn to gauge the time between a sound tone and a stimulus, a much harder problem requiring the ability to predict a future event based on past experience, the neurons survived.

Here's some more good news: the animals that were a bit slow to master the tasks—the plodders and workers—ended up with more new neurons than the fast learners. Scientists assume that means,

again, that the more effort, the greater the gain—just like at the gym or when learning calculus.

But the type of workout is important here: crossword puzzles and memory games may not challenge your neurons enough. The puzzles have to be difficult for you, and repeating already-learned skills makes you better at those skills but doesn't apparently improve cognition. It seems the tasks that rescued the most neurons were the ones that are hardest to learn, and that the more engaging and challenging the problem, the greater the number of neurons that stick around. By the way, those can be learning tasks that are fun such as learning to play the violin or rock guitar or how to speak Italian—as opposed to, say, learning inorganic chemistry (unless, of course, inorganic chemistry is fun for you). Anecdotal evidence and some human research have said just the same thing, but so far without the human brain biology to prove it.

Anecdotal accounts suggest that effortful learning may also help some dementia patients. When Stors and colleagues presented her group's animal research at a meeting about Alzheimer's disease and other forms of dementia, the health professionals in the audience were intrigued. They report having seen benefits from such exertions in their patients. And they noted that patients who can fully engage themselves in cognitively demanding activities may be able to delay the progression of this mind-robbing disease.

Brain Training Programs: Help or Hype?

Because studies show brains are like muscles (use it or lose it), many experts are suggesting we do brain training exercises. And many of those experts recommending the exercises are among the producers of cognitive training programs, now a $225 million–plus industry.

Are these sometimes pricey programs as good as exercising your brain on your own (and for free) by playing chess, say, or learning a new language or how to play the mandolin? Possibly not, and if they are, it's hard to say if any one is better than the others. The bulk of the research is murky.

COULD WEIGHT GAIN MAKE YOU A FATHEAD?

Could obesity be bad for your brain? Well, it appears to shrink your gray matter. A section of the Pittsburgh Healthy Women Study looked at weight gains of forty-eight women over an average of fifteen years. Those who had gained the most weight but were completely healthy otherwise showed a decrease in brain gray matter. Scientists conducting the study aren't sure what, if anything, this means, or if being overweight is a cause, but it chalks up one more possible strike against obesity, which by itself raises the risk of brain injury from stroke or heart attack.

And, yes, there's probably a gene for that. In fact, three genes active in the brain have been associated with obesity. If that isn't bad enough, it's also linked to some other bad things. The latest, NRXN3 gene variant, is also associated with alcohol dependence, cocaine addiction, and illegal substance abuse.

Neuroscientist Peter Snyder of Brown University reviewed nearly twenty software studies and concluded that as a group, these training programs were underwhelming. The studies have flaws that induce confounding factors, such as a lack of control groups and follow-up, Snyder warns. In fact, more than a third of those he reviewed were too shoddy even to include in the analysis he published in early 2009 in the journal *Alzheimer's & Dementia*. From his perspective, software companies remain hard-pressed to prove that their products do much, especially over the long term, and few programs have demonstrated the flexibility to boost skills that were not practiced or to increase actual thinking ability. Others have noted that brain programs that involve repetition make you better at repeating that specific task and do not necessarily improve your thinking skills.

Writer Kaspar Mossman sampled a range of programs for *Scientific American Mind.* After eight weeks of testing, he concluded he had learned some useful things about the software but didn't feel any smarter. It could be because he's only in his thirties—not old enough to have any cognitive problems (yet): program developers

claim these interactive exercises work best for the brains of people who are having slippage.

If you want to try the programs, what workout works best? You can experiment by taking advantage of the many free trials offered online for these products and see what works for you. What matters most is whether you enjoy using one of these programs, whether it challenges you at the right level, and whether you stick with it.

Or take Synder's advice. The best memory enhancer, he says, is physical exercise, followed by a good diet and an active social life.

Wait. Does that mean reading this book doesn't count?

What's Next? And What About My Brain?

Good questions. So far, we've been looking mostly at animal brains that can be dissected for detailed study.

Scientists are eager to find out how to prompt neurogenesis in human brains—in healthy individuals, as well as in people with brains damaged by Alzheimer's disease, trauma, or stroke. Knowing how neurogenesis works would tell us which treatments, from deep brain stimulation to drugs to gene therapy and stem cell replacement, can best prompt new neurons in the human hippocampus or anywhere else in the brain. We'd also be able to tell if (or which) brain-exercising activities help your physical brain.

They'd also like to know how to better encourage neuroplasticity and understand how to direct epigenesis—to be able to direct some injured brains to make them more nimble and self-healing in cases of mental illness, anxiety, and depression, to help those needing to rewire a brain damaged by autism or a genetic injury, and to learn how to turn genes on and off as needed.

They're mulling many theories and working in many areas of research, spurred and supported by the billions being invested in research on Alzheimer's disease (see "Alzheimer's Disease: The Memory Epidemic," p. 41).

But first researchers need to know more about the basics. Which molecular mechanisms and which neurotransmitters are involved?

Which receptor proteins? And when exactly do those mechanisms operate? Does learning help new neurons to become integrated into neuronal networks, or does it promote the survival of those that are already connected? And how do they do this? Why do we make new brain cells in the first place? And can we prompt the production of extra brain cells to boost healthy brains? It appears that learning promotes the survival of new neurons but does not seem to control the number of new cells produced.

Another important concern will be how to control the amount of neurogenesis a particular treatment prompts, because the overproduction of new neurons can also be dangerous. In some forms of epilepsy, for example, neural stem cells continue to divide past the point at which new neurons can form useful connections. Neuroscientists speculate that these aberrant cells not only end up in the wrong place but also don't mature and could contribute to the miswiring of the brain that causes seizures. So researchers must first better understand the process.

To know (and do) all that, we need better ways to look inside a living human brain without cutting it open. Seeing what goes on in humans when new brain cells are created and exactly how they die or stick around would give tremendous insights into preventing or reversing many brain conditions. Scientists are working toward that with ever more innovative neuroimaging techniques (see "Looking Inside Your Brain," p. 71).

As for helping your brain cells today, lifestyle changes might make the difference, and those might be summed up as brain boosters, butt busters, blueberries, and bliss (see the list of "Six Drug-Free Ways to Boost Your Brain," p. 29). These include challenging mental activities and environments with lots of interesting and stimulating toys; vigorous physical exercise; diets rich in deeply colored vegetables and fruits known to be high in antioxidants and vitamins; and meditation and other calming activities that relieve stress, which is known to be a killer for your new brain cells.

And there's a bonus: all of these are good for the rest of your body as well.