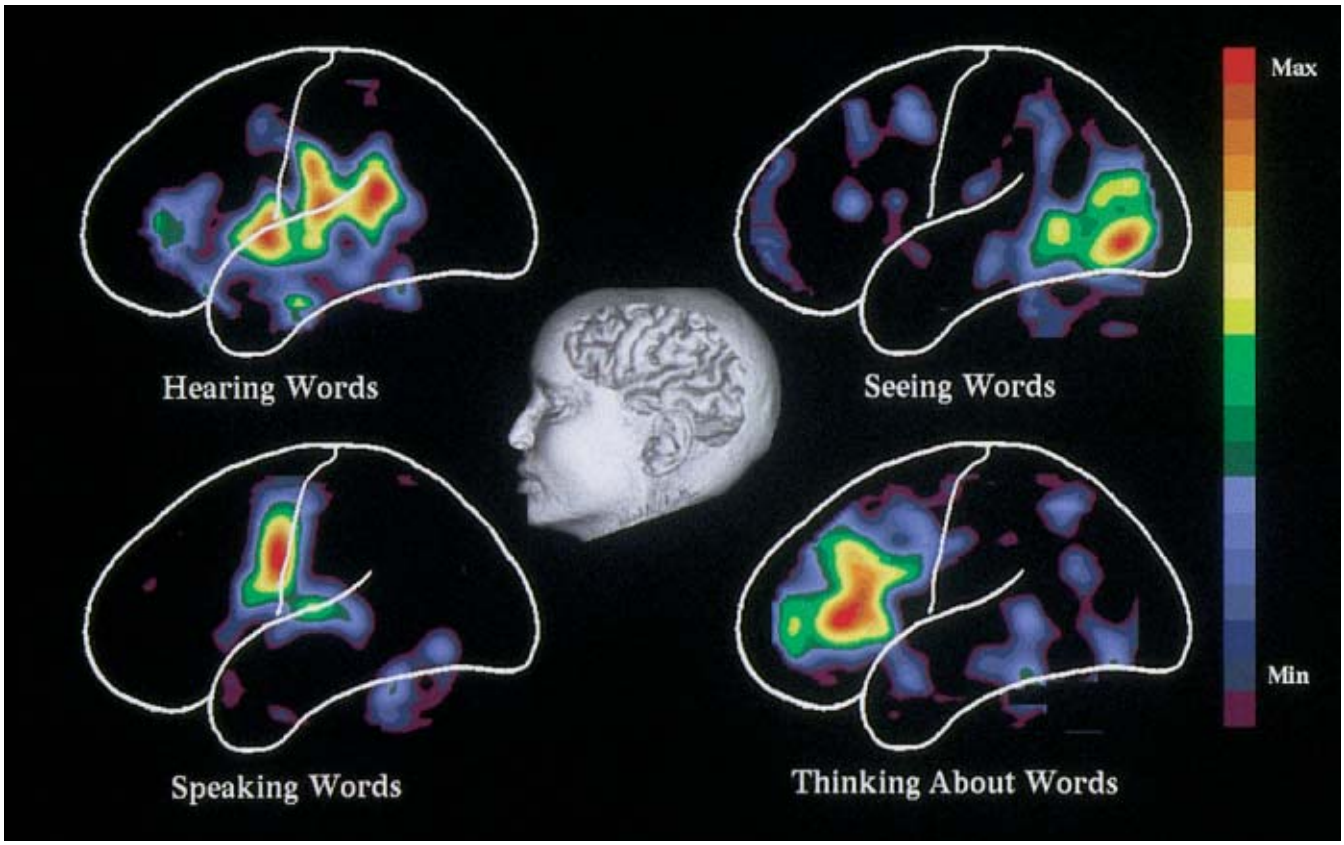
The Dana Sourcebook of Brain Science



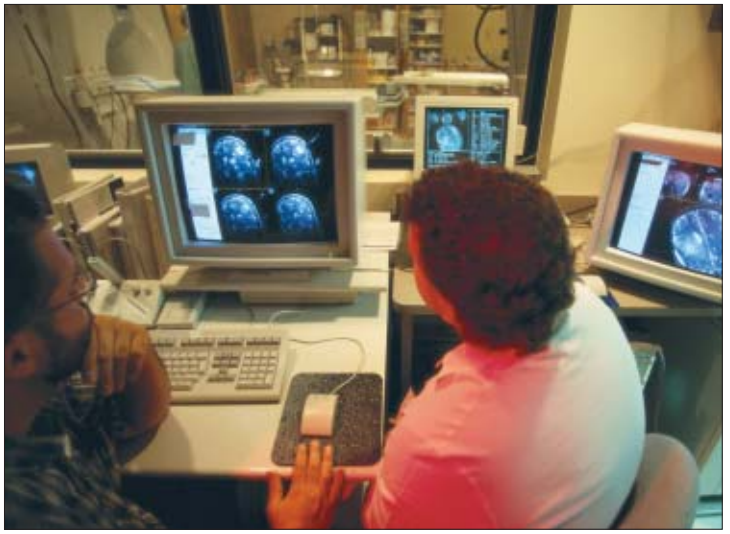
Resources for Secondary and Post-Secondary Teachers and Students

Third Edition

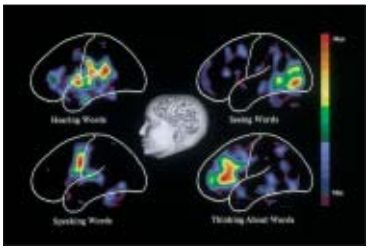
The Dana Sourcebook of Brain Science Third Edition

The brain: the most complex entity we know. The three-pound mass of pinkish-gray tissue is what makes us distinctively human. The brain encases 100 billion or more nerve cells and it can send signals to thousands of other cells at a rate of about 200 miles an hour. Because of its daunting complexity, the brain is the locus of many of our most serious remaining diseases and disorders—from Alzheimer's to learning disabilities.

An unexpectedly close genetic cousin. In a landmark event in biology, a team of international scientists in 2002 showed the genetic makeup of the common mouse to bear remarkable similarities to that of humans. Because roughly 50% of our genes are devoted to developing and maintaining the brain and the central nervous system, being able to compare two complete mammalian genomes for the first time should speed up efforts to understand brain-related diseases and disorders.



Computer technology opens a window on the living brain. Before the early 1970s, only neurosurgeons had seen a living human brain. Rapid advances in computer-generated imaging have allowed brain scientists and doctors to go inside the head and examine the structure and function of the brain in the living patient. Advances in the next few decades are expected to allow scientists to investigate how brain circuits work, how one part of the brain modifies the functions of other parts, and how these circuits adapt to new situations or damage to existing circuits.



About the cover:
These images demonstrate, by Positron Emission Tomography (PET scanning), that certain areas of the brain activate as the brain performs specific language tasks.

"Every aspect of our lives depends on the normal functioning of our brains. Our education depends on it; the education of our children depends on it; our relationships to our fellow humans depend on it; our hopes and aspirations are all represented in our brain. And all of these human qualities are at risk if something goes wrong with one's brain."

—W. Maxwell Cowan, M.D., Ph.D.,

Neuroscientist, Educator (1931–2002)

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DANA PRESS

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David Balog, Editor

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Scientific Lives

Part One: A Life of Research, Advancing Our Knowledge of How the Brain Works

Editor's note: *One way to study the brain is to become a researcher, conducting experiments, analyzing data, publishing results, and teaching. A world-renowned scientist and researcher on the development and regeneration of nerve cells, Bernice Grafstein, Ph.D., is professor of physiology and Vincent & Brooke Astor Distinguished Professor of Neuroscience, Department of Physiology, Weill Medical College of Cornell University.*

Bernice Grafstein, Ph.D.

A Leader in Spinal Cord Research and for Women in Neuroscience

Bernice Grafstein, Ph.D.

Dr. Bernice Grafstein has a particular interest in advancing the careers of young neuroscientists through her role as a teacher of neuroscience and also as a member of the board of trustees and a vice president of the Grass Foundation. She is particularly impressed by the creativity and technical sophistication of students who are applying for support from the Foundation. "Students attracted to neuroscience seem to have an extra amount of motivation and commitment."

The number of women joining the field of neuroscience is certainly increasing, reflected by the growing numbers of women—now roughly 10,000—who are members of the Society for Neuroscience, the largest organization in the field. And striking to Dr. Grafstein are the outstanding women who specialize in the study of nervous system regeneration and development. "There may be something inherently attractive to women in the concepts of growth and repair."

Writing in *In Search of the Lost Cord: Solving the Mystery of Spinal Cord Regeneration*, (Dana Press/Joseph Henry Press, 2001) author Luba Vikhanski describes Dr. Bernice Grafstein's groundbreaking work: "Unlike in mammals, regenerating nerve cells in fish and amphibians readily reconnect to their appropriate targets. Dr. Grafstein's pioneering studies with radioactive tracing showed that fish nerve cells undergo massive changes in metabolism when they regenerate, a finding that would lead to many of the current studies on the activity of neuronal genes involved in regeneration."

Spinal cord injury remains one of our most tragic, devastating medical conditions. It often strikes the young and can cause serious incapacitation for 40 years or more. As a scientist who has been interested in development and regeneration of nerve cells for several decades, Dr. Grafstein says she is heartened by the recent increase in attention to the problem of spinal cord injury. She cautions, however, that we still have much work to do to investigate the most basic elements of the process of axonal reconnection, let alone the immensely more difficult problems of regenerating or replacing the cells that have been killed by the injury.

"How close we are to a solution depends on the amount of effort that can be directed to solving these problems," says Dr. Grafstein. "And that in turn depends on the amount of support that can be made available. I hope that by the end of the next decade my friends with spinal cord injury will find available treatments that can improve their conditions and help them build a significantly better quality of life." ■

Part Two: Treating Patients With Brain Diseases and Disorders

Editor's note: *In addition to conducting research and teaching, brain scientists can also be "hands-on" doctors and surgeons. Benjamin S. Carson, Sr., M.D., one of the world's leading neurosurgeons, is director of pediatric neurosurgery at Johns Hopkins Medical Institutions. He is professor of neurosurgery, oncology, plastic surgery, and pediatrics at the Johns Hopkins School of Medicine.*

Benjamin S. Carson, Sr., M.D.

A Brain Surgeon Talks About "Second Chances"

Benjamin Carson, M.D.

Not long ago, doctors whose practices focused on the brain had few tools to intervene significantly in their patients' lives. That has changed quickly. Brain doctors are now aggressively treating patients for stroke, seizures, acute trauma, psychoses, addiction, and even some neurodegenerative disorders.

One of these pioneers is Dr. Benjamin Carson. During his career he has gained international distinction for successful, delicate high-risk surgeries such as hemispherectomies—removing one side of the brain to treat those suffering from otherwise untreatable severe multiple seizures.

Dr. Carson speaks often to young students and emphasizes his own transition from poor inner-city kid in Detroit with failing grades to one of the most prestigious positions at one of the world's most renowned medical institutions. "Is it ever too late if you miss the boat the first time around? Well, I have to tell you, when I was a youngster, many people would have said it was too late for me. No one certainly would have thought that I was going to grow up to be a physician."

His mother, Sonya, was determined to help, and she ordered Ben and his brother Curtis to read two books each week, which she, with only a third-grade education, pretended to review. "Once my mother made us start reading, what a tremendous change took place," says Dr. Carson.

Becoming a successful student didn't protect him from racist treatment, nor from his rage against it. In high school, a teacher scolded Ben's white classmates for letting a black student win the outstanding-achievement award. Then one day, Ben tried to stab a student who had changed the station on a radio. The student had a large metal belt buckle and the knife blade struck it and broke. Frightened by his anger, Ben ran home and prayed for hours. Devoutly religious like his mother, he says he has not lost his temper since.

Dr. Carson went on to win a college scholarship. "Later, I bombed out of my first set of comprehensive medical exams. The counselor suggested that there were a lot of things I could do besides medicine."

Dr. Carson at that point thought back to his mother's earlier encouragement to read. "I decided to concentrate on reading, which then made medical school a snap. Taking advantage of how we learn is incredibly important."

Dr. Carson believes in today's students. He is president and co-founder of the Carson Scholars Fund, which recognizes young people of all backgrounds for exceptional academic and humanitarian accomplishments. He says, "We need to start putting our resources where it counts and honoring our academic superstars." ■

Revealing the Workings, the Wonder of the Human Brain

Do each of the following, in succession. (<u>This is not a test</u>):

1. Visualize a place you'd like to be. Maybe it's lounging on a sunny summer day at the beach. Maybe it's in your living room, watching a favorite movie. Create the image of that place in your mind, and hold it for a minute or two.

2. Listen to the sounds in the room around you. Really listen. What do you hear? Low voices in conversation? Muffled laughter in the hall? Phones and computers ringing and beeping? See how many sounds you can differentiate.

3. Silently tap your fingers on the desk, one tap, one finger at a time, in succession. Then reverse the order of tapping. Then tap each finger twice, in succession; then in reverse. Then three times….

4. Starting at 100, count backward by 7s.

5. Remember some event from your past. The first time you rode a bike all by yourself; your grandmother baking your favorite cookies; the first time you kissed someone other than a relative. Put yourself back in that place, and recall everything you can about it: Who was there with you? What were you wearing? What emotions were you feeling?

6. Now pinch yourself. Pick a tender spot on the inside of your elbow, and pinch the skin just hard enough to feel pain.

In performing these six tasks, you've just activated a good portion of your brain. Even something as "simple" as tapping your fingers in succession requires a phenomenal act of coordination among millions of nerve cells throughout the brain, all acting together in perfect timing to produce the signals that command your fingers to move.

If you had been lying inside a *PET* or *fMRI* scanner—tools of modern *neuroscience* that enable scientists to take images of the living brain as it works—the scans would show distinct areas of your brain "lighting up" as you did each task. Tapping your fingers in succession would activate groups of *neurons* in at least four distinct areas of the brain: the *prefrontal cortex,* where your brain makes the conscious decision to do the task; the *premotor cortex*, where you formulate the instructions for doing the task; the *motor cortex,* a sort of relay station that sends those instructions on to the arm and hand muscles that move the fingers; and the *cerebellum,* which supervises the whole process and adjusts your actions as necessary in response to external cues, such as where your hand is in relation to the desk. All of this takes place in a mere fraction of a second. Not such a "simple" task after all, from the brain's perspective.

Task number one, visual imagery, lights up the *visual cortex* in the back of the brain, as well as pathways leading to it from the eyes, along the optic nerve. Differentiating individual sounds around you activates the *auditory cortex* and associated areas. Counting backward by 7s is a complex *cognitive* task, and it calls upon the brain's center for higher thoughts in the prefrontal cortex.

Recalling a *memory* from your past will likely activate the *hippocampus*, an inner-brain structure involved in memory, as well as other areas of the brain that correspond to the type of memory. For example, remembering the first time you rode a bike, a motor task, will light up the motor area of the brain; recalling the smell of Grandma's cookies would activate the *olfactory* center.

Lastly, when you pinched yourself, *pain receptors* in the nerves of the skin sent signals back to the brain to alert it to the location and intensity of the pain and to initiate corrective action if necessary (i.e., stop pinching!). If the pain was intense, the brain might release *endorphins,* natural *hormones* that block the transmission of pain signals. *Narcotic* drugs such as morphine imitate the action of these natural endorphins to fight pain.

The Most Complex Machine Known to Man

You've just taken a brief tour of your brain. It has taken scientists hundreds of years to figure out the bits of information you've just learned in a few minutes. If that seems like a long time for a little bit of information, consider the complexity of the problem. The human brain is, as neuroscientist Joseph LeDoux, Ph.D. says in *The Emotional Brain,* "the most sophisticated machine imaginable, or unimaginable." It is composed of more than

Note: Terms in italics are defined in "A Glossary of Key Brain Science Terms," beginning on page 124.

100 billion nerve cells, **each** of which forms as many as 10,000 connections with other neurons. A typical brain weighs about three pounds, just two percent of the total body weight of a 150-pound person. But the brain uses between 20 percent and 25 percent of the body's oxygen and a substantial amount of the calories we consume in the form of the blood sugar *glucose*. The brain is also a nonstop factory of *neurotransmitters* that are critical to every thought and feeling we experience. About half of the 30,000 or so *genes* in the human *genome* are committed to building and operating the *central nervous system* (the brain and *spinal cord*). The Human Genome Project and the privately run effort of Celera Genomics, which have produced a map of the human genome and seek to understand the specific roles of each gene, have been completed and are expected to reveal many of the brain's most complex mysteries.

In the process of deciphering the genetic code that is written in our *DNA*, learning the "blueprint" of our bodies is also likely to pave the way for a better understanding of the brain-based disorders and diseases that plague mankind and open new avenues for treating these disorders. This is an undertaking with enormous implications, because more than 55 million Americans are afflicted with a brain disorder—conditions that range from learning disabilities to *depression* to traumatic brain injury. That's nearly one in five of us. Look around you. If there are 25 students in your class, statistically 5 of you will be personally affected. Everyone of us will personally know or care for someone who is affected by a brain disease or disorder.

Evolution of the Brain

The modern human brain is the product of millennia of "evolutionary tinkering," says Dr. LeDoux. To figure out how it works, we need to "pick the brain apart in the hope that we will see what evolution was up to when it put the device together."

About half of the 30,000 or so genes in the human genome are committed to building the central nervous system (the brain and spinal cord).

For centuries, "picking the brain apart" was, literally, how scientists learned how the brain worked. Actually, they usually picked apart the brains of other animals for clues as to how the human brain worked. As it turns out, the human brain is remarkably similar to the brains of other mammals, from rats right up to our closest cousins in the evolutionary tree, the great apes. In evolutionary terms, most of the structures in our brain are, in fact, primitive—that is, they have existed in much the same form for eons. These include the parts

continued on page 10

Leon N. Cooper, Ph.D.

Scientific Research Saves Money, Saves Lives

By Leon N. Cooper, Ph.D.

A Nobel prize-winning physicist, Dr. Cooper is professor of science and director of the Institute for Brain and Neural Systems at Brown University.

Scientific research yields an intellectual harvest that is sometimes beautiful, often useful, usually expensive, but extraordinarily rewarding. I would argue, in addition, that it saves money and makes money.

Economic growth is fueled by technology rooted in research discoveries. The last 50 years have seen *magnetic resonance imaging*, laser surgery, computers, and modern telecommunications (to take just a few examples) emerge from prior basic research. Let us pursue a single instance. Computers and telecommunications, which make a gargantuan contribution to GDP (Gross Domestic Product), require integrated circuits based on transistors. The importance of the transistor is generally grasped; but it is less commonly appreciated that the transistor could not have been invented without fundamental advances in quantum physics just 10 or 20 years earlier.

On this spectrum, biomedical research occupies a special position. It has a profound impact on human suffering and, in addition to generating revenue, it reduces costs by reducing or delaying chronic illnesses—among the most expensive components of the cost of health care.

The gains *neuroscience* has made, in just a few years, in areas as diverse as learning and memory, emotion and stress, behavior and pain…translate into new hope for treating developmental disorders, schizophrenia, addiction, alcoholism, manic-depressive illness, and other maladies that inflict misery on millions. This progress also translates into economic benefits. The figures are only suggestive (and more study would be welcome), but it is estimated by the Ad Hoc Group for Medical Research Funding that just *delaying* the onset of aging-dependent illnesses like Alzheimer's could reduce annual spending for nursing home care by as much as $35 billion.*

True, new technologies can increase expenditure. It is expensive to use magnetic resonance imaging to plan neurosurgery for epilepsy, or to implant the newly approved neural prosthesis that enables some quadriplegics to feed themselves, or to treat manic-depressive illness or multiple sclerosis with new drugs. But these expenditures extend lives that would have been shorter, save lives that would have been lost, and preserve a quality (and productivity) of life that would have been diminished. In a way, it is like comparing the cost of a Model T of Henry Ford's day with the complex electronic device that we now call a car. It is simply not the same vehicle. And most of us, when the length and quality of our lives are at stake, prayerfully accept the new and more expensive technology.

Much of the current effort to find causes and treatments of disease involves genetic technology built on the basic research on DNA by James D. Watson, Francis Crick, and their colleagues—work that goes back at least half a century. Today identifying the genes involved in neurological conditions such as Huntington's disease, manic-depressive illness, and some forms of alcoholism is a critical step toward diagnosis and effective treatments.

Think of the increased cost and misery, or the lost revenue, if the polio vaccine or the transistor had been delayed by just 10 years. In addition to reducing human misery, our investment in a healthy and diversified portfolio of fundamental research in all sciences will more than repay its cost. We may not be aware of what we will lose if we do not continue to invest adequately, but lose we surely will.

*"NIH Research…Preparing for the Senior Boom," The Ad Hoc Group for Medical Research Funding, Washington, DC, February Issue, 1997.

(Adapted from "Scientific Research: Who Benefits? Who Pays?" published in *Cerebrum: The Dana Forum on Brain Science,* Pilot Issue, Dana Press, New York, 1997.)

continued from p. 8
of the brain that control functions basic to survival, such as breathing, heart rate, and digestion. Such functions are centralized in the *brain stem*, located in the base of the brain, where the spinal cord meets the brain.

What Makes Human Brains So Special?

Clearly, humans have so-called specialized functions that rats, or even great apes, do not. So what makes humans so special? The key seems to lie in the prefrontal cortex, the forward-most section of the *cerebral cortex*, which is the brain's outermost layer of *gray matter*. This is the brain's command and control center, where higher cognitive functions are centralized, including the abilities for thinking, reasoning, believing, planning, and social *consciousness*—things that set us apart from other animals. The prefrontal cortex is more highly developed in humans than in any other primate, and it may not even exist in other mammals. (This is an area of continuing scientific exploration.)

In addition to examining the brains of other animals, scientists have made great strides in understanding brain function by observing people who have suffered trauma to the brain. Some of the most important breakthroughs in the biology of memory systems in the brain, for example, came from the study of a young man known as H.M., who underwent a radical surgery in which large sections of his *temporal lobes* were removed to control epileptic seizures. The surgery worked, but it left H.M. with a severe memory disorder in which he could learn, but not retain new information —he couldn't recall having met someone moments after that person had left the room. By observing H.M.'s behavior, and correlating it to the missing parts of his brain, scientists were able to learn which parts of the brain were responsible for certain behaviors. His case single-handedly shaped the course of memory research for decades.

While H.M. and legions of other brain-injury survivors spurred important advances in understanding the brain, for much of scientific history the brain was a black box, a mystery so profound it was long considered to be the realm of philosophy or religion, not science. The 15th-century philosopher René Descartes promoted the idea that the "mind" was separate from the brain or body—an idea that has stubbornly persisted even in this age of modern medicine, argues Antonio Damasio, M.D., Ph.D. in *Descartes' Error.* Indeed, medical science has only recently begun to recognize the links between psychological phenomena and physical health, or the power of the mind to influence healing in the body.

That Bump on Your Head Means You're…

The history of brain science is filled with odd twists and turns, not unlike the convoluted *sulci* and *gyri* (grooves and ridges) of the brain's outer surface. Perhaps one of the oddest twists, a field dubbed "phrenology," emerged in the late 1700s. Early proponents of phrenology argued that individual

brain structures, or "organs" as they called them, were highly specialized to individual personality traits, an idea coincidentally ahead of its time. (We now know that many brain structures have very specialized functions.) But phrenology is perhaps best known for a belief that is now viewed as one of the more bizarre footnotes of science—that each human trait could be traced to specific bumps and indentations on the head. Further, phrenologists believed that the size of the bumps was directly correlated to the prominence of that particular emotion or attribute in the person's overall personality makeup. A protruding forehead, then, might mean you were exceptionally "mirthful," or a depression at the top of your head meant you had low self-esteem.

Phrenology was a mere "bump" on the road to modern neuroscience. The drive to understand the brain's mysteries picked up speed as scientific methods advanced. As the 19th century ended, two scientists—an Italian physician named Camillo Golgi and a Spanish anatomist named Santiago Ramon y Cajal—forever changed our understanding of the brain and shared the 1906 Nobel Prize in Medicine or Physiology for their work. While Golgi's theories about brain function were later disproved, his techniques, in which he stained brain tissue with silver nitrate and other substances to reveal its inner structure, are still used today. Just as important, Golgi "opened scientists' eyes to the true complexity of the human brain," notes Bruce S. McEwen, Ph.D., a leading neuroscientist at Rockefeller University. Golgi, they say, was the first to see the brain as a network of connected cells. Even though he was wrong about how the cells were connected, his work spurred others, including Cajal, to look at the brain differently. Cajal advanced what later became known as "the neuron theory," which proposed that nerve cells were not structurally connected, as Golgi thought, but were separate cells connected in some other, unknown way.

Chemical, Electrical Pulses Spark Brain Cell Communication

Over the next couple of decades, scientists began to tease out the details of nerve cell communication. They learned that the connections Cajal had hypothesized to be the underpinnings of all human behavior were actually formed through a complex chemical signaling process. In this relay race of life, they learned, one cell squirts out a neurotransmitter, a chemical messenger, that crosses the synaptic gap between nerve cells and latches onto *receptors* on the surface of a neighboring cell. It wasn't long before dozens of neurotransmitters were discovered and systematically analyzed to determine their roles in *cognition*, behavior, and disease processes.

By the 1970s, it had become clear that brain function was the result of a complex interplay of chemical transmitters jolted into action by electrical impulses. The pulses were generated by ion channels within the neuron, which acted like the starting gun for the relay race of *interneuronal* commu-

nication. Today, scientists continue to elaborate the processes of cell-to-cell communication in exquisite detail, and a new arm of science has evolved that is now exploring the events that occur "beyond the receptor" within the *post-synaptic* cell.

The 1970s and 1980s were important decades for brain science. The development of PET *(positron emission tomography)* during this period enabled scientists to capture anatomical images of the living, functioning human brain and to begin to inventory the neurotransmitters involved in various behaviors or brain disorders. PET takes advantage of the fact that nerve cells *metabolize* the sugar glucose to derive the energy needed to perform their roles in brain function. By measuring changes in glucose uptake by nerve cells, PET enables scientists to determine which areas of the brain are activated during specific tasks (such as the finger-tapping exercise discussed earlier).

The introduction of PET got people thinking about other strategies for mapping the brain, and *MRI* (magnetic resonance imaging) soon followed. Rather than measuring how much glucose cells metabolize, MRI uses intensely powerful magnets and radiowave pulses to capture images of the brain's structure (standard MRI) and function (fMRI). Standard MRI relies on the fact that molecules within cells, when placed in the strong magnetic field of an MRI scanner, "line up" in a certain fashion, much like the needle on a compass lines up with the Earth's magnetic field. When pulses of radio waves are applied to tissues with such alignment, the nuclei of individual molecules resonate the signals back in varying patterns that correspond to the chemical make-up of each area of tissue being studied. Scientists can then reconstruct anatomical images based on the patterns of resonance.

In recent years, sophisticated computer techniques have enabled brain imagers to take MRI to the next level, creating images that depict brain function in addition to anatomical structure. Using a standard MRI scanner, scientists can track which areas of the brain are active. When a specific region of the brain is active, neurons in that area use more oxygen. fMRI takes advantage of the different magnetic properties of oxygenated and deoxygenated blood, blood that has not been used by brain cells and blood that has been used. The relative concentrations of oxygenated and deoxygenated blood are measured and charted onto standard MR images of the brain to show which areas are "working."

Brain Function: The Sum of Many Parts

Imaging techniques such as PET and fMRI have revolutionized the field of brain science, enabling the precise mapping of brain functions and structures and permitting scientists to search out the roots of brain disorders or injuries. In addition, they have helped advance a "systems" view of brain function. According to this view, no one structure or area of the brain acts alone to drive a specific behavior or mental task. While certain brain

areas may be specialized for certain tasks, brain function relies on networks of interconnected neurons. These specialized pathways enable the brain to analyze and assimilate information from external (e.g., sensory) as well as internal (e.g., hormones) cues in order to respond with appropriate physical and psychological behaviors.

Systems neuroscience helps explain how people such as victims of stroke or head trauma, whose brains have been injured in a discrete site, can, over time, redevelop the functions lost as a result of the injury. Nerve cells in their brains in effect forge new pathways, bypassing the injured site and forming new connections, as if finding a new route to get to work after discovering that a bridge is out on the usual route. This ability to adapt, which scientists call *plasticity*, seems to be particularly strong in young brains, but "old" brains routinely learn new tricks, scientists have found.

Plasticity, in fact, plays a critical role in the entire life cycle of the brain, from its development in infancy, to its continual reshaping as learning occurs, to its ability to adapt to age-related changes that can lead to mental deterioration in later life. Now, new evidence suggests the brain may be even more plastic than previously thought. Turning one of the oldest tenets of neuroscience on its head, scientists recently discovered that nerve cells can regenerate, making the idea of brain repair following trauma or disease thinkable. Revealed at the end of the 20th century, this scientific breakthrough is sure to influence brain science for at least the next century.

Constructing the World's Most Sophisticated Machine

There is perhaps no time in the human life cycle during which plasticity is more important than in the period of nervous system development. A newborn baby's brain, scientists have learned, is not just a miniature version of an adult's. Instead, it is a work in progress, the world's most sophisticated machine in construction phase. Like the scaffolding that shapes the framework of a building, an initial framework of interneuronal "wiring" is present at birth, pre-set by nature via the genetic blueprints provided by the mother and father. The materials are also there: babies are born with virtually all of their lifetime store of nerve cells. (See developments in *stem cell* research, p. 23.) What remains is the "finish work" of the brain's communications architecture, the fine-tuning of a *quadrillion* cell-to-cell connections.

In humans, the fine-tuning phase unfolds over several developmental years. *"Nurture"* largely directs the completion of the wiring process, literally shaping the structure of the brain according to a child's early sensory experiences. During critical periods (or stages) of brain development, these early experiences stimulate neural activity in certain synaptic connections, which in turn become stronger and thrive. A "pruning" process ruled by a philosophy of "use it or lose it" ensues, during which *synapses* that are not routinely stimulated may wither and die. Within that period, "windows" of opportunity, during which the brain may be

specially "primed" for learning certain skills such as language, open according to the developmental schedule of the brain regions underlying those skills. Since it's well known that humans can continue to learn and modify behavior throughout life, it's clear that the windows never really slam shut, even though they may become a bit sticky.

Children who fail to get the stimulation they need for proper brain development can become tragedies. In the 1990s, studies of Romanian orphans whose cries for comfort were never answered or whose smiles were never encouraged, found lingering impairments in the children's basic social and thinking abilities and in their physical development. Numerous studies have also shown that babies who are held and caressed regularly do better developmentally and may reap the benefits throughout life.

The first few years of life are especially important, as they are periods of rapid change in the synapses. But new understandings about the developing brain indicate that the process of fine-tuning connections among neurons continues, to varying degrees, into adolescence. In fact, "brain development" probably never really ends—older adults are also capable of forming new synaptic connections and do when they learn new things. But the rapid-paced period during which external stimuli are critical to "normal" brain-building generally begins to dwindle around the mid-teen years.

Growing Pains in the Teenage Brain

Adolescence marks a turning point of sorts for the brain, as some of its structures are nearing maturity, while others are not yet fully developed. The prefrontal cortex, for example—the brain's center for reason, advance planning, and other higher functions—does not reach maturity until the early 20s. Since this part of the brain seems to act as a kind of cerebral "brake" to halt inappropriate or risky behaviors, some scientists believe sluggish development may explain difficulties in resisting impulsive behavior that some adolescents exhibit at times. The brain also has ultimate control over the ebb and flow of powerful hormones such as *adrenaline*, testosterone, and estrogen, which themselves play critical roles in the changing adolescent body.

The teenage brain is also struggling to adapt to a shift in the circadian rhythm, the brain's internal biological clock, which drives the sleep-wake

Numerous studies have also shown that babies who are held and caressed regularly do better developmentally and may reap the benefits throughout life.

cycle. The secretion of *melatonin* sets the timing for this internal clock, a hormone the brain produces in response to the daily onset of darkness. In one study, researchers found that the further along in puberty teens were, the later at night their melatonin was secreted. In practice, that means teens' natural biological clock is telling them to go to sleep later, and to stay asleep longer.

The Aging Brain: Attitude Counts!

While the teenage brain faces its share of challenges as it weathers the storm of adolescence, aging undoubtedly poses the greatest challenge to the normal life cycle of the brain. But contrary to popular belief, the slow march of mental decline many people associate with aging is not inevitable. While many people do experience memory lapses as they age, even as early as their 40s, this too is not preordained. Scientists who study the aging brain have identified an intriguing set of circumstances and personal attributes that seem to protect some people from the age-related declines in mental ability that so many aging Americans fear. In fact, brain research is turning up a surprising amount of evidence that, when it comes to maintaining mental sharpness into old age, attitude counts.

Marilyn Albert, Ph.D., a neuropsychologist at Johns Hopkins Medical School, and her colleagues have been following a large group of "high-functioning" elderly people in an effort to determine what specific attributes tend to characterize people who maintain high levels of mental abilities into their 70s and beyond. Moderate to strenuous physical activity and higher levels of formal education have been found to be key predictors of cognitive maintenance. But perhaps the most surprising correlate with successful aging is a psychosocial factor that scientists call "self-efficacy."

Dr. Albert defines self-efficacy as "the feeling that what you do makes a difference in the things that happen to you every day. It boils down to feelings of control." Scientists have theorized that our self-efficacy beliefs influence the types of activities we pursue, as well as how much effort we put into them, and how persistent we are if the task proves difficult. If we have doubts about our ability to accomplish something, we may be less likely to try it, or may give up more easily. A cycle ensues: If we fail to engage in challenging activities, our risk for cognitive decline increases as we age. We might be anxious or stressed about what we can no longer do, which sets off a cascade of stress hormones that can themselves contribute to memory lapses, and may damage brain systems in other ways as well. Scientists say that taking steps to assert control over one's life and surroundings, even in seemingly small ways, may help us to maintain our mental faculties well into old age. And, they say, it's never too early to begin.

Genetics and Stem-Cell Research: Breathtaking Vistas on the Great Biological Frontier

With all the advances neuroscience has

seen in the past decades, the future holds even greater promise. New techniques in cellular, molecular, and genetic biology are opening up vast opportunities for scientists to explore.

Two major scientific accomplishments have recently focused public attention in these areas: the near complete sequencing and mapping of the human genome and discoveries related to *stem cells*, found in both human embryos and in adults.

The mapping and sequencing of the human genome, completed in 2003, is the crowning achievement of nearly two decades of effort by dozens of research laboratories. This identification of the make-up of the human genome basically provides the blueprint of the human body, with the 23 pairs of chromosomes and roughly 30,000 genes found in each of the approximately 100 trillion cells in the human body. Some researchers estimate that half of all human genes and the multiple proteins they produce play a role in developing and maintaining the central nervous system (the brain and the spinal cord). (For a more in-depth look at genes and the brain, turn to p. 18.)

Having access to the human genome sequences will help brain researchers in four areas: helping brain medicine diagnose disease, determining genetic versus environmental effects, deciphering the underlying mechanisms of disease, and developing effective medications and treatments.

Another major development in cellular biology has come in discoveries related to stem cells. Stem cells are "blank," undifferentiated cells that can grow into heart cells, kidney cells, or other cells of the body. Originally thought to be found only in embryos, stem cells have unexpectedly been discovered in adult brains and other parts of the body.

In experiments, researchers have shown that stem cells can be transplanted into various regions of the brain, where they develop into both neurons and glia. Moreover, researchers now believe that other types of stem cells—from bone marrow, muscle, or skin—can be made to differentiate into neurons (and even neurons of specific types) when grown in culture and treated with appropriate inducing factors.

The potential use of such stem cells for the treatment of neurodegenerative disorders such as Parkinson's disease and to replace damaged neural tissue could provide a whole new dimension to research and ultimately to treatment of some of our most difficult brain diseases and disorders. (For a more in-depth look at stem-cell research, turn to p. 23.)

As scientists learn more about cellular and genetic biology, they are discovering new keys that may unlock the mysteries of the devastating brain disorders that continue to ravage humankind. A large group of leading brain scientists from around the world has outlined specific areas of neuroscience in which rapid advances are forecast. Already, progress has been made in each of these areas. True breakthroughs that will change the way we think about the brain and its disorders are imminent.

Neurologist Guy M. McKhann,

M.D., of Johns Hopkins University, predicts great advances in the next few decades in imaging, which actually now does not take place in real time with brain activity—that is, the images show brain systems' activity milliseconds after it begins. "The big advance," he says, "will be to develop functional imaging techniques that show us—as it is happening—how various areas of the brain interact. That is, we will see not only the location of brain activity but also its speed. Whatever the method, this souped-up imaging will enable us to investigate how brain circuits work, how one part of the brain modifies the functions of other parts, and how these circuits adapt to new situations or damage to existing circuits."

Dr. McKhann also says that we will be able to use imaging to study cell transplants in the brain. "Transplanted cells and their changes can be tracked by molecules on their surfaces. Specific markers can be attached to those molecules as tags that can be spotted by imaging, like radio collars on wolves moved to a new terrain. Other cells, scavenger cells that are part of our immune system, can be tracked into and out of the brain as they respond to injury or to therapies."

Alzheimer's disease, one of our most serious medical and societal problems, will be part of a new era of active intervention and treatment, says Dr. McKhann. "We have had a remarkable education about Alzheimer's disease in the last few years. We have a good idea of the basic mechanism: A fragment of a protein, *amyloid,* which is normally present in the brain, accumulates and is toxic to nerve cells. With this knowledge, our current approaches to treatment try to prevent the accumulation of amyloid or to accelerate its removal.

"I ask myself how many of the advances in the last 25 years of brain science I would have predicted," says Dr. McKhann. "Not many. Some came from logical, sequential explorations of how the brain works. Others were great leaps that kicked over strongly held beliefs. Others came through luck, albeit the luck of very patient and alert investigators. The same combination will shape the next 25 years of brain research." ■

The big advance will be to develop functional imaging techniques that show us—as it is happening—how various areas of the brain interact.

Genes and the Brain

Imagine a homework assignment in which you must read and understand the "Book of Life," a story with 3.3 billion letters. Printed out, the letters would fill a volume of books that would reach as high as the Washington Monument. Oh, and the letters are all either A, C, G, or T, arranged in seemingly endless combinations. Some of the "words" are millions of letters long, and you'll need to figure out where one ends and another begins. Then you'll need to find out what the words mean (there's no dictionary), and how they interplay with all the other words in the book.

That is essentially the task that was undertaken by the Human Genome Project, a government-funded effort to "read" the human genome, and a parallel effort by Celera Genomics, a private company. The genome contains the complete instruction manual for Homo sapiens, written in chemical code along the twisted *double-helix* strands of DNA that are carried within each of the 100 trillion cells in the human body (except in mature red blood cells).

The mapping and sequencing of the human genome, completed in 2003, culminates nearly five decades of investigation following the first description of the double helix model of DNA by James Watson and Francis Crick in 1953. Watson and Crick's view of DNA successfully described how molecules of nucleic acid could not only carry tremendous amounts of information, but could also copy themselves accurately each time a cell divides.

With the mapping and sequencing of the human genome, for the first time scientists can see the entire landscape of all the human chromosomes and how the genes are organized on the chromosomes. Encoded in the twists of our DNA are about 30,000 genes, the critical "words" in the Book of Life. They determine every inherited trait we have, from the color of our eyes to the size of our feet, and possibly even behavioral traits such as an inclination to be aggressive or our desire for affection. More important, they tell us what diseases we may be susceptible to and those we may be protected from, as well as what medicines we might respond to in the event of illness.

In short, understanding the Book of Life has the potential to change everything about health, medicine, and life in general. Welcome to the Genomics Era.

Genomics will affect every field of medical science, but its significance to brain science is particularly great. As much as half of the genome's instruction manual—as many as 15,000 genes—is thought to be devoted to the workings of the central nervous system (the brain and spinal cord) and peripheral nerves. One surprise of the genome projects was that humans have only about twice as many genes as fruit flies and roundworms, two "simpler" species used as models for biological systems in science and medicine. Many of the "extra" genes in humans are thought to be devoted to the development, structure, and function of the brain—a testament to the complexity of the organ that most differentiates us from every other living thing on earth.

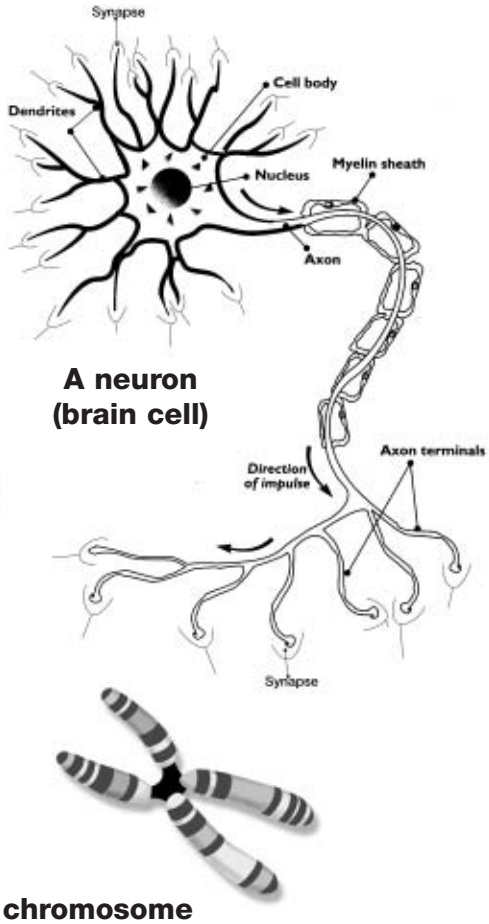
Not So Different from a Fruit Fly

Still, experts remind us that at the level of individual brain cells (neurons) we're not all that different from fruit flies. Many of the most basic mechanisms of brain function—how cells communicate with one another or how memories are processed, among others—are basically the same in humans and fruit flies, as well as in mice, chimpanzees, and other species. In the spirit of "if it's not broken, don't fix it," such processes have been conserved by the forces of evolution. Much of the human brain's complexity is more likely because we have so many more neurons interconnected in so many more ways. Think of it as your home PC versus a huge supercomputer: the basic operating systems are the same, but the supercomputer has far more processing power.

The sequencing of the human genome and, more important, determining the function of all those genes—will reveal the brain's deepest secrets: why we act the way we do; why some things are easier to learn than others; how our brain develops from conception through adulthood, including the critical teenage years when the brain undergoes a dramatic "pruning" process to streamline its circuits. It will also give us new information about the genetic components of brain diseases, which include a wide array of disorders ranging from attention-deficit disorder to Alzheimer's disease and mental illnesses such as depression and schizophrenia. Scientists have struggled for years to find the genes at the root of many of these brain disorders; with the sequence in hand, the searches will be much speedier.

Basic Genetics—A Brief Guide

A human cell
Each of the 100 trillion cells in the human body (except mature red blood cells) contains a copy of the entire human genome—all the genetic information necessary to build a human being. The cell nucleus is a separate compartment in the cell that contains six feet of DNA packed into 23 pairs of chromosomes. We each inherit one set of 23 chromosomes from our mother and another set from our father. Egg and sperm cells carry single sets of 23 chromosomes.



A neuron (brain cell)

A chromosome
In the nucleus of any normal human cell there are 23 sets of chromosomes. Within each of the 46 chromosomes is bundled a double-stranded helix of DNA. Each of the human chromosomes contains genes, the major functional units of DNA.

DNA
The material from which the 46 chromosomes in each cell's nucleus are formed is called DNA (deoxyribonucleic acid). DNA contains the codes for the body's approximately 30,000 genes, governing all aspects of cell growth and inheritance. DNA has a double-helix structure—two intertwined strands resembling a spiraling ladder. DNA consists of just a few kinds of atoms: carbon, hydrogen, oxygen, nitrogen, and phosphorus. Combinations of these atoms form the sugar-phosphate backbone of the DNA—the sides of the ladder.

A gene

Each gene is a segment of DNA, typically several thousand base pairs long. Genes are copied into a molecule of *RNA (ribonucleic acid)*, which is translated to make a specific molecule, usually an *amino acid*. Combinations of the atoms carbon, hydrogen, oxygen, nitrogen, and phosphorus form the four chemical bases in DNA: adenine (A), thymine (T), guanine (G), and cytosine (C). The bases form interlocking pairs that can fit together in only one way: A pairs with T; G pairs with C. Each such pair is called a base pair of DNA.

A protein

Proteins, which are made up of *amino acids,* are the body's workhorses, essential components of all organs and chemical activities. Their function depends on their shapes, which are determined by the roughly 30,000 genes in the cell nucleus.

SNP

Pronounced "snip," *SNPs* (single nucleotide polymorphisms) are one-letter variations in the DNA sequence. SNPs contribute to differences among individuals. The majority have no effect; others cause subtle differences in countless characteristics, such as appearance, while some affect the risk for certain diseases.

C G G T A C T T G A G G C T A Person 1
C G G T A C T C G A G G C T A Person 2

Mutation

Mutations are changes in DNA spelling that can result in abnormal proteins that do not function normally and therefore cause health problems.

Three DNA bases are deleted in the mutated sequence below, resulting in the deletion of an amino acid (phenylalanine) from the CF protein. People with the abnormal protein develop cystic fibrosis.

Normal CF (Cystic Fibrosis) sequence

ATT ATC ATC TTT GGT GTT TCC

Mutated CF sequence

ATT ATC TTT GGT GTT TCC

Sources:
National Human Genome Research Institute: (*www.nhgri.nih.gov);* Howard Hughes Medical Institute: *Blazing a Genetic Trail*, (*www.hhmi.org*); Public Broadcasting System, WGBH: *DNA Workshop* (*www.pbs.org/WGBH*); CNN: "Scientists Sequence First Human Chromosome," (*www.cnn.com*).

Here's Your Genome

What does all this mean to you? Imagine a time in your future when you can visit a human genome laboratory and a week later, get back a DVD with your personal genome spelled out. It comes with an editorial describing your life story, as told by your genes. It tells you what illnesses for which you may be at risk and which *recessive* genes you may have that could be passed along to your children. Armed with information about your risk, you could take steps to protect yourself. These might include lifestyle changes that reduce the likelihood of your exposure to "triggers" in the environment that might set the disease process in motion, or taking medications genetically formulated to alter the function of the gene or genes that put you at risk.

Sound like a brave new world? With the knowledge of our genome, the potential for changing medicine for the better, and the world we live in, is tremendous. Moreover, a significant part of genetics research is being devoted to understanding the ethical, legal, and social implications of the sequencing effort and to finding ways to safeguard against abuses and ensure the privacy of individuals in the Genomics Era.

While the sequence of the human genome is now a matter of public information, the task before genomics scientists has merely begun. Now, the challenge is to create the "dictionary" that explains each word in the Book of Life: what it means, what roles it plays in development and biological function, and what goes wrong when disease or illness strikes. This phase will be the most difficult by far. When complete, everything we now know—about science, medicine, and life overall—will forever change. ■

Stem Cells and Brain Research

Fred H. Gage, Ph.D.

By Fred H. Gage, Ph.D.

Dr. Gage, is professor, the Laboratory of Genetics, The Salk Institute for Biological Studies, La Jolla, CA. His current areas of specialization are regeneration and neurogenesis in the adult nervous system.

Almost every day a newspaper article, news magazine piece, or television news story extols the miraculous possibilities of replacing diseased organs with tissue made in the laboratory from stem cells or raises nightmarish specters of unregulated harvesting of stem cells to create clones. Stem-cell research does offer real promise and does raise real concerns, but unfortunately the public has not been adequately informed about the science behind the debate.

The hopes and promises for the use of these cells as therapies for devastating and currently untreatable diseases are being counterbalanced by the concerns over the ethical issues associated with the source of the cells. The discussion of stem cells also has been linked to discussions of cloning humans, as well as to the use of fetal tissue for transplantation.

Trying to untangle unrelated issues and clarifying what is currently known versus what is believed to be true can help us make informed decisions. An informed public will make rational decisions about the use of stem cells and can provide knowledgeable support in advancing this potentially useful field of biomedical research.

So, What Is a Stem Cell?

In its simplest form, a stem cell is any cell that can divide and produce a cell like itself (self-renewal) and produce another progeny that gives rise to a mature cell of any organ of the body—that is, blood, brain, liver, and so on. Some stem cells are "totipotent" cells; that is, they can give rise to a fully developed organism. For instance, a fertilized egg has this potential for about four days. These cells can be produced through human reproduction or in the laboratory through in-vitro fertilization (IVF). Within six days after fertilization, the totipotent stem cell divides, matures, and gives rise to more restricted cells called "pluripotent" stem cells. These cells can self-renew and can give rise to any cell of the body. Pluripotent cells have lost the potential to form an organ and certainly cannot form a fully developed organism. This complex cellular

development takes place before organs begin to form in the embryo or even before the embryo leaves the fallopian tubes and implants in the uterus.

These more restricted pluripotent cells are called embryonic stem cells (ES cells) and are the focus of both the promise and concern currently being expressed at national and international levels.

The promise is based on the fact that these cells can divide indefinitely and may be able to be used to replace missing, damaged, or dying cells in any organ of the developing and adult body. Certain diseases, in which specific types of cells are damaged, as in diabetes, Parkinson's disease, heart disease, and cancers, are likely to be the first targets for such therapeutic applications.

The concern about human cloning is unrelated to the current debate over stem cells, because of the clear finding that stem cells of any sort, and particularly the pluripotent stem cells, are not required for cloning.

Where Can Stem Cells Be Obtained, and How Do Various Types of Stem Cells Differ?

Once an embryo implants in the uterus and begins to make specific organs, at about 25 days after fertilization, separate groups of more mature stem cells take up residence in the different organs (blood, skin, brain, etc.) and contribute to making the cells of each organ. These cells remain in the organ throughout life and can be obtained at any time in development as well as in adulthood, but are more abundant early during development, when the fetus is growing. These later cells are called organ-restricted, "multipotent" stem cells (sometimes referred to as adult stem cells, because a limited number remain in and can be isolated from adult organs).

Great interest and effort are being put into investigating both ES cells and multipotent stem cells, but it is not clear whether the multipotent (adult stem) cells live as long or are as viable as the pluripotent ES cells. Multipotent cells are certainly not as versatile or potent as embryonic cells.

Our knowledge is currently too limited for making a decision as to which cells will be the best or most efficacious for which therapy. In fact, it is quite likely that, through a careful comparison of ES cells and multipotent cells, a clearer understanding will emerge as to the best, safest, and most ethical way to use stem cells for treatment of human diseases.

Pluripotent embryonic cells can be obtained from the surplus fertilized eggs produced by fertility clinics through IVF, a life-giving procedure that helps infertile couples conceive a child. Most of these surplus fertilized eggs are not used and are discarded. This fact contributed to the recent decision in the United Kingdom to approve financial support for the evaluation of new human embryonic cells to develop therapies for human disease. The United States approved a plan permitting the use of limited number of existing ES cell lines in 2001. In the United States, unregulated research continues to be carried out by private companies using private funding.

Approval of federal support for the generation of new ES cells would guarantee that extensive guidelines could be enforced for federally funded research. Oversight of federally funded research would cover such issues as the source of cells, informed consent, and measures to ensure safety and the ethical use of ES cells.

It is important to remember that the information that is gained from research sponsored by federal funding is open to the public and available for scientists to use for their own studies and potential therapeutic applications.

The biomedical research community generally supports the study of embryonic cells for their potential value in treating a variety of unresponsive diseases, but like most citizens of this country, the scientific community would support fully enforceable guidelines that would permit the best open and ethical information to be obtained.

Only by obtaining accurate, responsible, and high-quality information can we as a country make informed decisions and explain our positions to our local and national representatives. ■

Advances in Brain Research

A Look at Remarkable Achievements and Far-Reaching Goals in Specific Areas of Brain Science and Brain Medicine:

■ The Adolescent Brain ■ Neuroethics ■ Stroke, or Brain Attack

■ Neuroimmunology ■ Stress ■ Alzheimer's Disease ■ Depression

■ Memory ■ Emotions ■ The Developing Nervous System

■ Spinal Cord Repair ■ Parkinson's Disease ■ Epilepsy

■ Multiple Sclerosis ■ Brain Injury ■ Brain Tumor ■ Pain

■ Addiction ■ Basic Brain Knowledge ■ Cell Replacement

■ Neural Repair ■ Electronic Aids ■ Drug Discovery



Behind the Scenes in the Adolescent Brain

Floyd E. Bloom, M.D., M. Flint Beal, M.D., and David J. Kupfer, M.D., Editors

Adolescence has been described as a busy time for the human brain. It's a time of transition as the brain, like the rest of the body, physically eases into adulthood and, in the process, the brain's gray matter absorbs an explosion of new external stimuli. In this article, the authors look at the unique external and internal developments of the teenage years: high school, peer pressure, sexuality. The list goes on, and as it does, the brain is challenged. In most cases it thrives; sometimes it does not.

A large part of adolescent development takes place in the *frontal lobes,* which house an incredible number of faculties that we use many times each day. Here are the brain sites that enable us to make sense of the floods of information constantly being gathered by our five senses; to know when we are experiencing an emotion, and even to think about it while we feel it; to understand and keep track of the passage of time; and to hold a thought or object briefly in the forefront of our mind while we proceed with another thought (an ability known as working memory). According to a recent animal study of frontal lobe development, several different "transporter" molecules, which help the neurons to take in neurotransmitter molecules and break them down for reuse, either increase in density during adolescence or reach a plateau, which in turn alters some signaling pathways and stabilizes others. Partly from refinements in the signal circuits of the frontal lobes and partly through accumulated experience, adolescence gradually brings greater independence along with new capacities to plan, to consider the possible consequences of an action, and to take responsibility for the conduct of one's life.

Not surprisingly for a major executive center, the frontal lobes must reorganize to meet new demands, and they do so at more than one level in the years leading up to adulthood. One of the most significant changes (which actually continues well into adulthood) is a major increase in the myelination, or insulation, of the nerve fibers going both into and out of the frontal lobes. Greater insulation here means faster signaling, and perhaps more highly branched signaling pathways, between frontal lobe neurons and those in any distant region of the brain. This is a development that we can understand on an everyday level. Clearly, the more information the executive center can gather in various modes—visual signals, the emphatic tone of someone's voice, the emotions of the moment—the more nuanced and appropriate the brain's responses can be.

At a day-to-day level, adolescents encounter increasing demands on their attention. For starters, entering middle school or high school means a lot more to keep track of. Instead of being with one teacher in one classroom all day, students move among a half-dozen different classrooms, with a homeroom somewhere else and a

locker at yet another place. And, typically today, it quickly becomes necessary to juggle various homework assignments and projects and to balance them against sports or after-school activities, paid or volunteer work, and an ever more complicated social life. Is it any wonder that researchers, psychologists, and sociologists alike are becoming concerned about the long-term effects of these very crowded schedules on the young, developing brain? Some experts warn that our society may be overencouraging the development of quick responses and mental multitasking in young people, at the expense of equally valuable life skills: planning, thinking things through, and predicting the consequences of actions.

Neuroethics Weighs the Benefits or Potential Misuses of Brain Research

By David Balog

***As the revolution in brain science and patient treatment continues, neuroscientists and numerous other professionals are beginning to consider daunting societal issues that have arisen as a result. David Balog is assistant editor of the Dana Press and editor of* The Dana Sourcebook of Brain Science: Resources for Secondary and Post-Secondary Teachers and Students, Third Edition.**

So important are the potential questions and answers regarding the use or misuse of the fruits of brain research that a new word, neuroethics, has been coined.

Consider some of the following medical situations:

- Drugs that improve concentration are already available; others that enhance memory are in development. How it should be decided whether these medications are used only to treat an underlying illness, such as Alzheimer's disease, or are also used to boost a healthy individual's mental performance?
- A specific gene, apoE4, increases risk for late-onset Alzheimer's, the most common form of the disease. Additional genes are likely to be identified. However, genes are responsible for only part of the risk of Alzheimer's. Are genetic counselors needed to help people interpret the emerging information?
- *Brain imaging* can reveal when people are lying or suffering from brain damage linked to impulsive violence. Some experts now question the reliability of this technology, while others wonder whether—and how—it will be used by police and the courts.[1]

A large group of professionals representing such diverse fields as neuroscience, biology, law, journalism, and religion gathered in 2002 for a first-of-its-kind conference, "Neuroethics: Mapping the Field." These professionals are beginning to reflect on the impact of neuroscience advances in areas such as moral vision, decision-making, conduct, and policies in both the public and private sectors.[2]

New knowledge about the brain will affect a wide range of fields including athletics, education, college admissions, policing, and social work. Advances in brain imaging could pose a particular dilemma. Neuroscientist Pierre J. Magistretti, M.D., Ph.D., has written, "If such tests were misused, they could infringe on an individual's privacy—for example in the context of health insurance contracts or seeking a job."[3] Our understanding of morality is even being transformed by neuroscience: Researchers have shown that learning right from wrong is influenced by myelination of brain tissue in the frontal cortex and in several other brain regions and systems, processes that typically are not completed until one's early twenties. Given this knowledge, do we as a society need to reassess our ideas of self control or obedience to the law?

Similarly, another conference participant said that patients with dysfunction in selected brain

regions, caused by disease occurring during development or adulthood, exhibit behavioral changes that may be indistinguishable from those of straightforward bad behavior. Since neuroscience can now investigate the mechanisms behind disturbed behaviors, this participant said that society must ponder how it treats individuals who are found to violate its rules and take into account those with medical conditions. Should those individuals receive treatment or punishment?

On the role of brain scientists in this new field, leading researcher Fred H. Gage, Ph.D., said, "Pursuing these new lines of scientific inquiry in a responsible way requires that we reexamine what we do as scientists. But as neuroscientists, we are well-positioned to help shape and contribute to the debate and discussion. One of the hallmarks of neuroscience as a field has always been the drive toward integrating information from disparate fields and specializations to increase knowledge. Sorting through the complex issues captured under the umbrella of neuroethics will provide an important opportunity for contributing to informed and rich discussions among and between scientists and the public."[4]

[1] MacDonald, A., "Information Overload: Scientific Advances Create New Challenges," *BrainWork: The Neuroscience Newsletter,* July-August 2002, p. 4.

[2] _____, "Dana-Sponsored Neuroethics Conference Begins to Define Issues, Conflicts in Emerging Field," *Dana Alliance Member News,* Vol. VI, No. 3, June/July 2002, p. 1.

[3] Magistretti, Pierre J., M.D., Ph.D., "Neuroethics: A Neuroscientist's Perspective," *Visions of the Brain: A Progress Report on Brain Research, Update 2003—Neuorethics: Conscience of the Brain*. Dana Press, New York, 2003.

[4] _____, "Alliance Attendees at Neuroethics Conference Look to Future," *Dana Alliance Member News*, Vol. VI, No. 3, June/July 2002.

Neuroimmunology: Harnessing the Power of the Brain and the Immune System

By Maia Szalavitz

Neuroimmunology, whose complex work focuses on the brain, the immune system, and their interactions, holds the potential for conquering ills as diverse as spinal cord injury, multiple sclerosis, and bodily reactions to pathogens, both naturally occurring and intentionally inflicted. Maia Szalavitz is a freelance writer who covers neuroscience and addictions. She has written for the New York Times, *the* Washington Post, Newsweek, *and other publications.*

They are the two most complex systems in the body and the only two with memory. Now, scientists are realizing that the new frontier in protecting human health may lie at the interface between these two worlds—the nervous system and the immune system.

In his book *The End of Stress As We Know It,* noted brain scientist Bruce McEwen, Ph.D., has written this concise description of our body's self-defense system:

> The immune system orchestrates the body's defenses against infection and injury, fighting off such intruders when possible and healing the damage that occurs when any invaders get past the front lines. Immune cells, generated in the bone marrow and carried by the blood, obey the prime directive of deciding

what is a healthy integral part of the body and what is not—in scientific parlance, distinguishing "self" from "nonself." Anything that's nonself is marked for destruction. The immune cells are the white blood cells, as opposed to the red blood cells that deliver oxygen to the body's tissues.

Although the immune system has been investigated intensively since Louis Pasteur created one of modern medicine's marvels, vaccination, 150 years ago, the study of the brain-immune system interaction is new. Unlike the brain, our body's command center, the immune system does not reside in one place. Immune cells rove freely through the blood and into most of our tissues and can respond relatively independently to local conditions.

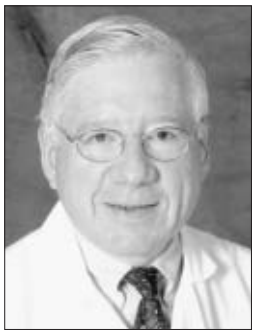
Over the past decade, scientists began to find that vital immune cells called T-cells bind to neurotransmitters such as endogenous *opiates* and norepinephrine, giving new support to the concept that the immune cells are equipped to receive messages from the brain. Scientists also spotted traffic flowing in the other direction: cellular chemical messengers, called cytokines, could affect the brain.

Scientists in laboratories across the country are now seeking to discover how the brain and immune system communicate, how immune cells travel through the body (and sometimes into the brain), and if and how and why the immune system gets the wrong messages from the brain and turns its attack on the body. Just how close is the brain-immune system relationship? One noted scientist, Esther Sternberg of the National Institute for Mental Health, NIMH, says, "The immune system can be viewed as a sensory organ, sending signals about pathogens the way the eyes send visual signals and the ears send auditory signals. The brain responds and produces hormones and neurochemicals that alter immune function."

Neuroimmunologists are beginning to focus on enhancing the power of our innate immune system against pathogens, both naturally occurring and intentionally inflicted. But how to form a first line of defense without triggering an autoimmune response that can cause a disease such as multiple sclerosis remains a daunting question. In the autoimmune disease multiple sclerosis, immune cells attack the insulating covering *(myelin)* of neuron fibers *(axons)*, profoundly affecting the nerve cells' ability to communicate. Other questions being explored include how specialized immune cells are able to penetrate the blood/brain barrier and attack delicate brain tissue. Investigations are also underway regarding cell inflammation after spinal cord injury. Scientists believe that spinal cord damage results not only from the injury itself, but also from the resulting cellular reactions.

As we discover what regulates immune power and how our brains have voluntary control over it, medical science could take possession of a tool of enormously diverse potential.

(Adapted from "The Brain-Immunology Axis," by Maia Szalavitz, *Cerebrum: The Dana Forum on Brain Science*, Vol. 4, No. 1, Winter 2002, Dana Press, New York.)



Defining Stroke or Brain Attack

By Cleo Hutton and Louis R. Caplan, M.D.

Stroke, or brain attack, is the third leading cause of death in the United States. In a 2003 book, Cleo Hutton's account of surviving a stroke is complemented by medical and scientific commentary from a leading expert in the field, Louis R. Caplan, M.D. Dr. Caplan explains Hutton's case in terms of what scientists and doctors have come to know about strokes.

The term stroke describes brain injury caused by an abnormality of the blood supply to a part of the brain. The word is derived from the fact that most sufferers are struck suddenly by the vascular abnormality. Abnormalities of brain function begin quickly, sometimes within an instant. *Stroke* is a very broad term that describes several different types of vascular diseases involving the blood vessels that supply the brain with needed nourishment and fuel. Since treatment depends on the type of stroke and the blood vessels involved, it is very important for the doctor to determine precisely what caused the vascular and brain injury and where the abnormalities are located.

Strokes fall into two very broad groups: ischemia and hemorrhage. Cleo had the most common type of stroke—ischemia—which means a lack of blood. Hemorrhage and ischemia are polar opposites: in hemorrhage, too much blood collects inside the skull; in ischemia, there is not enough blood supply to allow survival of the affected brain tissue. About four strokes out of every five are ischemic. When a part of the brain is not getting adequate blood, it may stop performing its usual tasks. A good comparison is the fuel pump in a car. If a fuel line is blocked and you step on the gas pedal, the car will not go because of the lack of fuel. But when the fuel line opens, the car will return to its normal behavior—and the car is not necessarily damaged. When the blood supply to a part of the brain is deficient for enough time, the tissue dies. The death of tissue caused by ischemia is called infarction. With *CT scans* we can tell whether the brain contains a hemorrhage, which looks white on the scan, or an infarct, which shows damage as black or gray.…

There are three major categories of brain ischemia: thrombosis, embolism, and systemic hypoperfusion. Each indicates a different reason for decreased blood flow. I find these terms easiest to explain by comparing them with house plumbing. Suppose that one day you turn on the faucet in the bathroom on the second floor and no water comes out, or it comes out in an inadequate drip. The problem could be a local one, such as a rust buildup in the pipe leading to that sink. This is analogous to *thrombosis*, a term used to describe a local process occurring in one blood vessel region. Atherosclerosis or another disease narrows the artery. When the artery becomes very narrow, the resulting change in blood flow causes blood to clot, resulting in total occlusion of the artery. Clearly this is a local problem in one pipe; a plumber would attempt to fix the blocked pipe. Similarly, physicians treat a narrowed (stenosed) or occluded artery by trying to open it or by creating a detour around it.

But a blocked pipe to a second-floor sink could also be caused by debris in the water system that came to rest in that pipe, rather than by a local problem that began within the pipe. When particles break loose and block a distant artery, we call it an embolism. (The place where the material originates is called the donor site; the receiving artery is the recipient site; and the material is called an embolus.) An artery within the head can be blocked by a blood clot or other particles that break loose from the heart, from the aorta (the major artery leading away from the heart), or from one of the major arteries in the neck or head. An embolism was the cause of Cleo's stroke.

Suppose instead that the plumber finds that the water did not flow normally in your second floor sink because the water pressure in your house is intermittently low and flow to all sinks and showers is faulty due to a leak in the water tank or low water pressure in the entire house plumbing. This situation is like systemic hypoperfusion: there is no local problem within the pipe to one sink, but instead a general circulatory problem. Ischemia can be caused by inadequate pumping of blood from the heart or a low volume of blood or fluid in the body.…

(Excerpted from *Striking Back at Stroke: A Doctor-Patient Journal,* by Cleo Hutton and Louis R. Caplan, M.D. Dana Press, Washington, DC, 2003.)

What Exactly Are Antidepressants?

By J. Raymond DePaulo, Jr., M.D.

Depression, in its unipolar form, may be the leading cause of disability worldwide; in its bipolar form—often called manic-depressive illness—it has both stimulated the creativity and diminished the will to live of some of the world's most brilliant artists, poets, scientists, and statesmen. J. Raymond DePaulo, Jr., M.D., professor of psychiatry at Johns Hopkins University School of Medicine, an active clinician, teacher, and researcher, has described depression as "a mystery disease," a paradoxical characterization of an illness for which brain science has produced an array of usually effective medications.

For all their differences, the many types of medications we call antidepressants are consistently better than placebo tablets in reducing symptoms in depressed patients. These medications do not, however, have the capacity to change anyone's personality, but rather act to restore the normal chemistry in the brain. Antidepressants go by many names based on their chemical structure or activity, such as the tricyclic structure or the *serotonin reuptake* inhibitor activity; that's not to suggest that every drug with a tricyclic structure and every drug that affects serotonin reuptake is necessarily an antidepressant. While demonstrating antidepressant activity, almost all these medications have other useful properties, particularly in anxiety disorders or in the regulation of blood pressure. That's why the word antidepressant can be confusing. I prefer to describe these medications in terms of their structure or function; for example, this drug affects serotonin or norepinephrine in this or that way.

The drugs we call antidepressants fall into four basic categories: tricyclics, selective serotonin reuptake inhibitors (SSRIs), monoamine oxidase inhibitors (MAOIs), and a number of newer drugs we can lump together under the necessarily vague designation of "others."

Serendipity has played an interesting role in the development of drugs that are currently being used to treat depressive illness. Swiss researchers were trying to make a better antihistamine when they created a compound containing a property that proved very helpful in treating psychotics and schizophrenics. The drug they created turned out to be Thorazine. Then, when researchers sought to make a better Thorazine they produced not an antipsychotic (a drug used to treat severe mental illness), but a tricyclic drug called imipramine. While imipramine didn't help people suffering from manias or schizophrenia, it did help people with depression. Once the tricyclics began to enjoy wide acceptance, pharmacists went back into the labs to attempt to make a better imipramine; they instead came up with Tegretol (also called carbamazepine), the first anticonvulsant mood stabilizer not derived from lithium. But happy accidents, as we all know, rarely happen in a vacuum. The discoverers of these compounds were astute enough to know how to see things they weren't looking for directly, and that's hard to do.…

While there are differences between types of antidepressants, they are outweighed by their similarities. In fact, some experts have argued that, when you come right down to it, all antidepressants are basically the same, not only because the response rates are so similar, but because the chemical structure of these various drugs is much the same and overlap in terms of activity. Generally speaking, these drugs act by blocking the reuptake of neurotransmitters such as serotonin and norepinephrine in varying degrees.

These drugs leave more of the signal-carrying neurotransmitter "out there" in the brain rather than allowing so much of it to be sucked back into the neurons and produce mental or emotional problems. Keep in mind that altering chemical balances in the brain is what these drugs do, and while they often evoke a favorable response in that the patient feels much better over time, what makes these drugs work, what their exact mechanism is in the brain that has an effect on depression, remains a mystery.…

(Excerpted from *Understanding Depression: What We Know and What You Can Do About It,* by J. Raymond DePaulo, Jr., M.D., with Leslie Alan Horwitz. John Wiley & Sons, Inc., and Dana Press, New York, 2002.)

The Developing Nervous System: Vision

By Norbert Herschkowitz, M.D., and Elinore Chapman Herschkowitz

Norbert Herschkowitz, M.D., and his educator-writer wife, Elinore Chapman Herschkowitz, study how brain development shapes a child's personality, beginning with conception. Here they discuss visual development, a feat of information processing whose complexity we are still learning to appreciate. Scientists now know that some circuits of the visual system are up and running even before we are born.

The View from Inside

The view really isn't much, perhaps at most a faint orange glow during the last weeks before birth. But even in the dark, your baby's visual system is under intense construction to prepare her for her life in the world of light. Already at around one month after fertilization, when the first traces of her brain as a whole come into view, tiny bulges that will become the baby's eyes appear.

Carla J. Shatz, now chair of the Department of Neurobiology at Harvard Medical School, showed in animal experiments that the basic wiring of the visual system begins to take place before any stimulation from the outside world reaches the baby's eyes. In the absence of light, special nerve cells in the retina of the eye called ganglion cells begin, probably under genetic influences, to fire off short bursts of electrical impulses. The impulses are transmitted from the retina along the optic nerve to the brain. The spontaneous electrical activity of these retina cells seems to be crucial for setting up the correct wiring. If it does not take place, vision will not develop normally.

The impressive groundwork takes place all by itself without any extra outside stimulation. However, adverse environmental conditions may prevent necessary developmental steps from taking place. The spontaneous firing of the nerve cells in the visual system is vulnerable to disruptions. Drugs that interfere with the transmission of electrical activity across the synapse (e.g., nicotine, benzodiazepines, or narcotics) could disturb the pattern of the fine connections and lead to later visual deficits.

By the time your baby is born, her visual system is basically set up. But it will need the stimulation of the outside world to complete the job—and there is plenty out there waiting.…

Looking Around

Once your baby has taken his first breath or two, his eyes blink at all the bright light in the delivery room and he stares astounded by all the unfamiliar sights. Now his sense of vision suddenly becomes important for helping him become acquainted with his world. While his sense of hearing has been exposed to a great variety of sounds in the uterus and his sense of touch has

been stimulated by contacts with his own body or the uterine wall, his visual system has been pretty much left in the dark until now.

Newborn babies seem eager to find out what's going on. Marshall Haith and his colleagues observed infants lying in a dark room. Even in complete darkness, the infants' eyes moved around as if they were looking for something to attract their attention. Since no light was entering the babies' eyes, the investigators concluded that the eye movements were "endogenous," that is, the result of direct activity of the brain rather than of outside stimulation.

A newborn baby sees faces as blurred figures surrounded by areas of light, and the baby's eyes can focus only on objects that are within about 8 to 30 inches. That is about the distance between a mother's face and that of her baby when she is holding him during feeding.

Newborns focus on strong lines and distinct contours. Studies have shown that they can tell the difference between the outline shapes of a triangle, square, circle, and cross. In human faces, the eyes and hairline are prominent features. Perhaps for this reason, mothers—and fathers—of newborn infants might think twice about changing their hairstyles too often….

(Excerpted from *A Good Start in Life: Understanding Your Child's Brain and Behavior,* by Norbert Herschkowitz, M.D., and Elinore Chapman Herschkowitz. Dana Press and Joseph Henry Press, Washington, DC, 2002.)

The Science of Attracting Axons—The Final Key to Spinal Cord Regeneration?

By Luba Vikhanski

For millennia, scientists and doctors have viewed damage to the spinal cord *as permanent. Science journalist Luba Vikhanski writes that startling new discoveries in the last 20 years have greatly improved our understanding of the "wiring" process of the fetal nervous system and opened a window on the workings of the mature spinal cord. Treatment and cures from this and other research paths could follow.*

As befits a mechanism perfected over 600 million years, axonal guidance is a smoothly scripted affair. *Axons* travel a long distance, sometimes more than a thousand times greater than the diameter of their cell bodies, before settling into their assigned spots. They negotiate this challenging journey by breaking it up into short segments, each perhaps a fraction of a millimeter long. At the end of each segment, the growth cone appears to pause, like a traveler at a crossroads, making navigating decisions. What helps it choose its course is the presence of guidance chemicals….

Axons have no problem following the attractive and repulsive cues in the embryo, but by adulthood something happens to the environment in the central nervous system, making it hostile to growth. Scientists hypothesize that the "go" signs that guided axons to the places in the fetus turn into "stop" signs in the adult organism. To pro-

duce regeneration, the guiding signs would have to be switched from "stop" back to "go." This idea is based on a fascinating property of all guidance molecules: They can be attractive or repellent at different times, or attractive for some growth cones but repulsive for others, which suggests that their guiding properties can be manipulated.

Scientists have proposed that the molecular "stop-go" switch may be the same for all guidance molecules. No one has yet proved this hypothesis, but in several studies a manipulation of guiding properties has already been accomplished. In one series of experiments, a team led by Dr. Mu-ming Poo, from the University of California at San Diego, in collaboration with [Dr. Marc] Tessier-Lavigne's lab, achieved a feat that sounds like an episode from a romantic novel. The scientists managed to transform repulsion into attraction. Using a molecular switch they identified, they altered the effect of two guidance molecules on the tips of growing nerve fibers: Instead of repelling the growing fibers, the molecules started to attract the fibers in a laboratory dish.

Scientists are trying to identify the key targets for such manipulation. Netrins, first identified in worms and chick embryos but later found to be present in fruit flies and in humans, are among the potential candidates. Timothy Kennedy, former postdoctoral fellow from Tessier-Lavigne's San Francisco netrin team, who now runs his own lab at McGill University's Montreal Neurological Institute, has shown with his colleagues that netrins are present in large amounts in the adult spinal cord of rats, and that their amounts change after injury. During development, netrins have been shown to attract the growth of some axons and repel the growth of others, but Kennedy believes that their role in the adult nervous system may be to block nerve fiber growth. By cranking up the attractive properties of netrins, he suggests, it may be possible to encourage spinal cord axons to regenerate in adults….

(Excerpted from *In Search of the Lost Cord: Solving the Mystery of Spinal Cord Regeneration* by Luba Vikhanski. Dana Press/Joseph Henry Press, Washington, DC, 2001.)

Allostatic Load Scenario 4: Too Little Is as Bad as Too Much

By Bruce McEwen, Ph.D.

Stress is just one of among a host of factors that contribute to what we call "allostatic load," says Bruce McEwen, Ph.D., professor of neuroendocrinology at Rockefeller University. Dr. McEwen defines allostasis as "the ability of the body to achieve stability through its own regulatory changes." Allostasis is affected by diet, sleep, exercise, whether or not we drink or smoke, and even our socioeconomic status. "If our allostatic load is high, our bodies work overtime to maintain balance."

The idea of checks and balances in the stress response brings us to the final way in which the protective systems of allostatis can trigger the damage of allostatic load: when the stress response is insufficient, resulting in underproduction of the stress hormones, particularly *cortisol*, wear and tear can also result.…How can this be? Surely if there are no stress hormones, there must be no stress and consequently no stress-related illness. But like most of human physiology, it isn't quite that simple. Cortisol acts somewhat like a thermostat; in fact, it clamps down on its own production. It slows the production of the two hormones that touch off the HPA *[hypothalamus-pituitary-adrenal]* axis: corticotropin-releasing factor in the hypothalamus and adrenocorticotropic hormone in the pituitary. Cortisol also reins in the immune system and reduces inflammation and

swelling from tissue damage.

When one of the participants in a checks-and-balances arrangement isn't doing its job, the others may go overboard in doing theirs. In some people, allostatic load takes the form of a sluggish response by the adrenals and a subsequent lack of sufficient cortisol. The most immediate result is that the immune system, without cortisol's steadying hand, runs wild and reacts to things that do not really pose a threat to the body. Allergies are one example of this process. In most people the immune system does not put things like dust and cat dander on a par with pathogenic (disease-causing) bacteria. But in people prone to allergies, the immune system goes on red alert in the presence of such usually innocuous substances, throwing everything it's got at the irritants: uncontrollable sneezing to expel the invaders, mucous secretion to entrap them, swelling caused by the influx of white blood cells to the infected area, pain, redness, and general misery. All of these symptoms are reduced by the action of cortisol….

A feeble HPA response can often manifest itself in conditions not always immediately associated with the immune system. Fibromyalgia, for example, is a condition of chronic pain that most doctors consider psychosomatic (and some consider imaginary, though the patients certainly don't). The connection with the immune system and cortisol becomes clear when we consider that pain is a part of the inflammatory response; pain warns us that there's a problem and encourages us to leave the affected area alone until the problem is resolved. But in many chronic pain states, as with other inflammatory disorders, there is no apparent threat. Rather, the system is responding in a maladaptive way, which the available supply of cortisol is too low to prevent.

(Excerpted from *The End of Stress as We Know It*, by Bruce McEwen, Ph.D., with Elizabeth Lasley. Dana Press/Joseph Henry Press, Washington, DC, 2002.)

Research and Future Treatments for Alzheimer's Disease

By Guy McKhann, M.D., and Marilyn Albert, Ph.D.

Alzheimer's disease expert Dennis J. Selkoe, M.D., has written,"In the past few years, we have not only identified the genes that cause Alzheimer's, we are also beginning to understand how they work. In their mutated forms, every one of the Alzheimer's genes that scientists have discovered work by subtly different mechanisms to increase the amount of amyloid beta-protein in the brain." Two of the world's leading neurological experts, Marilyn Albert, Ph.D., of Harvard University and Guy McKhann, M.D., of Johns Hopkins University, take a detailed look at the promising outlook for treating one of our most notorious medical disorders.

It is imperative that ways to prevent and treat this disease be found. If prevention efforts could delay the average onset of the disease by only five years, it would have enormous impact. If the sharp increase in numbers of cases could be delayed until people reached age 90, many people would die of other causes before they ever got Alzheimer's disease.

Every pharmaceutical company worth its salt is therefore working on how to slow the progression or delay the first symptoms of Alzheimer's disease. In general they are working in several basic areas. The first approach is to prevent the accumulation of the abnormal form of amyloid protein. These fragments, called AB or A-beta,

vary in length, but one particular length is especially toxic to nerve cells. Researchers are concentrating on either preventing this toxic fragment from accumulating or removing it from the brain. Genetically engineered "Alzheimer mice," who show the same toxic buildup in their brains as human patients do, are invaluable to this research…

The second approach involves getting the body to use its immune system to remove the amyloid from the brain. A person is injected, that is immunized, with the offending fragment of amyloid, and then makes antibodies to this fragment. The person's own antibodies attack and remove the amyloid. In the Alzheimer mice, the antibodies not only removed the amyloid plaques, they kept them from forming.

A third approach is to try to keep alive the nerve cells in which amyloid is already accumulating. Two agents are currently being studied: vitamin E and estrogen. Substances called trophic factors also may help sustain these endangered cells. The brain normally deploys trophic factors in very small quantities to maintain the health of nerve cells. With the techniques of *molecular biology*, researchers can now make large amounts of these substances and try them out as drugs for treatment. The problem is getting trophic factors into the areas of the brain affected by the disease. One approach is to use genetic engineering—to put the gene that directs the production of the trophic factor into a bacterium that's been rendered harmless, then put the bacterium into the brain to deliver the gene to the brain cells. This sounds like science fiction but actually works in experimental animals. Preliminary trials of this gene therapy are under way in people.

The final strategy is to decrease the inflammation in the brain that occurs in response to the abnormal amyloid's attack on nerve cells. This approach takes its cue from recent advances in treating arthritis' inflammation in the joints with anti-inflammatory medications like aspirin, Motrin, or the recently FDA-approved COX-2 inhibitors. Studies are ongoing to see if these anti-inflammatory drugs have a role in treating Alzheimer's disease.

(Excerpted from *Keep Your Brain Young: The Complete Guide to Physical and Emotional Health and Longevity,* by Guy M. McKhann, M.D., and Marilyn S. Albert, Ph.D. Dana Press and John Wiley & Sons, Inc., New York, 2002.)

How Your Brain Forms Memories

By Guy McKhann, M.D., and Marilyn Albert, Ph.D.

How can physical matter, atoms and molecules, amassed in however intricate an arrangement in the three pounds of tissue that make up the human brain, retain for short periods, or for decades, the color and taste and smell of a ripe apple or the thought that the universe is curved? For centuries, this query has remained one of the most profound questions for science. The first Nobel Prize in Physiology or Medicine of the 21st century went to three neuroscientists, Eric R. Kandel, M.D.; Paul Greengard, Ph.D.; and Arvid Carlsson, M.D., in part for their fundamental work on memory formation. Drs. McKhann and Albert provide a closer look at memory here.

Can you drive your brain to be better than it is genetically programmed to be? Little evidence supports the possibility. However, it is clear that you can attain optimal functioning and maintain it by stimulating usage. Each nerve cell communicates with thousands of others. But when you form new memories, you strengthen a particular series of connections, the way a heavily trodden pathway in the woods

becomes more visible and easier to follow. Among nerve cells, two different things are happening. First, changes take place in the physical connections between nerve cells to make one pathway easier to use than others. These changes occur at the very end of the pathway, at the synapses, where nerve cells connect with one another. Second, some of the chemicals released at the synapses, the neurotransmitters, are specialized for memory. One of these neurotransmitters is acetylcholine. Many of the drugs being developed to attempt to modify memory involve increasing the effectiveness of this neurotransmitter.

Mentally and physically stimulating activities promote this constant "rewiring" of the brain, strengthening its pathways and stimulating the production of substances required for the growth and maintenance of nerve cells. In some instances, brain cells will make new connections. More commonly the balance between existing connections is altered, by strengthening some and weakening others.

Years ago scientists thought of the brain as being "hard-wired," meaning that during development, nerve cells would assume their proper positions and make myriad interconnections. Once in place and interconnected, it was thought that nerve cells did not change. This notion is clearly wrong. Research in the last few years has shown that new nerve cells may even develop in areas of the adult brain, including the hippocampus, the area that is important for making new memories. No one knows what regulates this replenishment of nerve cells, but recent evidence suggests that one factor may be physical and mental activity.

Genetics of Memory

Genetics also plays a role in how well memory functions. The behavior of animals is a good example. Certain breeds of dog, such as Labradors, are supposed to be gentle but perhaps a little dumb, meaning they do not learn new information easily. German Shepherds, on the other hand, generally learn quickly but are not particularly gentle. The same phenomenon is well known in laboratory animals. Some strains of mice can be taught to find food in a maze much more easily than others. Now that we know that genes can be either more or less active, it is possible to breed mice that are selectively smart or dumb. This line of research is one of the approaches that may eventually lead to drugs that will enhance memory for people.

But what about us humans?...Some people may simply not have genetic vulnerabilities that lead to diseases like Alzheimer's disease. On the other hand, they may have other genes working that protect their brains from the decline in the ability of nerve cells to function normally. Research to explore these alternatives is already under way in animals, such as mice, in which the genetic properties can be manipulated.

(Excerpted from *Keep Your Brain Young: The Complete Guide to Physical and Emotional Health and Longevity,* by Guy M. McKhann, M.D., and Marilyn S. Albert, Ph.D. Dana Press and John Wiley & Sons, Inc., New York, 2002.)

The Power of Emotions

By Joseph E. LeDoux, Ph.D.

New York University neuroscientist Joseph LeDoux, Ph.D., and other neuroscientists have begun to examine the way the brain shapes our experience—and our memories—to generate the varied repertoire of human emotions. Specifically, as Dr. LeDoux explains, he chose to begin his inquiry by examining an emotion that is common to all living creatures: fear.

Brain Pathways in Fear Learning

Years of research by many workers have given us extensive knowledge of the neural pathways involved in processing acoustic information, which is an excellent starting point for examining the neurological foundations of fear. The natural flow of auditory information—the way you hear music, speech, or anything else—is that the sound comes into the ear, enters the brain, goes up to a region called the auditory midbrain, then to the auditory thalamus, and ultimately to the auditory cortex. Thus, in the auditory pathway, as in other sensory systems, the cortex is the highest level of processing.

So the first question we asked when we began these studies of the fear system was: Does the sound have to go all the way to the auditory cortex in order for the rat to learn that the sound paired with the shock is dangerous? When we made *lesions* in the auditory cortex, we found that the animal could still make the association between the sound and the shock, and would still react with fear behavior to the sound alone. Since information from all our senses is processed in the cortex—which ultimately allows us to become conscious of seeing the predator or hearing the sound—the fact that the cortex didn't seem to be necessary to fear conditioning was both intriguing and mystifying. We wanted to understand how something as important as the emotion of fear could be mediated by the brain if it wasn't going into the cortex, where all the higher processes occur. So we next made lesions in the auditory thalamus and then in the auditory midbrain. The midbrain supplies the major sensory input to the thalamus, which in turn supplies the major sensory input to the cortex. What we found was that lesions in either of these subcortical areas completely eliminated the rat's susceptibility to fear conditioning. If the lesions were made in an unconditioned rat, the animal could not learn to make the association between sound and shock, and if the lesions were made on a rat that had already been conditioned to fear the sound, it would no longer react to the sound.

But if the stimulus didn't have to reach the cortex, where was it going from the thalamus? Some other area or areas of the brain must receive information from the thalamus and establish memories about experiences that stimulate a fear response. To find out, we made a tracer injection in the auditory thalamus (the part of the thalamus that processes sounds) and found that some cells in this structure projected axons into the amygdala. This is key, because the amygdala has for many years been known to be important in emotional responses. So it appeared that information went to the amygdala from the thalamus without going to the neocortex.

We then did experiments with rats that had amygdala lesions, measuring freezing and blood-pressure responses elicited by the sound after conditioning. We found that the amygdala lesion prevented conditioning from taking place. In fact, the responses are very similar to those of unconditioned animals that hear the sound for the first time, without getting the shock.

So the amygdala is critical to this pathway. It receives information about the outside world directly from the thalamus, and immediately sets in motion a variety of bodily responses. We call this thalamo-amygdala pathway the low road because it's not taking advantage of all of the higher-level information processing that occurs in the neocortex, which also communicates with the amygdala.…

(Excerpted from *States of Mind: New Discoveries About How Our Brains Make Us Who We Are,* Roberta Conlan, editor; Dana Press and John Wiley & Sons, Inc., New York, 1999.)

Use It or Lose It

Take Active Measures Now to Combat Disuse Atrophy

By David Mahoney and Richard M. Restak, M.D.

Authors David Mahoney, businessman and philanthropist, and neurologist Richard Restak, M.D., point out that the 20th century's increase in life span (30 years longer average life expectancy) and spectacular gains in neuroscience and medicine will make the 100-year life span commonplace in another generation or two. This advance will happen only if we take proactive measures in such matters as handling stress properly and seeking out lifelong mental activity.

Certain cells in areas of the brain beneath the cortex (called subcortical nuclei) are sometimes irreverently dubbed the "juice machines." They give us enthusiasm and general "get up and go" energy. When Samuel Johnson said, "The question is not so much 'Is it worth seeing?' but rather 'Is it worth going to see?'" he was unknowingly referring to the subcortical nuclei, which generate enthusiasm and energy.

With aging, almost everyone undergoes some loss of cells in the subcortical nuclei. It's what we notice when we joke that our get-up-and-go "got up and went." Since this is natural, our task is to recognize that we are "mellowing" rather than losing any of our abilities. Our attention to those abilities, as intact as ever, helps us maintain mental vigor.

Every talent and special skill that you've developed over your lifetime is represented in your brain by a complex network of neurons. And each time you engage in any activity that involves your talents and skills, the neuronal linkages in that network are enhanced. Think of the brain cells as shaped like trees composed of long branches subdividing into smaller and smaller branches. As the result of brain growth and the person's experience in the world, tremendous overlap and connectivity develop among the tree branches. Neuroscientists, struck with the tree analogy, refer to this process as "arborization."

Eventually nerve cells form active circuits based on these branchlike linkages. The more often the circuits are activated, the easier it is to activate them the next time. Subjectively, you experience this as the formation of a habit. With time the activity gets easier to do; the more the skill or talent is practiced, the better you get at it. But if you neglect your talents and skills, they begin to wane, and over time it becomes harder and harder to perform at your best. If enough time passes you will experience great difficulty returning to your former level of excellence. That's because the neuronal circuits have fallen into disuse: greater degrees of effort are required to activate them. But no matter how long you've neglected a skill, you'll never find yourself in the same situation as the person who never learned the skill in the first place.

Neuronal circuits, once established, never entirely disappear. It's the ease of facilitating them that varies. This law of facilitation and disuse atrophy applies to every activity, whether physical or mental. Neglect your tennis or your golf for enough time and your skills in these very different activities will deteriorate.

Remember that the brain is an ever-changing organ. If one part gets rusty and suffers atrophy from disuse, its functions are taken over by other areas that are used more. When we stop challenging ourselves and expanding, or at least maintaining our skills, the brain cells involved in the neuronal networks drop out and link into other networks. Eventually the skill has almost entirely disappeared. We say almost because some neurons, though a much smaller number, always remain in the network.

(Excerpted from *The Longevity Strategy: How to Live to 100 Using the Brain-Body Connection,* by David Mahoney and Richard Restak, M.D. John Wiley & Sons, Inc., and Dana Press, New York, 1998.)

The member scientists of the Dana Alliance for Brain Initiatives and the European Dana Alliance for the Brain announced in 2001 their joint vision and goals statement. That document, reprinted here in its entirety, outlines the potential for new treatments and therapies and speaks to the importance of continued basic research and the need to keep the public informed of progress in neuroscience.

Imagine a World

In which Alzheimer's, Parkinson's, and Lou Gehrig's (ALS) diseases and retinitis pigmentosa and other causes of blindness are commonly detected in their early stages, and are swiftly treated by medications that stop deterioration before significant damage occurs.

In which spinal cord injury doesn't mean a lifetime of paralysis because the nervous system can be programmed to re-wire neural circuits and re-establish muscle movement.

In which drug addiction and alcoholism no longer hold people's lives hostage because easily available treatments can interrupt the changes in neural pathways that cause withdrawal from, and drive the craving for, addictive substances.

In which the genetic pathways and environmental triggers that predispose people to mental illness are understood so that accurate diagnostic tests and targeted therapies, including medications, counseling, and preventive interventions, are widely available and fully employed.

In which new knowledge about brain development is used to enhance the benefits of the crucial early learning years and combat diseases associated with aging.

In which people's daily lives are not compromised by attacks of depression or anxiety because better medications are developed to treat these conditions.

Although such a vision may seem unrealistic and utopian, we are at an extraordinarily exciting time in the history of neuroscience. The advances in research during the past decade have taken us further than we had imagined. We have expanded our understanding of the basic mechanisms of how the brain works, and are at a point where we can harness the healing potential of that knowledge.

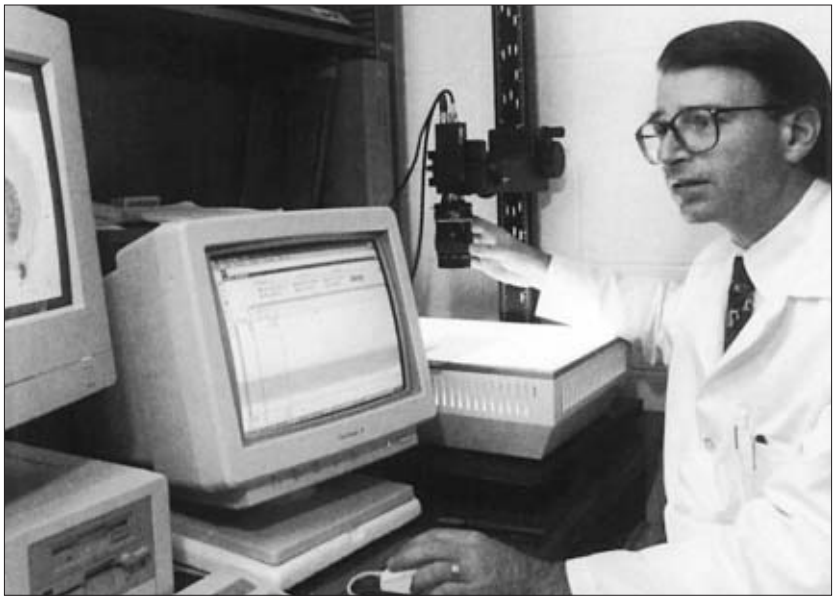
We have already begun to devise strategies, new technologies, and treatments to combat a range of neurological diseases and disorders. By setting therapeutic goals, and applying what we know, we will develop effective treatments—and, in some instances, cures.

For all that has been learned in neuroscience recently, we are learning how much we do not know. That creates the urgency to continue basic research that looks at the broader questions of how living things work. This will help to formulate the complex questions that lead to scientific discovery.

The coordinated work of thousands of basic and clinical scientists in multiple disciplines, ranging from molecular structure and drug design to genomics, brain imaging, cognitive science, and clinical investigation, has given us a pool of information that we can use to build into therapeutic applications for all neurological diseases and disorders. As scientists, we will continue to move forward not just as individuals exploring our particular areas of interest, but also in concert with colleagues in all areas of science, mining opportunities to collaborate across disciplines.

Public confidence in science is essential if we are to be successful in our mission. To this end we recognize that dialogue between researchers and the public will be essential in considering the ethical and social consequences of advances in brain research.

The Dana Alliance for Brain Initiatives and the European Dana Alliance for the Brain represent a community of neuroscientists willing to commit to ambitious goals, as seen in 1992 in Cold Spring Harbor, New York, where an American research agenda was set forth and again in 1997 when the newly formed European group followed suit with its own goals and objectives. Both groups now are moving the goalposts to capitalize on the gains that have been made. We are setting new goals to guide what can be achieved in the near term and project even further into the future. By allowing ourselves to imagine what benefit this new era in neuroscience is likely to bring, we can speed progress toward achieving our goals.



A scientist analyzes a potentially useful drug via computer imaging.

The Goals

Combat the devastating impact of Alzheimer's disease.

In Alzheimer's disease, a small piece of the protein amyloid accumulates and is toxic to nerve cells. The mechanism of this accumulation has been worked out biochemically and in genetic studies in animals. Using these *animal models,* new therapeutic drugs and a potentially powerful vaccine are being developed to prevent the accumulation of this toxic material or enhance its removal. These new therapies, which will be tried in humans in the near future, offer realistic hope that this disease process can be effectively treated.

Discover how best to treat Parkinson's disease.

Drugs that act on *dopamine* pathways in the brain have had significant success in treating the motor abnormalities of Parkinson's disease. Unfortunately, this therapeutic benefit wears off for many patients after 5-10 years. New drugs are being developed to prolong the action of dopamine-based treatments and to slow the selective loss of nerve cells that causes this disease. For those in whom drug therapies fail, surgical approaches, such as deep brain stimulation, are likely to be of benefit. Newer forms of brain imaging have made it possible to determine if these treatments are rescuing nerve cells and restoring their circuits back toward normal.

Decrease the incidence of stroke and improve post-stroke therapies.

Heart disease and stroke can be strikingly reduced when people stop smoking, keep their cholesterol levels low and maintain normal weight by diet and exercise, and when diabetes is detected and treated. For those with strokes, rapid evaluation and treatment can lead to dramatic improvement and less disability. New treatments will be developed to further reduce the acute impact of stroke on normal brain cells. New rehabilitation techniques, based on understanding how the brain adjusts itself following injury, will result in further improvement.

Develop more successful treatments for mood disorders such as depression, schizophrenia, obsessive compulsive disorder, and bipolar disorder.

Although the genes for these diseases have eluded researchers over the past decade, the sequencing of the human genome will reveal several of the genes for these conditions. New imaging techniques, along with new knowledge about the actions of these genes in the brain, will make it possible to see how certain brain circuits go awry in these disorders of mood and thought. This will provide the basis for better diagnosis of patients, more effective use of today's medications, and the development of entirely new agents for treatment.

Treatments and cures for some of our most devastating, chronic disorders will be found in brain research and public support for it.

Uncover genetic and neurobiological causes of epilepsy and advance its treatment.

Understanding the genetic roots of epilepsy and the neural mechanisms that cause seizures will provide opportunities for preventive diagnosis and targeted therapies. Advances in electronic and surgical therapies promise to provide valuable treatment options.

Discover new and effective ways to prevent and treat multiple sclerosis.

For the first time, we have drugs that can modify the course of this disease. New drugs, aimed at altering the body's immune responses, will continue to decrease the number and severity of attacks of multiple sclerosis. New approaches will be taken to stop the longer-term progression caused by the breakdown of nerve fibers.

Develop better treatments for brain tumors.

Many types of brain tumors, especially those that are malignant or have spread from cancer outside the brain, are difficult to treat. Imaging techniques, focused-radiation treatments, different forms of delivery of drugs to the tumor, and the identification of genetic markers that will assist diagnosis should provide the basis for development of innovative therapies.

Improve recovery from traumatic brain and spinal cord injuries.

Treatments are being evaluated that decrease the amount of injured tissue immediately after an injury. Other agents are aimed at promoting the rewiring of nerve fibers. Techniques that encourage cellular regeneration in the brain to replace dead and damaged neurons will advance from animal models to human clinical trials. Electronic prostheses are being developed that use microchip technology to control neural circuits and return movement to paralyzed limbs.

The Strategy

Create new approaches for pain management.

Pain, as a medical condition, need no longer be woefully undertreated. Research into the causation of pain and the neural mechanisms that drive it will give neuroscientists the tools they need to develop more effective and more highly targeted therapies for pain relief.

Treat addiction at its origins in the brain.

Researchers have identified the neural circuits involved in every known drug of abuse and have cloned major receptors for these drugs. Advances in brain imaging, by identifying the neurobiological mechanisms that turn a normal brain into an addicted brain, will enable us to develop therapies that can either reverse or compensate for these changes.

Understand the brain mechanisms underlying the response to stress, anxiety, and depression.

Good mental health is a prerequisite for a good quality of life. Stress, anxiety, and depression not only damage peoples' lives, they also can have a devastating impact on society. As we come to understand the body's response to stress and the brain circuits implicated in anxiety and depression, we will be able to develop more effective ways to prevent them and better treatments to lessen their impact.

Take advantage of the findings of genomic research.

The complete sequence of all the genes that make up the human genome will soon be available. This means that we will be able, within the next 10 to 15 years, to determine which genes are active in each region of the brain under different functional states, and at every stage in life—from early embryonic life, through infancy, adolescence, and throughout adulthood. It will be possible to identify which genes are altered so that their protein products are either missing or functioning abnormally in a variety of neurological and psychiatric disorders. Already this approach has enabled scientists to establish the genetic basis of such disorders as Huntington's disease, the spinocerebellar ataxias, muscular dystrophy, and fragile-X mental retardation.

The whole process of gene discovery and its use in clinical diagnosis promises to transform neurology and *psychiatry* and represents one of the greatest challenges to neuroscience. Fortunately the availability of microarrays or "gene chips" should greatly accelerate this endeavor and provide a powerful new tool both for diagnosis and for the design of new therapies.

Apply what we know about how the brain develops.

The brain passes through specific stages of development from conception until death and through different stages and areas of vulnerability and growth that can either be enhanced or impaired. To improve treatment for developmental disorders such as autism, attention deficit disorder, and learning disabilities, neuroscience will build a more detailed picture of brain development. Because the brain also has unique problems asso-

ciated with other stages of development such as adolescence and aging, understanding how the brain changes during these periods will enable us to develop innovative treatments.

Harness the immense potential of the plasticity of the brain.

By harnessing the power of neuroplasticity—the ability of the brain to remodel and adjust itself—neuroscientists will advance treatments for degenerative neurological diseases and offer ways to improve brain function in both healthy and disease states. In the next ten years, cell replacement therapies and the promotion of new brain cell formation will lead to new treatments for stroke, spinal cord injury, and Parkinson's disease.

Expand our understanding of what makes us uniquely human.

How does the brain work? Neuroscientists are at the point where they can ask—and begin to answer—the big questions. What are the mechanisms and underlying neural circuits that allow us to form memories, pay attention, feel and express our emotions, make decisions, use language, and foster creativity? Efforts to develop a "unified field theory" of the brain will offer great opportunities to maximize human potential.

Major developments in cellular and molecular biology are contributing significantly to our understanding of basic brain function.

The Tools

Cell replacement.

Adult nerve cells cannot replicate themselves to replace cells lost due to disease or injury. Technologies that use the ability of neural stem cells (the progenitors of neurons) to differentiate into new neurons have the potential to revolutionize the treatment of neurological disorders. Transplants of neural stem cells, currently being done on animal models, will rapidly reach human clinical trial status. How to control the development of these cells, direct them to the right place, and cause them to make the appropriate connections are all active areas of research.

Neural repair mechanisms.

By using the nervous system's own repair mechanisms—in some cases, regenerating new neurons and in others restoring the wiring—the brain has the potential to "fix" itself. The ability to enhance these processes provides hope for recovery after spinal cord injury or head injuries.

Technologies that may arrest or prevent neurodegeneration.

Many conditions, such as Parkinson's disease, Alzheimer's disease, Huntington's disease, and ALS, are the result of degeneration in specific populations of nerve cells in particular regions of the brain. Our present treatments, which modify the symptoms in a disease like Parkinson's disease, do not alter this progressive loss of nerve cells. Techniques that draw on our knowledge of the mechanisms of cell death are likely to offer methods to prevent neurodegeneration and, in this way, stop the progression of these diseases.

Technologies that modify genetic expression in the brain.

It is possible to either enhance or block the action of specific genes in the brains of experimental animals. Mutated human genes that cause neurological diseases such as Huntington's and ALS are being used in animal models to assist in the development of new therapies to prevent neurodegeneration. Such techniques have also provided valuable information about normal processes such as development of the brain, learning, and the formation of new memories. These technologies provide an approach to the study of normal and abnormal brain processes more powerful than there has ever been available before, and in time, they may be used clinically in the treatment of many brain disorders.

Advanced imaging techniques.

There have been remarkable advances in imaging both the structure and the function of the brain. By developing techniques that image brain functions as quickly and accurately as the brain does, we can achieve "real-time" imaging of brain functions. These technologies will allow neuroscientists to see exactly which parts of the brain are involved as we think, learn, and experience emotions.

Electronic aids to replace non-functional brain pathways.

In time it may be possible to bypass injured pathways in the brain. Using multi-electrode array implants and micro-computer devices—which monitor activity in the brain and translate it into signals to the spinal cord, motor nerves, or directly to muscles—we expect to be able to offer the injured hope for functional recovery.

Novel methods of drug discovery.

Advances in structural biology, genomics, and computational chemistry are enabling scientists to generate unprecedented numbers of new drugs, many of which promise to be of considerable value in clinical practice. The development of new, rapid screening procedures, using "gene chips" and other high through-put technologies, will reduce the time between the discovery of a new drug and its clinical evaluation, in some cases, from years to just a few months.

Our Commitment, Bench to Bedside

Today, neuroscience research benefits from an unprecedented breadth of opportunity. We have expanded our understanding of brain function, disease onset, and disease progression. A sophisticated arsenal of tools and techniques now enables us to apply our knowledge and to accelerate progress in brain research.

As scientists, we are committed to continue making progress "at the bench." To attack major brain disorders, such as Alzheimer's, stroke, or Parkinson's, will require continued basic research from which clinicians can move toward development of new treatments and therapies. We have a responsibility to continue such research and to enlist its support by the public.

We also have the obligation to explain those areas of scientific research that soon may have direct application to human beings. To progress beyond laboratory research, we need to take the next clinical steps in partnership with the public, translating science into real and genuine benefits "at the bedside."

As our tools and techniques become more sophisticated, they may be considered threatening in their perceived potential for misuse. It is important to recognize the understandable fears that brain research may allow scientists to alter the most important aspects of our brains and behavior, changing the very things that make us uniquely human. Public confidence in the integrity of scientists, in the safety of clinical trials—the cornerstone of applied research—and in the

assurance of patient confidentiality must be continually maintained.

Putting research into a real-life context is always a challenge. People not only want to know how and why research is done, they also want to know why it matters to them. Allaying the public's concerns that the findings of brain science could be used in ways that might be harmful or ethically questionable is particularly important. Meeting both of these challenges is essential if those affected by neurological or psychiatric disorders are to reap fully the benefits of brain research.

Our mission as neuroscientists has to go beyond brain research. We accept our responsibility to explain in plain language where our science, and its new tools and techniques, are likely to take us. We, the members of the Dana Alliance and the European Dana Alliance, willingly embrace this mission as we embark on a new decade of hope, hard work, and partnership with the public. ■

Suggested Activities

Classroom Video: *Exploring Your Brain: "Topics in Brain Science"*

Section 1: Looking Inside the Brain

Background:

For the last century, scientists have been able to use the x-ray machine to examine the bony parts of the living human body, but they were not able to x-ray the living human brain. Since the 1970s, however, new computer technology has been developed that goes far beyond the capabilities of the x-ray and allows scientists to examine a living individual's functioning brain. Because of this new technology, scientists have learned a great deal about how we think, feel, and perceive.

KEY WORDS:

CAT (computer-aided tomography), PET (positron emission tomography), MRI (magnetic resonance imaging), *fMRI (functional magnetic resonance imaging),* cortex, neural

SUGGESTED RECALL QUESTIONS:

1. **Where is the visual cortex of the brain?**
   The visual cortex is located in the back of the brain.
2. **Where is the part of the visual cortex specific to recognizing faces? What size is it?**
   It is located on the left, not far from the ear, and is about the size of a pea.
3. **How does functional MRI, the technique used by Dr. Nancy Kanwisher in the video to image the brain, work?**
   It uses an intense magnetic field that reveals which parts of the brain are getting more blood or less. More blood flows to brain areas that are working harder. Activity is mapped by a continuous series of high-speed digital images. Taken together, these images provide an idea of what happens over time in a particular region of the brain.

4. **Why is there an area of the brain dedicated to reading faces?**
   Humans are social primates. It is important for us to determine if the people we meet are friendly or not, interested or detached, confident or afraid. It is of such importance that an entire area of the brain is dedicated to this one task.

EXAMPLES OF DISCUSSION QUESTIONS:

1. **Does the new imaging technology allow scientists to "read" our minds?**
   New technology can, for example, identify the separate areas in the brain where facial imaging takes place and where site imaging takes place. As shown in this segment, by looking at an MRI image of the brain, scientists can tell whether the person is thinking of a place or a person; they cannot determine what place or what person.
2. **What is the difference between the brain and the mind?**
   The brain is a physical organ of the body in the same way the heart is an organ. Scientists tend to study the mind as a set of activities, e.g., thinking, feeling, and sensing, that emanate in the brain. The brain is a physical entity that is measurable; the mind is a concept that describes some of the things the brain does.

LEARN MORE ABOUT IT:

See "Brain Imaging Timeline," on the back cover of this book.

Recommended Web sites:

The Whole Brain Atlas, www.med.harvard.edu/AANLIB/home.html

National Institute on Drug Abuse, www.drugabuse.gov,
NIDA Notes (online publication)

Classroom Video: *Exploring Your Brain: "Topics in Brain Science"*

Section 2: Sports and the Brain

Background:

Learning any motor skill involves a complex relationship between the body and the brain. As the body learns a particular movement through constant repetition and practice, the brain is also learning. At each new skill level, the brain stores what it has learned in a separate area while it continues to learn. Once a skill is mastered, an athlete finds ways to trigger the brain to remember what it has learned. Some athletes learn to focus solely on the activity so that the brain is not in any way distracted.

KEY WORDS:

Conditioning (as in training), motor skills, coordination

SUGGESTED RECALL QUESTIONS:

1. **Why is it difficult to hit a baseball the first time you try?**
   The first time a person tries to hit a baseball, neither the brain nor the corresponding muscles have learned how to respond to the oncoming ball and coordinate the swing of the bat. Both have to learn this new skill.
2. **How does the brain learn motor skills?**
   In order to perform a motor skill, the brain has to coordinate many different muscles at the same time. This makes learning a skill somewhat complex. Nevertheless, the brain has an efficient way of consolidating new information, saving what it needs and discarding what it does not. Certain parts of the brain are active during motor learning and become inactive once the skill is mastered. New procedural memories are formed in areas of the brain dedicated to short-term memory. But they don't stay there. Instead, these memories are stored elsewhere in the brain for future retrieval.
3. **According to Dr. David Van Essen, what must an athlete do in order to perform successfully?**
   An athlete must analyze not just one but several objects moving simultaneously in many different directions. The visual system controls the flow of that information into the specialized subsystems of the brain that make sense of the shapes and movement trajectories of those objects.

EXAMPLES OF DISCUSSION QUESTIONS:

1. **Is there such a thing as a born athlete?**
   No person is born with the ability to hit a home run. All athletic skills are learned by the brain and the body. Individuals may be born with the potential to develop bigger and stronger muscles, but the ability to coordinate the muscles to perform well is always learned.
2. **What are the most important skills an athlete must develop?**
   Perfect coordination between the brain and the body and the ability to "trigger" the brain to remember what it has learned. Athletes often refer to this ability as being "grooved" or "in the zone." To hit a home run, both the body and the brain have to be well trained and perfectly coordinated. If a person's muscles are tired or the brain is distracted, the person is likely to pop up, ground out, or miss the ball completely.

LEARN MORE ABOUT IT:

Read "Behind the Scenes in the Adolescent Brain," p. 26.

Recommended Web sites:

National Institute of Child Health and Human Development,
www.nichd.nih.gov
National Institute of Mental Health,
www.nimh.nih.gov

Classroom Video: *Exploring Your Brain: "Topics in Brain Science"*

Section 3: The Broken Brain

Background:

Sports are a major cause of brain injuries to children and young adults. Studies show that 7 to 10 percent of all football players will sustain at least one concussion while playing. Pat LaFontaine, a star American-born professional hockey player, had to retire from the National Hockey League after 14 years and six concussions. Multiple concussions can result in memory loss, difficulty with thinking and concentrating, and even more serious problems. Doctors and brain researchers are cautioning all athletes about the dangers of brain injuries.

KEY WORDS:

Concussion, neurologist, trauma, symptomatic, migraine headaches, neuropsychological

SUGGESTED RECALL QUESTIONS:

1. **What is a concussion?**
   A concussion is much more than being "knocked unconscious." Neurologists define a concussion as any change in mental status resulting from trauma. Such changes can include headaches, nausea, sleeplessness, moodiness, and an inability to focus one's attention.
2. **How did Pat LaFontaine's brain injuries affect his family relationships?**
   He became depressed, had a personality change, and even had difficulty reading stories to his children.

EXAMPLES OF DISCUSSION QUESTIONS:

1. **Why might an athlete, whether a professional or a student-athlete, not report problems following a head injury?**
   According to Pat LaFontaine and Dr. James Kelly, athletes are taught to play with injuries and sickness and not to complain. The mind-set among athletes seems to be that you must play and overcome adversity in order to get back in the game.
2. **What can be done to help reduce the number of serious sports-related injuries?**
   Coaches, trainers, and athletes can learn more about the brain and brain injuries. Standardized neurological tests need to be configured to sports situations and used by officials of the various sports. Better equipment can be developed. Brain research to determine how the brain recovers from an injury and what can be done to promote healing must continue.
3. **If a young person suffers a concussion playing sports, should that person quit playing that sport?**
   The person does not have to quit the sport forever but should not risk further damage until the injury is healed. The brain can recover from concussions if it has time to heal. Multiple concussions, especially in a short period of time, can increase the risk of serious brain injury.

LEARN MORE ABOUT IT:

Recommended Web sites:

Brain Injury Association, www.biausa.org
Brain Injury Services of America, www.braininjurysvcs.org
Think First Foundation, www.thinkfirst.org

Classroom Video: *Exploring Your Brain: "Topics in Brain Science"*

Section 4: Stress and the Brain

Background:

If an animal senses that it is in a stressful situation, its brain tells its body to prepare for a fight or take flight. The body responds by preparing extra hormones to create more energy and by increasing the rate the heart pumps blood to the muscles. For most animals, this stress reaction lasts for just a short time and it saves lives. As a body is preparing for fight or flight, however, all other systems, such as physical growth and warding off diseases, are placed on hold. This means that people for whom stress has become a way of life are endangering every other system in their bodies. Researchers have learned by studying primates whose systems are similar to human beings that those who learn to have control over their lives and are able to reduce or avoid stress live longer and healthier lives.

KEY WORDS:

Fight or flight, adrenaline, hypothalamus, *pituitary gland, adrenal gland,* cortisol, lymphocytes, primate

SUGGESTED RECALL QUESTIONS:

1. **Why are zebras better equipped to deal with stress than humans? (Or, put another way, why don't zebras get ulcers?)**
   It is not so much that zebras are better equipped for stress than humans, but that their environment is better suited for their response to stress. According to Dr. Robert Sapolsky, humans have constructed a network of social stressors. Since we are obliged to live in this framework, stress builds up. Over time, chronic psychological stress can lead to cardiovascular damage and other serious health problems.

2. **How do the brain and the body react to stress?**
   Stress, such as the threat of attack, forces various changes in the body. First, adrenaline causes an increase in heart rate and blood pressure so that blood can be sent to muscles faster. Second, the brain's hypothalamus signals the pituitary gland to stimulate the adrenal gland (specifically the adrenal cortex) to produce cortisol. This stress hormone, a longer-acting steroid, helps the body to mobilize energy. At the same time, long-term projects like digestion are put

on hold. However, prolonged exposure to cortisol can damage the body. Chronic high blood pressure can cause vascular damage and the long-term shut down of digestion can lead to ulcers.

EXAMPLES OF DISCUSSION QUESTIONS:

1. **Why do some people experience more stress than others?**
   Individuals who feel they have control over their lives appear to experience less stress. It also depends on personality and temperament. Aggressive, competitive types are more likely to define a situation as stressful than a passive, accommodating personality. A universal stress producer seems to be social isolation.
2. **What are the major causes of stress among young people in America today?**
   Most young people today do not have to confront life-threatening situations very often. The stress they experience is usually psychological—for example, fear of failure, fear of rejection, fear of abuse (physical or verbal), and fear of the unknown.
3. **What can people do to eliminate or reduce stress in their daily lives?**
   There are thousands of books on this subject advocating everything from mind exercises to body exercises to therapy. What they all have in common is learning what we can control and finding helpful ways of responding to or balancing out the inevitable things we can't control.

LEARN MORE ABOUT IT:

Read "Allostatic Load Scenario 4: Too Little Is as Bad as Too Much," p. 34.

Recommended Web sites:

National Institute of Mental Health, www.nimh.nih.gov
National Center for Post-Traumatic Stress Disorder, www.ncptsd.org

Classroom Video: *Exploring Your Brain: "Topics in Brain Science"*

Section 5: Pain and the Brain

Background:

When individuals injure any part of their bodies, the pain is transmitted to the spinal cord and on to the brain. Even if the injury is a broken bone in the foot, the pain is perceived in the brain. All of us experience acute pain when we suffer injuries and the pain may be minor or intense. But acute pain lasts only for a while, then it subsides and eventually goes away completely when the injury has healed. Chronic pain does not go away.

KEY WORDS:

Acute, chronic, sickle cell disease

SUGGESTED RECALL QUESTIONS:

1. **Is pain important to survival?**
   Yes. Dr. Steven Hyman says that in certain circumstances, pain is essential for learning, which in turn is necessary for survival. A child who touches a hot stove or a sharp object and feels acute pain learns not to do those things again.
2. **Is chronic pain a sign of personal weakness?**
   No, according to Dr. Hyman. "People are suffering…and it's not because they are weak or because they are not trying hard enough. It is literally because the brain is hard-wired for pain to be a negative emotional experience."
3. **How does acute pain differ from chronic pain?**
   Acute pain is well understood. Chronic pain is far more complicated. According to Dr. Allan Basbaum, if the pain is severe and persists, it causes long-term changes in the spinal cord. These changes can be thought of as "memories," which last a long time and which sensitize the entire body's pain system, making the individual hypersensitive to ordinary stimuli.
4. **How does sickle cell disease cause chronic pain?**
   Sickle cell disease deprives tissues of the oxygen they need. Many sickle cell patients suffer every day with dull, throbbing pain and then, unpredictably, acute pain can strike at any time.

EXAMPLES OF DISCUSSION QUESTIONS:

1. **What are some ways people have learned to help themselves manage chronic pain?**
   They distract their brains by doing something else—for example, painting, dancing, or meditating. By distracting the brain, they eliminate or reduce the brain's awareness of the pain signals it receives.
2. **Why are some people unsympathetic to another person's pain?**
   Pain is personal and not visible to others. People have no way of knowing another person's pain; they can only relate it to their own pain experiences. A person who has never experienced severe chronic pain may assume the other person is exaggerating. Some people believe that individuals are supposed to "play over pain" and "tough it out." Frequently, these are people who have never experienced chronic pain.

LEARN MORE ABOUT IT:

Recommended Web sites:

American Chronic Pain Association, www.theacpa.org

American Pain Foundation, www.painfoundation.org

National Chronic Pain Outreach Association, www.chronicpain.org

Classroom Video: *Exploring Your Brain: "Topics in Brain Science"*

Section 6: Depression and the Brain

Background:

Millions of Americans struggle with depression, a brain disorder that researchers now know affects almost every system of the body. Depression often accompanies other diseases such as alcoholism and heart disease. Research indicates that depressed heart patients are three to four times more likely to die within six months than patients who are not depressed. Unfortunately, too many doctors and patients are unaware of the relationship between depression and other diseases, which means they fail to identify depression and fail to treat it aggressively.

KEY WORDS:

Chemical imbalances, physiologic processes, syndrome, cardiologist

SUGGESTED RECALL QUESTIONS:

1. **Is depression a real disease or just a convenient excuse made up by people to explain their behavior?**
   Depression is a real disease, caused by a chemical imbalance in the brain. Also, depression is a disease that can affect many systems in the body.
2. **Does depression affect adults only?**
   No. For singer and songwriter Judy Collins, depression began in her teenage years and is as vivid to her now as it was then.
3. **Can depression travel through families?**
   Yes. In her particular case, Judy Collins described her depression as a family legacy. In fact, scientists are currently investigating the hereditary, genetic bases for depression.
4. **How widespread is depression in the United States?**
   More than 17 million Americans suffer from this disease.

EXAMPLES OF DISCUSSION QUESTIONS:

1. **What is the difference between sadness and depression?**
   Sadness is a normal reaction to an unhappy experience. It can be very intense, but people usually get over it and get on with their lives. Depression is a dis-

ease that involves a chemical imbalance in the brain. If left untreated, depression can last weeks, months, or even years, and it can be severely debilitating.

2. In what way are depression and alcoholism diseases?
Doctors do not know exactly what causes depression or alcoholism. Research indicates there may be multiple genetic factors involved. Science has proven, however, that people who suffer from either disease have a chemical imbalance in the brain that is treatable in the same way other diseases are treatable—that is with medications and other treatments.

LEARN MORE ABOUT IT:

Read "What Exactly Are Antidepressants?," p. 31.

Recommended Web sites:

Depression and Related Affective Disorders Association (DRADA), www.drada.org

National Alliance for Research on Schizophrenia and Depression, www.narsad.org

National Alliance for the Mentally Ill (NAMI), www.nami.org

Audio Program: *Gray Matters: "Alcohol, Drugs and the Brain"*

Section 7

Background:

Substances of abuse are a cultural phenomenon as ancient as civilization itself. Only recently, however, have scientists begun to study their effects on us, and more specifically, their effects on our brains. Why do people get addicted to drugs, tobacco, and alcohol? Why is it so hard to kick a habit? It stands to reason that since drug use is self-destructive, people would naturally avoid it. This obviously is not the case. What is not so obvious, however, is why people turn to addictive drugs. People use drugs, tobacco, and alcohol to feel good, without regard to the fact that long-term effects are very bad. Research is only now showing us how genetic and environmental factors all play a part in our susceptibility to substance addiction.

KEY WORDS:

Alcoholism, dopamine, emotional memory, neurotransmitter, *physical dependence*, addiction

SUGGESTED RECALL QUESTIONS:

1. **What percentage of Americans smoke on a daily basis?**
   25 percent, one in four.
2. **What percentage of American high school students use tobacco?**
   35 percent, more than one in three.
3. **How many adult Americans have used an illegal drug at some point in their lives?:**
   a) 70,000 b) 700,000 c) 7,000,000 d) 70,000,000
   Answer: d
4. **Can drug use modify your brain?**
   Yes.
5. **True or false: Nicotine is NOT an addictive substance.**
   False
6. **How can alcohol abuse affect memory loss and *dementia*?**
   Alcohol abuse can lead to or increase both.

EXAMPLES OF DISCUSSION QUESTIONS:

1. **How do drugs give people pleasure?**
   Drugs are rewarding because they directly or indirectly stimulate the brain's natural reward system and cause dopamine to be released. Dr. Steven Hyman: "Drugs are much more reliable and potent than normal stimuli. Instead of running that marathon, or for a scientist, working for months and writing a good paper and getting it accepted—a lot of work for a little dopamine in the brain—people who use drugs find that they can literally short-circuit all of these natural processes."
2. **Why do some people fall quickly into addiction, while others can experiment and then walk away?**
   Dr. Hyman: "You know, it's hardly heroic that we use alcohol well. And there's no special act of will. And this gets back to the issue of vulnerability. That is, people who will take drugs enough to potentially get addicted seem to seek them out and enjoy them. They seem to have fewer warning signs." Dr. Alan Leshner: "It's not true that you take a drug and you become addicted for the rest of your life. Some people do. Most people don't. However, most people (who routinely use) ultimately will become addicted to an addicting substance. The question is, what determines how readily and what determines how intensively a single individual will respond to the drug and become addicted to the drug"?
3. **Is alcoholism polygenic (i.e., involving more than one gene)?**
   Yes, according to Dr. Enoch Gordis. "Alcoholism is a polygenic disorder almost certainly. That is, it's not one gene causing the disease. Almost all the complex disorders, especially those involving behavior, are probably polygenic. And that means the task is harder, because no single gene is responsible for the whole condition. These are genes for vulnerability or risk, not destiny.

And that's a very important distinction." Currently, 24 genes have been mapped in rodents that are relevant to drug addiction. Addiction genes have not yet been found in humans, but it is only a matter of time and technology before the genetic component of human addiction is more fully understood.

4. Why would a person who can hold his liquor have an increased risk of becoming an alcoholic?

We have learned that the ability to hold your liquor is actually a warning sign—not an advantage. Dr. Gordis described a long-term study by psychiatrist Mark Schuckit with some college students: "He [Dr. Schuckit] tested their reaction to alcohol on several scales. How much they became wobbly in standing, how much they actually had a subjective feeling of being high. And also certain hormonal measurements which he did at the time. And he found two things. First of all, early on, he found that those with a family history tended to be less sensitive to the effect of alcohol—less sensitive. But whether or not you had this family history, lack of sensitivity or reduced sensitivity to alcohol on his testing at the age of 20 was predictive of an increased risk of alcoholism at the age of 30."

5. According to Dr. Leshner, how can drug addiction be limited to a specific environmental context?

Regarding a study that revealed an alarmingly high number of soldiers were using heroin in Vietnam but did not get readdicted when they returned to the United States, Dr. Leshner comments: "The heroin addicts in Vietnam developed their heroin addiction in a certain environmental context, Vietnam. When they came back to the United States, they were never exposed to that context again...they were never exposed to all of the cues, all of the stimuli, associated with their initial drug use....

6. Citing Dr. Hyman's statement, describe the three kinds of changes that occur in the brain as a result of long-term drug use.

Dr. Hyman: "The first kind of adaptation is caused only by alcohol and by opiates, not by nicotine particularly, and not by cocaine or amphetamines. And these are adaptations that lead to what has been called physical dependence." In the second type of change, drug users start losing the ability to experience normal pleasure. They feel depressed and they crave drugs. The third change from chronic drug use involves what Dr. Hyman calls your emotional memory. Dr. Hyman: "This is a system that's there to say, yes, that was good, let's do it again, and let's remember exactly how we did it. So memories that are associated with the drug taking become nearly indelible. And we know from experience that people who are fully detoxified from drugs remain at really high risk of relapse for a very long time, maybe for the rest of their lives. Alcoholics Anonymous says that people are only recovering and not recovered. And a great deal of this, I think, has to do with these emotional memories. And these can be triggered by even trivial reminders of drug use in the environment. A smoker might have a festive meal, a Thanksgiving dinner, and intensely crave a cigarette. Someone who had used opiates or cocaine might meet friends that he used to use drugs with or see some drug paraphernalia and get intense waves of craving."

LEARN MORE ABOUT IT:

Read "Drugs and the Brain: A Celebration of Alcohol," p. 102.

Recommended Web sites:

National Institute on Alcohol Abuse and Alcoholism,
www.niaaa.nih.gov

National Institute on Drug Abuse,
www.nida.nih.gov

National Institute of Mental Health,
www.nimh.nih.gov

Audio Program: *Gray Matters: "Alcohol, Drugs and the Brain"*

Section 8

"Happy day...when all appetites controlled, all poisons subdued, there shall be neither a slave nor a drunkard on the earth."

Abraham Lincoln, 1842

Background:

The allure of getting high is so powerful, so seductive, how then do we get people off drugs and keep them from relapsing? These are the questions put to modern science. Rational drug design has helped to develop effective dopamine-blocking agents. Scientists realize, however, that biological treatment mechanisms can only complement psychological and emotional therapies for those addicted to alcohol and drugs.

KEY WORDS:

Relapse, *psychological dependence,* physical dependence, agonist compound, rational drug design, dopamine transport blockers, anabuse, naltrexone, methadone, Zyban

SUGGESTED RECALL QUESTIONS:

1. **What is methadone?**
   A maintenance drug used to treat heroin addiction.
2. **What recent advance in methadone treatment has occurred and why is it helpful to addicts?**
   A longer-acting form of methadone enables addicts to avoid sometimes stigmatizing trips to a clinic to receive medication.
3. **What is naltrexone and how does it work?**
   Naltrexone is a drug that works to treat alcohol addiction by blocking the opiate receptors in the brain.

4. **True or False: Addiction is a complex phenomenon; therefore no single treatment can work for everyone.**
   True.
5. **True or False: Dealing with relapse is so difficult because the individual is often subject to the same problems that he tried to solve with drug use.**
   True.
6. **How do new drugs for cocaine treatment work?**
   They use antibodies to catch cocaine in the bloodstream before it gets to the brain, depriving the addict of a high and hopefully weakening dependence on the drug.

EXAMPLES OF DISCUSSION QUESTIONS:

1. **According to Dr. Alan Leshner, what is psychological dependence as opposed to physical addiction to drugs?**
   Dr. Leshner says that physical addiction plays a surprisingly small role in drug addiction: "What does matter in addiction is what people used to call psychological addiction, but which I prefer to think of as the essence of addiction. And that's uncontrollable, compulsive drug use. Sometimes, that's a hard concept for people to think about. But think about the crack addict who has sold her children in order to get drugs. Nobody wants to sell their children, but the drug becomes such a consuming part of the individual's core personality at that point in time that there is nothing else but drug and the craving for the drug. That's what addiction is. Addiction is not about does it or doesn't it give you the chills when you stop taking it. We can manage the chills. We can't seem so easily to manage the behavioral elements of it, and those are the things that matter clinically."

2. **Describe the function of methadone at the molecular level.**
   Dr. Leshner: "A maintenance drug like methadone, we call it an agonist compound, actually binds to and occupies the receptors in the brain where the drug of abuse acts. So that methadone works primarily by occupying the opiate, the mu opiate receptors in the brain, and therefore the individual doesn't feel the need to occupy his or her own mu opiate receptors...."
3. **How could cocaine drugs, called dopamine transport blockers, work in dealing with cocaine addiction?**
   Dr. Bertha Madras: "One of the approaches that we've taken is to try to find drugs that lodge on this dopamine transport system like cocaine that are much longer acting, but also enter the brain very slowly, unlike cocaine. Because there is accumulating evidence that the speed at which cocaine enters the brain, which is seconds, and the speed at which it comes off its targets, which is minutes, is part of the process of producing the euphoria as well as the

potential addictive properties. So we're trying to develop compounds, medications, and replacements for cocaine that are analogous to methadone and that would have different profiles of time on and time off."

4. **Pat Summerall, the host of the program, admits that he would not have quit drinking if his family had not confronted him. Would you confront a friend or family member with an addiction, or would you let him sort out his problems alone?**
   Ask students to give their opinions or share their experiences, if possible.

5. **Discuss how much progress has been made in alcoholism treatment in recent years, as highlighted on the audio.**
   Dr. Enoch Gordis: "I think we've learned more about alcoholism in the last 20 years than we have probably in most of the history of this before. It is only in the last few years that treatment has been subjected to the same rigorous scientific inquiry and analysis that every other branch of medicine has customarily used for new treatments for many, many years." Dr. Charles O'Brien: "I think that too often people think of addiction as a kind of broken arm, or a case of pneumonia where you get treatment and then it's cured. And because this is really a chronic memory, the brain has changed as a result of using a drug hundreds or thousands of times. Once you get into treatment you can't expect to wipe all that out. The memories are indelible. We have to aim for improvement and not expect total cure."

LEARN MORE ABOUT IT:

Recommended Web sites:

National Institute on Alcohol Abuse and Alcoholism,
www.niaaa.nih.gov
National Institute on Drug Abuse,
www.nida.nih.gov
National Institute of Mental Health,
www.nimh.nih.gov

Audio Program: *Gray Matters: "The Arts and the Brain"*

Section 9

Background:

Neuroscientists and learning specialists are gaining more knowledge about how children learn and how the arts can contribute to that process. As a result of imaging technologies that permit us to "see" the neural development of the brain, we now know how important the first three years of life are to a child's cognitive development. The arts—music, drama, creative writing, and visual

arts—can play a valuable role in this process by engaging a child in activities ideal in promoting the "wiring" for learning.

KEY WORDS:

Cognitive development, mental schema, repetition, motor cortex, collateral benefits, meaning, and memory

SUGGESTED RECALL QUESTIONS:

1. **How many neurons are added every single minute to the developing brain during gestation?**
   a. 250 b. 2,500 c. 25,000 d. 250,000
   Answer: d

2. **True or false: Researchers at the University of Illinois found that rats raised with playmates, toys, and a variety of stimuli grew 25 percent more neurons than those deprived of that same stimulation.**
   False. Despite recent evidence that points to neuronal production in the dentate *gyrus* of the hippocampus during adulthood, increasing the number of neurons in the brain by 25 percent is unlikely. Instead, what researchers at the University of Illinois found was an increase in the number of synapses, or connections between neurons, in the brains of rats raised in stimulating environments.

3. **How do mental schema help us make sense of the world?**
   They help us to understand the elements of the world and how they fit together. Repetition is important for building schema. Infants and young children need repetition to help them make sense of the world. Being able to predict a pattern gives them a sense of security and comfort, which allows them to explore new ideas and learn more complicated things.

EXAMPLES OF DISCUSSION QUESTIONS:

1. **Describe what's going on in your brain when you read music and how this might help learning in general.**
   To paraphrase Dr. Weinberger, we begin with the various senses. You envision you are looking at the score, then take those notes and translate them into what they represent. This is symbolic manipulation. Then you execute that program through your motor cortex, which requires the coordination of muscle activity. You then hear what you've played and that feeds back into what you need to do next. Playing music seems to be the ultimate form of brain exercise. More brain cells, more circuits, and more systems become interconnected. Those multiple interconnections give you more pathways to solve problems and you become more flexible in the way you approach and think about problems and the way you actually solve them.

2. A study conducted by Columbia University shows that students who were involved in music and the arts were much more tolerant of other people's ideas, more flexible in their approach to solving problems, and more willing to take intellectual risks. Discuss why you think this might be the case.
Mary Jo Thomson, a Minneapolis-based art teacher and the project director for a United States Department of Education program in New York City and Minneapolis called "artful teaching and learning," suggests the following explanation: "I think what happens to the process of visual thinking is that [children] start to move off the idea that there's only one way to look at something and there's only one right way to understand things. That the world is more complex and that there's much more nuance and subtlety in the world than there is black and white, right and wrong. Once we start to examine things more artfully you find that there's always a tension, there's a give and take in whatever it is. Children become more open to living within that ambiguity, being able to explore it and ask those harder questions."

3. Anne Green Gilbert is head of Seattle's Creative Dance Center. She claims that "The brain only has memory when there is meaning." What do you think of this statement? Can there be memory without meaning?
This discussion depends on your definitions for memory and meaning. If we think about memory as any kind of imprint, then we might consider a footprint left in the sand as memory. Does it have meaning? It certainly refers to something having been there, but whether it is meaningful in itself is questionable. Insofar as memories in the brain are concerned, some are equally devoid of meaning. Implicit memories, for instance, motor learning and fixed action patterns, are acquired by rote.

4. Why is movement increasingly important as a tool for learning in today's society?
Scientists at the University of Illinois have found that the cerebellum takes at least a couple of years before it starts to work well, and that if a child isn't given opportunities to move a lot during the first few years of life, synapse development in the region suffers. This biological imperative, however, is at odds with a society that encourages the sedentary lifestyle. There are stages in visual development when the brain is primed and ready for the next batch of wiring. At each of these stages, it is argued, movement is needed for the improved development of different synergies, from singing to social and emotional behavior.

LEARN MORE ABOUT IT:

Recommended Web sites:

Learning Disabilities Association of America,
www.ldsamerica.org

National Coalition of Creative Arts Therapies Associations (NCCATA),
www.ncata.com

Audio Program: *Gray Matters: "The Arts and the Brain"*

Section 10

Background:

Brain scientists are exploring the neural underpinnings of art—how the arts are perceived by the brain and which cells and circuits come into play. Are artists' brains wired differently than other people's brains? How might the arts be used as therapy for people with brain injury, stroke, or Alzheimer's disease? How can the study of synesthesia open a window on brain function and cognition?

KEY WORDS:

Art therapy, movement therapy, plasticity, neural networks, synesthesia and synesthetes, metronome

SUGGESTED RECALL QUESTIONS:

1. What are some of the goals of arts therapy?
The process of creating art can foster individual expression, self-awareness, and communication with others.

2. What is the potential benefit of movement therapy?
One therapist believes that dance or other forms of creative movement can, however temporarily, lift the moods of depressed or even suicidal teenagers, by helping them release anxieties and frustrations.

3. What is synesthesia? Name some famous synesthetes.
Synesthesia refers to the crossing of sensory signals (e.g., having music evoke a perception of a particular color, or having a particular taste evoke a tactile sensation). Novelist Vladimir Nabokov was a synesthete and wrote about his experience. Others include musician Franz Liszt and physicist Richard Feynman.

4. True or false: Most artists are synesthetes.
False.

EXAMPLES OF DISCUSSION QUESTIONS:

1. How can art and music therapy offer healing potential for the brain?

According to Dr. Michael Thaut, "If music and rhythm help a high performer to learn better and better, would it help a low-end performer to also learn better and better, except that they start from a different level?" It did, he discovered, for patients disabled by Parkinson's disease, stroke, and traumatic brain injury, though it was not the music, he found, but its rhythm. "It can be folk music, it can be classical music, it can be a metronome. A metronome, in many cases, may work just fine. The liking of the music for the patient is an additional bonus or motive to succeed in therapy. And so that's important too. But that's not what really drives the effect of music on coordinating and retraining the movement."

2. How else can art therapy help a damaged brain?

One researcher believes art therapy can give people with brain damage a sense of mastery, a tool for self expression, and a way of processing information, without words, thus simplifying a potential information overload. Another brain scientist believes the power of art therapy lies in enhancing brain plasticity, the power of the brain to change and form new connections—a key component of recovery after injury, disease, or insult.

3. How common is synesthesia?

Dr. Ramachandran speculates that as many as 1 in 200 people may be synesthetes. He indicates, however, that synesthesia is seven or eight times more common among artists—painters, poets, and writers, who are especially gifted at mixing words, images, color, and sound. Though this increases the proportion of synesthetes in a specific population to 7 or 8 in 200, this does not mean that most artists are synesthetes.

4. Dr. Ramachandran observes that the fusiform gyrus (occipitotemporal gyrus), the region of the brain responsible for seeing numbers, lies beside the part of the brain involved in seeing colors, which is itself adjacent to a primary auditory area. He considers "sloppy wiring" between these regions as a possible source of synesthesia. Why would the brain make "sloppy" connections?

The brain does not make sloppy connections. Instead, Dr. Ramachandran suggests that these redundant connections are left over from infancy. This may be due to a genetic condition. In his words, "the normal brain is born with excess connections, so in childhood and infancy and in the fetus, there are far more connections than you need. Everything is connected to everything. Then you start pruning away these connections to create the characteristic modular organization of the adult brain—with a different area for color, number, language—and so on. Now if this gene is defective, if the pruning is

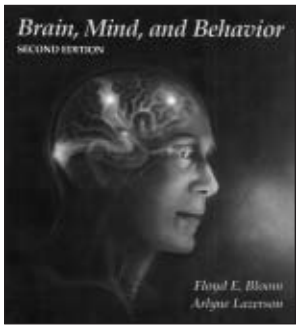
defective, the pruning does not take place. You end up having the number area and color area connected in these people. Therefore, every time they see a number, they see a color." (As a further note, the fusiform gyrus is implicated in face recognition, as distinct from recognition of other objects.)

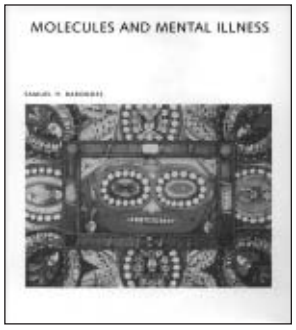
LEARN MORE ABOUT IT:

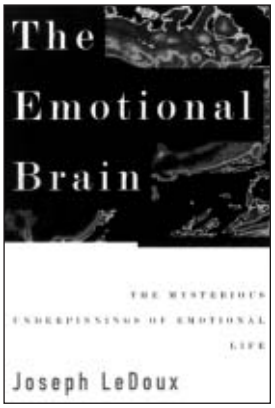
Recommended Web sites:

National Coalition of Creative Arts Therapies Associations (NCCATA),
www.ncata.com

National Institute of Neurological Disorders and Stroke,
www.ninds.nih.gov







The Great Brain Books

Voted by Scientists of the Dana Alliance for Brain Initiatives

Reprinted from *Cerebrum: The Dana Forum on Brain Science*, Vol. I, No. 1, Spring 1999 © Dana Press.

The most frequently cited "brain statistic" is not the number of patients on antidepressants or the percentage of our genes devoted to shaping our brains. It is probably the estimate that our knowledge of the brain has doubled in the 1990s.

Scientists first responded to this flood of information by writing general books about the brain for lay readers (a category that includes scientists writing outside their research specialties). More recently, books about specific *aspects* of the brain and brain research, also for the lay reader, have begun to appear. Why? As research accumulates, new areas of brain research reach the critical mass of information required to deal with questions of interest to such readers. This seems to be happening in research on emotion and the brain, for example, where Joseph LeDoux's *The Emotional Brain* and Antonio R. Damasio's *Descartes' Error* are examples. (In contrast, outstanding books about vision and the brain began appearing well over a decade ago, after some 30 years of intensive research in that area.)

Whatever else may have doubled in this decade, coverage of brain research by the media certainly has. This has nurtured an informed, curious audience for more information and ideas. As a result, publishers are bringing out more brain books than ever before.

Where should the reader begin? What are the great books, past and present, that capture the unfolding story of the brain and how brain research is changing our ideas about memory and emotion, lifespan and language, neurological disorders, and psychiatric syndromes?

The Survey

We decided to ask members of the Dana Alliance for Brain Initiatives, neuroscientists concerned with informing the public about the progress and promise of brain research, to give *Cerebrum* readers their recommendations.

We began by defining 12 categories, such as "Chemistry of the Brain," "Consciousness," and "Memoirs and Personal Experience." We then asked a dozen widely-read scientists and experienced science book editors to nominate books in each category. From these we created a ballot sent to members of the Dana Alliance, who were asked to vote their first, second, and third choice in each category. Write-ins were encouraged as well. Some 35 Dana Alliance scientists across the country responded by our deadline. Using a point-scoring system, their votes were tabulated to produce the winning books.

A few comments on the brief reviews that follow. We try to give original publication dates; few fields of science threaten the new book with such rapid obsolescence (but some books survive, as you will see). Where possible, though, we also mention new editions, especially expanded and updated editions.

That raises another issue. We have included books now out of print. Some scientists wrote to us, pointing this out and asking if readers would be frustrated. Possibly, but we decided to list the books. First, many readers, including most college students, will have easy access to a library. Second, we saw an opportunity for publishers. Why should these outstanding books be out of print? (They may not be for long. Perhaps because his new book, *Mood Genes*, became an immediate hit, Samuel H. Barondes's out-of-print *Molecules and Mental Illness* is back in a new paperback edition.)

We thank all Dana Alliance members who responded, with special thanks to those who wrote comments on their ballots. Books listed here are not endorsed by the Dana Alliance, of course; they are the choices of responding Dana Alliance members.

Book lovers (not to mention authors) have strong opinions. This would be a sorry survey if it did not spark disagreements. An internationally known psychologist nominated a book that an equally well-known neuropharmacologist derogated, in his note to us, as "basically a modern 'myth of mental illness' anti-reason, anti-psychiatry screed.'" Some told us that books were in the wrong category, or not for lay readers. A psychiatrist wrote that our category "Neurological Diseases and Disorders" implied that these books were not part of psychiatry, and added, "A very sad idea!" Perhaps that category is better described as "Mental and Neurological Disorders."

One scientist who received our nomination form wrote, "I've gone over your *Cerebrum* survey and I'm amazed at how many of the more modern books I really haven't read." He thoughtfully recommended some "older historical books...which set the stage for modern research."

Following are the 12 categories with brief introductions and reviews of the books voted best. There is one exception. Category 11 is "Books for Children and Young People." We received not a single nomination in that category. We nevertheless included it in the survey, hoping for some write-ins. We will mention them.

1. General Books About the Brain

Where can you get one book to bring to Neuroscience 101? Of the three books below, *Brain, Mind, and Behavior* is most accessible to the lay reader. *Images of Mind* comes next. *Essentials of Neural Science and Behavior* is a textbook, which makes it a questionable choice for lay readers. It received multiple nominations, however, and then the fourth highest total score in the survey, more than any other general book on the brain. *Brain, Mind, and Behavior*, a truly general account of neuroscience for lay readers, is now almost 15 years old, but a new edition was published in 2000.

Essentials of Neural Science and Behavior

Edited by Eric R. Kandel, James H. Schwartz, and Thomas M. Jessell. Appleton & Lange, 1995. $74.95. 743 pp.

This is a textbook, for undergraduates with some biology experience, and may be difficult for lay readers. Three primary authors, all at Columbia University, are joined by a dozen more to present the subject—from neuron to memory—with many illustrations, all technical, and appropriate mathematical formulas and models of compounds. Scientists in the *Cerebrum* survey, however, voted overwhelmingly for this book as a general introduction to neuroscience for lay readers. At 743 pages, it is our list's most comprehensive introduction to brain science.

Brain, Mind, and Behavior

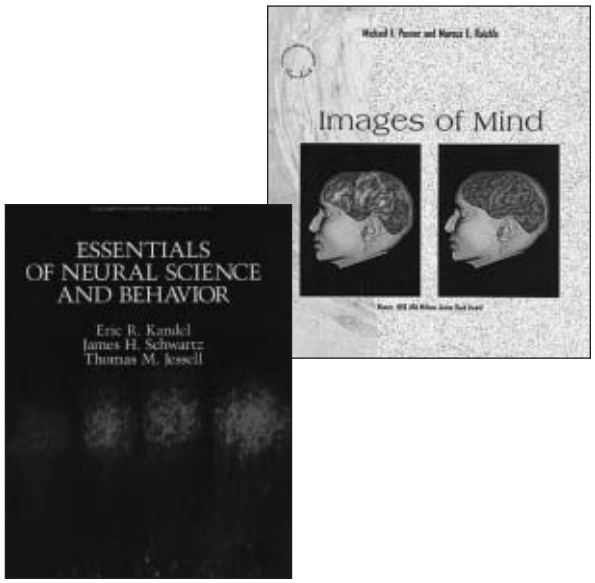
By Floyd E. Bloom and Arlyne Lazerson. W.H. Freeman & Company pb, 2000. $71.00. 457 pp.

Is there one book that "says it all" for the newcomer to neuroscience? If it isn't this one by Bloom (chairman of neuropharmacology at Scripps Research Institute and former editor of *Science*) and Lazerson (a science writer), it just may not be possible. Written to accompany a PBS-TV series, *Brain, Mind, and Behavior* systematically moves from monomine transmitters to thinking and consciousness, with glorious color illustrations all the way. The book is eminently readable by a smart high-school senior, but it addresses as well subtle controversies and questions in research. A 14-page glossary ices the cake.

Images of Mind

By Michael I. Posner and Marcus E. Raichle. Scientific American Library, 1997 (1994). $19.95. 257 pp.

No recent development has transformed neuroscience more than imaging technology. What brain research area has been untouched by its power? As a result, this volume—by a foremost cognitive psychologist (Posner) and a pioneer of positron emission tomography (Raichle)—is not just a book on imaging; it is also a general brain book. Chapters deal with mental images, interpreting words, mental operations, attention, brain development, and mental disorders. Visuals, including brain scans, are generous, but so is the lucid text. *Images of Mind* is more than a survey; it reports research by the authors at major PET centers.



2. Chemistry of the Brain

Authors know that brain chemistry ordinarily doesn't bring in the crowds. Rising to the challenge, two top scientists have written understandable introductions to the brain from a chemical perspective and, thanks to Scientific American Library, packaged their stories in lavishly illustrated books. Both are clear brief introductions to brain science as well as to the more specific topic. The third book on this list, almost as famous as its subject, is mostly psychological and philosophical—a meditation on where the amazing successes of brain chemistry are taking us.

Drugs and the Brain

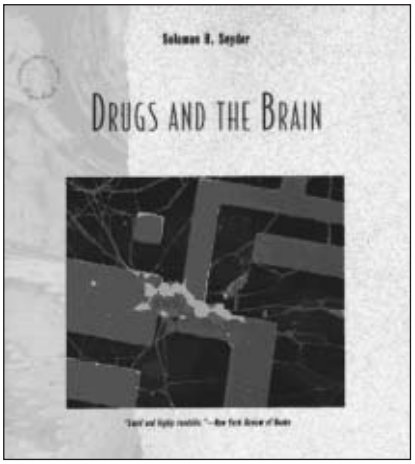
By Solomon Snyder. Scientific American Library pb, 1996 (Scientific American Books, Inc., 1986). $24.95. 228 pp.

Drugs and the Brain received the most votes and the highest score in the entire survey. Its author, director of the department of neuroscience at Johns Hopkins University, unites expertise in psychiatry, pharmacology, and neuroscience, is a world leader in neuropharmacological research, and writes well. He tells the story of brain research from the viewpoint of brain chemistry and pharmacological agents (some known over thousands of years) and what they reveal about our brains. The 1996 paperback (Scientific American Library) updates the story with molecular biology, gene cloning, and discovery of neurotransmitter receptors, as well as the practical story of new drugs such as Prozac for depression and clozapine for schizophrenia. This book takes even interested beginners from a cold start to a grasp of neuroscience's best line of attack on brain mysteries. The Scientific American Library series offers superb scientific illustrations and other good visuals.

Molecules and Mental Illness

By Samuel H. Barondes. W. H. Freeman pb, 1999 (Scientific American Library, 1993). $12.00. 215 pp.

This book teaches molecular biology while telling the story of biological psychiatry. Barondes, chairman of psychiatry at UC San Francisco and director of Langley Porter Psychiatric Institute, is an expert explainer (as he showed again in *Mood Genes*, also on this list). He guides you through heredity, molecular genetics, cellular neuroscience, and psychopharmacology with fascinating sidelights and fine Scientific American Library illustrations (you've never seen ion channels like these). Much technical material is in boxes, although discussions of specific drug reactions get mildly complicated. When he turns to psychiatric disorders and what molecular biology has to say about their causes and treatment, Barondes creates vivid portraits of manic-depressive illness, major depression, schizophrenia, and disabling fears and compulsions. At the end, the entire story is recapitulated in verse ("And by yet another tactic/You may switch from fright to fight/By increasing GABA's binding/To a GABA binding site.") With so much to offer, this book should not have gone out of print, and its return is welcome.



Listening to Prozac: A Psychiatrist Explores Antidepressant Drugs and the Remaking of the Self

By Peter D. Kramer. Penguin Books pb, 1997 (Viking Penguin, 1993). $15.00. 448 pp.

What if a widely available drug, with few side effects, could alter personality—make the shy outgoing, the sedate energetic, the timid bold? To many, that was Prozac. As it became a pharmaceutical bestseller, Dr. Kramer looked at the implications in a long, contemplative, readable book that also became a bestseller. If Prozac transformed personalities of relatively healthy patients, what did this mean for our view of psychiatry? Mental illness? Biology as destiny? Kramer raised and deliberatively deepened the issues. Elaborations went into more than 60 pages of notes. In the 1997 edition, Kramer's "Afterword" looks at his book's history, new developments, and—as always—larger issues.

3. Issues of Development and Life Span

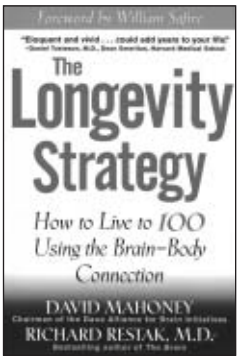
The categories used in our survey have their limits, clearly revealed here. Studying development of the brain is a prime strategy in neuroscience, not only to increase general understanding of brain structure and function but also to make progress against genetic defects and developmental disorders that can devastate the human brain. Of interest, therefore, is that none of the books listed in this category addresses development of the human brain and the investigations that have illuminated it. For that, readers will have to look to the three general books on the brain, as well as to books on specific aspects of the brain such as vision, that address development.

Books in the present category address three fascinating but more specific aspects of life-span and development: the health of our brains as we age; the extraordinary new research on temperament—what is given, what we can modify; and the brain from an evolutionary point of view.

The Longevity Strategy: How to Live to 100 Using the Brain-Body Connection

By David Mahoney and Richard Restak. John Wiley & Sons, Inc. and Dana Press pb, 1999 (1998). $14.95. 250 pp.

David Mahoney, the business executive and philanthropist who was chairman of the Dana Alliance for Brain Initiatives, teamed up with the neurologist and neuropsychiatrist Richard Restak for this roadmap to a healthy longevity. They provide thirty-one practical, research-based tactics for maintaining cognitive and emotional well-being, physical health, and financial stability through the lifespan. In a fresh perspective on the relationship between brain and body, they point out both the emerging health links between the two and how mindful use of the brain's capabilities can support the reader's goal of aging well. The work has a charm not always found in health-science books, thanks to the authors' cheerful citation of their personal experiences and the remarks of figures in sports, films, and public affairs on the fine points of aging and health.



Galen's Prophecy: Temperament in Human Nature

By Jerome Kagan. Westview Press pb, 1998 (Basic Books, 1995). $35.00. 376 pp.

Psychologist Jerome Kagan, who heads the interdisciplinary Mind, Brain, Behavior Initiative at Harvard, takes a perceptive look at what research into infant and child development can teach us about human nature, in particular the biological influences on temperament. He sees in his more than 15 years of research on what he calls "inhibited" and "uninhibited" children confirmation of Galen of Pergamon's second-century description of melancholic and sanguine adults. Weaving in an insightful analysis of the philosophical, historical, and social issues, he argues that free will is not undermined by these inborn temperamental biases; we may not be able to control our emotions but we can control our actions. Extensive endnotes on the science and methodology help keep the flow of the text clear but make the book valuable to professional as well as lay readers.

Evolving Brains

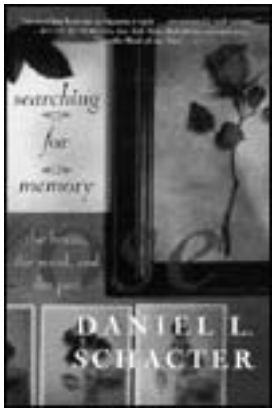
By John Morgan Allman. Scientific American Library pb, 2000 (1999). $22.95. 224 pp.

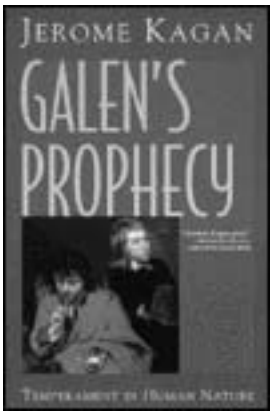
Evolving Brains barely had been published when it was voted a Great Brain Book in this survey. That might be because Allman brings a rare combination of neuroscience, evolutionary biology, and developmental biology to his work. Or it might be because he is a distinguished contributor in his own right to brain research (on vision), who now has written a fascinating account of the uncanny, unconscious genius of evolution brilliantly improvising the brain in response to the needs of the gut, the blood, the hunt, and, always, the next generation. You will be yelling to your kids, "Did you *know* that...?" Beautifully illustrated.

4. Cognition, Learning, and Memory

In a sense, these are the "payoff" topics of brain research: new knowledge of the functions of the brain that we depend on for our day-to-day effectiveness and over which we can exercise significant control. Larry R. Squire transformed our thinking about memory with his insights into the distinctly different types of memory that seem to operate in the human brain. Daniel L. Schacter's recent work has been inspired by the public controversy over "recovered memories" and their use in the courtroom. Steven Pinker, director of the Center for Cognitive Neuroscience at the Massachusetts Institute of Technology, is represented twice on this list. His book *The Language Instinct* was published before *How the Mind Works* (under our category "Consciousness"). They made him a celebrated writer on the brain, as popular with the public as with the critics.

Not represented in this category is a new genre of memory book: the review of what science can tell us about heading off memory loss or even strengthening memory through exercise (mental and physical), appropriate nutrition, and other steps.





Memory and Brain

By Larry R. Squire. Oxford University Press pb, 1987. $31.95. 315 pp.

Looking back at two decades of productive research on memory, Squire sets out to integrate the work of psychologists and neurobiologists into a coherent account of the nature of memory: synaptic changes, storage, learning, information processing, and types of memory. On the latter issue he can cite two dozen papers of his own, establishing the distinction between declarative ("what") and procedural ("how") types of memory. Squire's narrative is clear and sober, free of technical jargon, and comes with a glossary. He sets the historical context of new discoveries. A decade after writing this book, Squire and his opposite number in neural studies, Eric Kandel (the "dream team" in the memory field), joined forces to write *Memory: From Molecules to Mind* (1999).

Searching for Memory: The Brain, the Mind, and the Past

By Daniel L. Schacter. Basic Books pb, 1996. $17.50. 398 pp.

We seldom notice memory's daily feats. Memory is just "us." Decades of research by scientists such as Professor Schacter, chairman of *psychology* at Harvard, have begun to map the multiple, complex systems that underlie those feats. In prose always readable (100 pages of notes and bibliography are optional), Schacter tells the story that brain research has found. We learn that with memory's power comes fragility, limitations seen not only in disease and aging but also in explosive issues such as "recovered memories" of child abuse that have put innocent teachers in prison. Schacter weighs it all with scientific rigor and human warmth.

The Language Instinct

By Steven Pinker. HarperPerennial pb, 1995. (William Morrow and Company, 1994). $15.00. 494 pp.

Steven Pinker, a psychologist, turns a phenomenon that most of us take for granted—language—into a wonder and mystery that, he proposes, is at the heart of human development. Disputing the theory that language is a cultural construct, he argues that it is ingrained, an "instinct." We use it, says Pinker, because language is "the product of a well-engineered biological instinct," as hardwired in humans as making a web is in spiders. Thinking about language as part of what makes us human, posits Pinker, we begin to see it in a new light. Includes notes and a brief glossary.

5. Consciousness

For human beings, at least, the brain is *about* consciousness. Consciousness is the way that we actually experience the functioning of the brain (more precisely, the results of its functioning) and its malfunctioning. For reasons to be found in the history of philosophy and psychology, however, most neuroscientists until recently actively avoided investigating consciousness—or even, as John Searle points out, mentioning it. That has all changed now. Consciousness is being examined from every conceivable point of view, by every discipline concerned with neuroscience, and major conferences are called to consider the results. The three books on this list are famous in the field and well known to lay readers.

One prominent neuroscientist who responded to our survey took strong exception to including *How the Mind Works* as a nominee for this cate-

gory. Pinker, this scientist commented, concludes his book by saying that consciousness cannot be studied and will probably never be explained. At least it is safe to suggest that, as brain research progresses, consciousness is likely to be the last remaining mystery. Francis Crick holds out hope that the mystery may give way by the end of the twenty-first century.

How the Mind Works

By Steven Pinker. W.W. Norton & Company pb, 1999 (1997). $12.95. 660 pp.

How does the mind enable us to do what we do, from calculating calculus (for those of us who can actually do that) to tying our shoelaces? Steven Pinker attempts to explain the brain's natural ability to perform feats that even the most sophisticated computer hardware would find impossible. For example, how does the mind affix an object in space (such as a doorknob), know what it does (turn to open a door), and which direction it turns (clockwise), and also know what the object doesn't do (make toast), all at the same time? Pinker also explores how the mind thinks, reasons, falls in love, and develops family bonds.

Bright Air, Brilliant Fire: On the Matter of the Mind

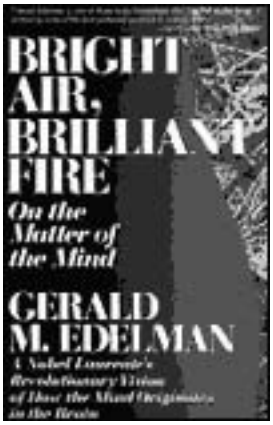
By Gerald M. Edelman. Basic Books pb, 1992. $22.00. 280 pp.

A Nobel laureate presents his complex and revolutionary vision of how evolution has led from simple cells to the intricate biology of our brains—and, in Edelman's view, our extraordinary minds and unique human consciousness. Following his ideas can be challenging, but Edelman takes great care in his writing to lay a clear path, expose problems, raise questions, and guide the reader along. This book, like many of Edelman's works, has its infuriated critics and its ardent devotees; it is essential reading in the neurobiology of consciousness.

The Astonishing Hypothesis: The Scientific Search for the Soul

By Francis Crick. Simon & Schuster pb, 1994. $11.20. 317 pp.

Nobel laureate Crick, co-discoverer with James Watson of DNA's structure, takes on the queen of scientific problems. His book is about consciousness and the case for scientific investigation of it. The "astonishing hypothesis" is that "all aspects of the brain's behavior are due to the activities of neurons" (that's *all*, including lofty aspects once called "soul"). Crick's challenge is to make real to us what it would mean to provide a complete explanation of awareness solely in neural terms. He does so by focusing on visual awareness and proposing research strategies (and specific experiments) for studying it, so several chapters deal with the brain's visual system. Crick is refreshingly frank about his chief competitor, the religious explanation of soul. "Now is the time," he writes, "to take the problem of consciousness seriously." Crick's brief introduction to the brain is superb, and he briefly annotates dozens of books for further reading.



6. Perception and Motion

Perception and motion are linked in the brain. Much is now known, for example, about how the brain "sees" and registers motion and position. Internal perception, or proprioception, is our direct experience of our body's position in space. And motion, of course, is often the output of the brain and nervous system in response to the input of perception. Nevertheless, no book in this category deals explicitly with motion. This is not surprising. Research on vision has tended to dominate the study of the brain over the past half century, so that today a great deal of what we know about the brain, including the neocortex, has to do with vision.

Eye, Brain, and Vision

By David H. Hubel. Scientific American Library pb, 1995 (1988). $32.95. 242 pp.

How do light rays falling on 125 million receptors in each of our eyes become the scene—in color, depth, and motion—that we perceive? In 1950 your question would have received, at best, a sketchy answer. By 1980 the answer required a fair-sized book (this one), and the primary visual cortex was the best understood part of the brain. For their role in that knowledge revolution, David Hubel and Torsten N. Wiesel received a Nobel Prize in 1981. Here Hubel tells the story for readers, he says, with scientific training but not biology expertise. Trained or not, readers who like science—and how a great scientist thinks—will enjoy this book. Color illustrations on most pages.

Eye and Brain: The Psychology of Seeing

By Richard L. Gregory. Princeton University Press pb, 1997 (1966). $22.95. 277 pp.

Richard Gregory, then at Cambridge University, wrote his book as "an *introduction* [his emphasis] to the psychology of vision." The period's headlong progress in research on vision and the brain would have guaranteed instant obsolescence, except that Gregory did new editions in '72, '77, and '79, then a greatly expanded edition in '97. Although in one way this is a primer, Gregory has a special slant: approaching vision through the analysis and categorization of visual illusions. In this, he is a pioneer, making the book unique (not to mention fascinating), with visual illusions to illustrate each chapter and to make you realize that deep mysteries remain.

A Vision of the Brain

By Semir Zeki. Blackwell Science Ltd. pb, 1993. $61.95. 366 pp.

We've come a long way from our grade school understanding of vision through the metaphor of a camera's lens, film, and eventual photo in hand. In decades of research on the visual cortex, Semir Zeki, a professor of neurobiology at the University of London, has come to believe that we see in order to obtain knowledge about and understand the world. In this elegant and detailed analysis of how and why we see—particularly color and motion—in a constantly changing visual environment, Zeki first reviews the historical twists and turns in studying vision. He then lays out his understanding of functional specialization, integration, and how our conscious perception of

what we see arises in the brain. Many color illustrations. Zeki is an international authority on visual arts and the brain.

7. Emotions and Behavior

Each of these books, though for somewhat different reasons, was hailed almost immediately as a classic. Sapolsky's book became a best-seller. Both LeDoux and Damasio are now cited in virtually every bibliography on the brain. Did the immediate excitement over these books owe anything to the fact that they were among the first to deal with emotions and the brain? In our survey, *The Emotional Brain* received the third-highest score of any book. Like some others on this list, it reports the author's own landmark research even as it addresses the broad topic.

The Emotional Brain: The Mysterious Underpinnings of Emotional Life

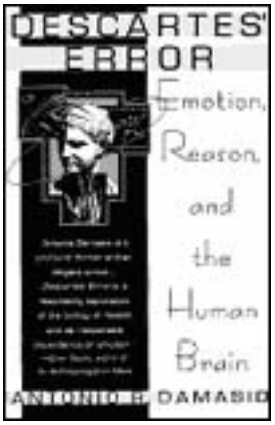
By Joseph LeDoux. Touchstone Books pb, 1998 (Simon & Schuster, 1996). $14.00. 384 pp.

Contemporary brain science did not begin by looking at emotions. Perception, even memory, seemed simpler. A couple of decades ago, this changed; publication of this book attests to the progress that has resulted. LeDoux and others traced how emotional stimuli move through the brain, and they discovered some big surprises (e.g., dual routes for reacting on red alert or more contemplatively). Building on this research, *The Emotional Brain* reasons its way through questions about the nature of emotions, conservation of emotional systems across species, conscious and unconscious emotional responses, and the relationship between feelings and emotions. LeDoux traces the history of thinking about the emotions. He set out to write for laymen, and succeeded; but that hasn't kept his book from becoming a "must cite"—a new launching pad for an entire field.

Descartes' Error: Emotion, Reason, and the Human Brain

By Antonio R. Damasio. Avon Books pb, 1995 (G.P. Putnam's Sons, 1994). $13.95. 312 pp.

The first modern European philosopher, René Descartes, saw mind and body as fundamentally separate. The idea infected Western thought with the premise that rationality and feeling, the mental and the biological, don't mix. Damasio challenges that dualism root and branch, marshaling evidence from basic and clinical research and interpreting it with rare philosophical acuity. New brain books seldom fail to reference *Descartes' Error,* suggesting an emerging classic. Reason and emotion, mind and brain, personality and biology are profoundly integrated on every level, Damasio declares—and the walls of philosophy shake. Miraculously, he makes it all eminently readable (now in 16 languages).



Why Zebras Don't Get Ulcers: A Guide To Stress, Stress-Related Diseases, and Coping

By Robert M. Sapolsky. W.H. Freeman and Company pb, 1998 (1994). $16.00. 368 pp.

Sapolsky is a scientist and science popularizer who made a big hit with this book. No surprise. Evolution of the fight-or-flight mechanism that, in a burst of physiological fireworks, can save a zebra from a lion, is often turned on—and left on—by the psychological and social stressors in our lives. Then the sympathetic nervous system's response to "danger" becomes the problem. Sapolsky explains all this, writing about glucocorticoids and insulin secretion with wit and charm. You don't have to wait for a tagged-on advice chapter; this book is a "how-to." There is a 1998 revised and updated version from Freeman with three new chapters.

8. Neurological Diseases and Disorders

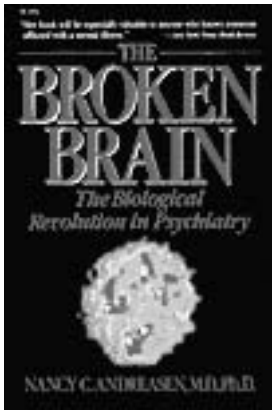
There are perhaps more books on specific diseases and disorders than on any other aspect of the brain. That is to be expected, with an estimated one out of five Americans experiencing some kind of brain-related problem. Clearly, though, scientists of the Dana Alliance took a scientific perspective on this category, voting for books that explain science rather than provide advice for patients and families. (In a future survey, a category of books for patients with brain disorders will be useful.)

The most popular writer on the brain, Oliver Sacks, is clearly a favorite with scientists as well. Two of his books are represented here. It is interesting, though, that one of the most celebrated brain books of all time, *The Man Who Mistook His Wife for a Hat*, tied for first place with a very new book, *Mood Genes,* by Samuel H. Barondes. Sacks, Barondes, Pinker, and Squire, by the way, all have two books on our list. *The Broken Brain* is another book that has survived the headlong changes in brain research for almost 15 years.

The Man Who Mistook His Wife for a Hat and Other Clinical Tales

By Oliver Sacks. HarperPerennial pb, 1990 (Simon & Schuster, 1970). $14.00. 243 pp.

Although today's best-known popular writer on the brain, Sacks has sacrificed no credibility with scientists, as attested by the two books on this list. Patients with lesions and disorders have been a crucial window on the brain for neuroscientists. In this famous book, Sacks presents a series of such cases, from Korsakov's syndrome, with its devastation of memory, to Tourette's syndrome, with its explosion of mental energy, in portraits that are profoundly revelatory and full of compassion for the afflicted individuals. Sacks, a master stylist, is a clinical neurologist at Albert Einstein College of Medicine.



Mood Genes: Hunting for Origins of Mania and Depression

By Samuel H. Barondes. W.H. Freeman and Company pb, 1999 (1998). $19.95. 237 pp.

The search is on for genes affecting complex mental disorders. These are not one-gene illnesses, nor illnesses inevitable if you have the genes. Thus the gene hunters face boggling complexities in laboratory and field. Right now the big search is for genes underlying mania and depression using linkage studies of families in Costa Rica. Samuel Barondes, a gene hunter, tells this story in terms of sufferers and scientists, bringing out the excitement, complexity, and controversies. He manages to teach science (e.g., a review of Mendelian genetics) as he goes. He concludes with frank comments on genetic testing—the risks, the hopes.

Awakenings

By Oliver Sacks. HarperPerennial Library pb, 1999 (1973). $15.00. 464 pp.

This Sacks classic is the account of victims of a decades-long sleeping sickness (encephalitis lethargica) who awaken to a new life after being treated with the drug L-dopa. As in *The Man Who Mistook His Wife for a Hat*, Sacks is able to enter into the world of someone with a neurological disease and help us understand both our common humanity and the medical science.

The Broken Brain: The Biological Revolution in Psychiatry

By Nancy C. Andreasen. HarperPerennial pb, 1985 (Harper & Row Publishers, Inc., 1984). $15.00. 278 pp.

In 1984 you could publish a book revealing that along with psychoanalysis and behavioral therapy there was something called "biological psychiatry," concerned with the "broken brain" (not the "troubled mind")—and have this book hailed as "must" reading for physicians. Andreasen, a distinguished psychiatrist, wrote that book, introducing it with chapters on the history of mental illness, the brain, the four major syndromes, diagnosis, treatment, and research. Many authors claim to write for laymen; Andreasen, a former English teacher, really did. Her subtext is that mental illness is a disease, no more shameful than cancer. Andreasen wrote that, in 1983, ideas whose expression she drafted in 1982 had become outdated, but 18 years have not dimmed the popularity of her book.

9. Memoirs and Personal Experience

Kay Redfield Jamison's *An Unquiet Mind* received the second-highest total score in our survey. One well-known scientist wrote to us that Jamison's book should be in the category "Neurological Diseases and Disorders" because it is not only a memoir but also an important contribution to understanding bi-polar disorder. (Jamison is coauthor with Frederick Goodwin of *Manic-Depressive Illness*, one of the best-known textbooks on bipolar disorder.) This is a valid comment, but it applies to all three highly personal memoirs in this category. Alice Wexler and Temple Grandin are not neuroscientists, but both are conversant with the scientific side of the stories they tell. Their books, like Jamison's, view a brain disorder from the inside with the trained eye of a scholar or a scientist.

An Unquiet Mind: A Memoir of Moods and Madness

By Kay Redfield Jamison. Alfred A. Knopf pb, 1997 (1995). $12.95. 224 pp.

Kay Jamison, professor of psychiatry at Johns Hopkins University and authority on manic-depressive illness, told the world with this book what only her colleagues knew—that she herself suffered from the illness. The brilliance and insight with which she told her story of a childhood, education, loves, and career laced with horrifying bouts of mania and depression became exhibit number one for her thesis: This illness can woo its victims with exalted flights of mind so exhilarating that taking lithium to save their sanity can become an agonizing decision. In this best-seller, Jamison makes that issue real for us—in personal, poetic, and scientific terms—as no other writer ever has.

The History of Neuroscience in Autobiography, Vols. 1 and 2,

Edited by Larry R. Squire. Society for Neuroscience, 1996 and 1998. $58.95/volume. 607 pp. 433 pp.

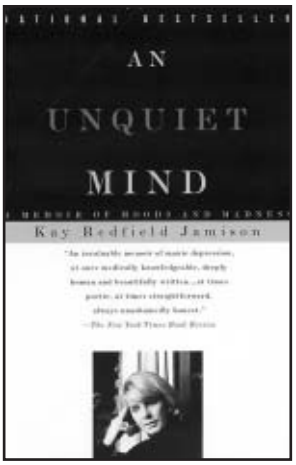
As president of the Society for Neuroscience, Larry Squire, a pioneer of memory research, conceived of this series and edited both volumes. Well-known neuroscientists from America and Europe contributed (17 in volume 1, 13 in volume 2), supposedly assigned to write autobiography, not a scientific article. Outcomes varied, with pieces running from fairly autobiographical (Herbert H. Jasper) to mostly scientific (Sir Bernard Katz). Still, this was a first attempt to get neuroscientists to write autobiography. The shorter second volume, two years after the first, eliminated technical material. There are good photographs of each scientist.

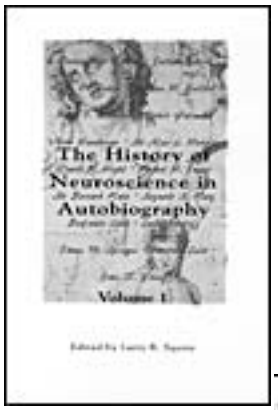
We have a tie for third place in this category. Both books are reviewed.

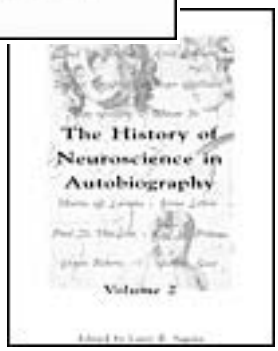
Mapping Fate: A Memoir of Family, Risk, and Genetic Research

By Alice Wexler. University of California pb, 1995. $18.95. 321 pp.

Genetic research is the ground of many of modern science's most compelling true-life adventure stories. In *Mapping Fate*, Alice Wexler skillfully interweaves the heartbreaking story of her family's odyssey with Huntington's disease—which killed her mother—and the dramatic, suspenseful, and eventually triumphant scientific search for the Huntington's gene, spearheaded by her sister Nancy and her father, Milton. The ethical, philosophical, and emotional issues of having a hereditary fatal illness, and being able to test for the gene before there is a cure, become inescapably personal in Wexler's beautifully written account.







Thinking in Pictures: And Other Reports from My Life with Autism

By Temple Grandin. Vintage Books pb, 1996 (Doubleday, 1995). $12.95. 222 pp.

This is not a book about the experience and science of autism, but an extraordinary report from deep within that seemingly unfathomable world. Temple Grandin, Ph.D., is a gifted animal scientist who has designed many of the livestock-handling facilities in the United States and who lectures widely on autism because she herself is autistic. She lucidly describes how she experiences and understands her world, and how she builds bridges to ours, and in so doing teaches us much not only about autism but also about thinking and feeling in animals and in ourselves.

10. The Brain in Relation to Other Fields

Our intention in creating this category was to find books that examine the implications of brain research for other fields—a central part of *Cerebrum*'s mission. Whether this took place in the nominating and voting the reader will decide. John R. Searle, a professional philosopher, is in a different field, but it is clear that his book is about the brain and easily could have been in our category "Consciousness." (Searle is the only professional philosopher on our list. That seems extraordinary, given the attention that philosophers and others have paid to the mind-brain question.)

Readers may wonder why *Neuronal Man* is in this category. Perhaps it is because Jean-Pierre Changeux is well known for his philosophical theory of "eliminative materialism," or because he states explicitly that his approach is "interdisciplinary." *The Placebo Effect*, edited by Anne Harrington, is literally an interdisciplinary work by multiple authors from different fields.

The Rediscovery of the Mind

By John R. Searle. MIT Press pb, 1992. $21.95. 270 pp.

This book is about the philosophy of mind, not the brain. How one chooses to study the brain, however, depends on one's view of mind. Searle's view is that mind is consciousness, which (however complex its emergence in the brain) is a natural phenomenon to be studied, not explained away or reduced to neural nets or "intelligent behavior." Having rejected materialism and dualism, and having admitted consciousness to the natural world, Searle analyzes its nature. His arguments are cogent, as is his dissection of materialism, which irks cognitive scientists whose investigations avoid all reference to mental life. But to study the brain while dismissing consciousness, says Searle, is like studying biology while explaining away the inconvenient emergence of life. Searle's prose is pellucid but does not make these matters escapist reading.

Neuronal Man: The Biology of Mind

By Jean-Pierre Changeux. Princeton University Press pb, 1997 (Fayard, 1983). $22.95. 348 pp.

Changeux, a distinguished French neurobiologist, wrote an introduction to neuroscience for general readers that became celebrated in Europe. He devotes more than the usual attention to history (the first known mention of the brain dates to 3000 B.C.) and to cross-species comparisons that probe why human brains are so relatively capable. Unlike some introductions to the brain, *Neuronal Man* has few illustrations, none in color, despite Changeux's reputation as an art collector and authority. It does have a glossary and an extensive bibliography. The 1997 Princeton Science Library edition has a brief preface by Vernon B. Mountcastle, the dean of physiological neuroscientists.

The Placebo Effect: An Interdisciplinary Exploration

Edited by Anne Harrington. Harvard University Press pb, 1999 (1997). $22.00. 260 pp.

Medical science has traditionally been uncomfortable with the paradox of placebos: "sham" treatments that can produce real, even dramatic, effects on healing. This insightful collection of essays and dialogue, based on a 1994 Harvard conference, confronts the dilemma—and the discomfort—head on. Looking at placebos from viewpoints as diverse as neuropharmacology and anthropology, molecular biology and religion, the contributors place placebos at the intersection of biology and culture, with much to teach us about the interaction of our minds and bodies.

11. Books for Children and Young People

We included this category in our call for nominations but netted nothing. Undaunted, we put the category in the survey itself, with plenty of room for write-ins. Below is a complete enumeration, with comments, of the few entries we received for ages 9-12. Obviously there are promising avenues, outside the scope of this survey, to search for children's books on the brain.

Brain Surgery for Beginners and Other Major Operations for Minors

By David West and Steve Parker. Millbrook Press, 1995, $9.99.

Focus on Drugs and the Brain (A Drug Alert Book)

By David Friedman and David Neuhaus. Twenty-First Century Books, 1991, $2.50.

The Body Book

Illustrated by Sara Bonnett Stein. Workman Publishing Co., 1992, $11.95.

12. Historical Classics

In this category we sought nominations for books from earlier eras that made an enduring contribution to brain science. *Cerebrum* asked scientists to consider books published before World War II—that is, before the era of modern neuroscience—but going back as far as they wished. What about Aristotle? What about John Locke's *Essay Concerning Human Understanding*? What about *The Anatomy of Melancholy*? For that matter, what about Sigmund Freud, an author who received not a single nomination?

In the nominations, a few early scientists were suggested (such as Aleksandr Luria), but none before the late nineteenth century. Our guess is that scientists interpreted "brain" and "science" rather literally, limiting their recommendations to professional scientists. Donald Hebb scored just one point lower than William James; Hebb is a figure who spans World War II, publishing his classic *The Organization of Behavior* in 1949. This book is now out of print.

Recollections of My Life

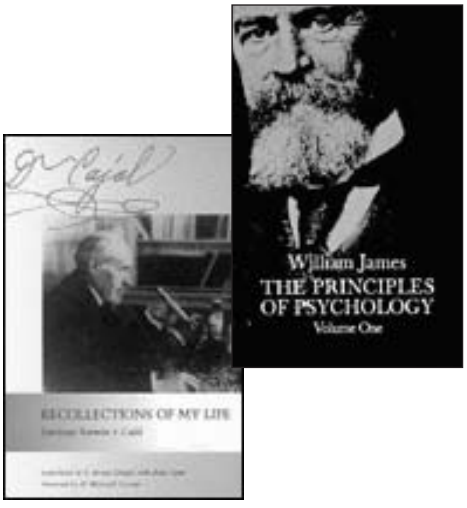
By Santiago Ramon y Cajal. MIT Press pb, 1996. (Published 1901-1917 in Madrid). $29.95. 638 pp.

One "founder" of neuroscience is Ramon y Cajal, a Spanish histologist born in 1852 whose massive writings and superb drawings are still the most cited sources on the nervous system. *Recollections* is the story not only of his methods (he perfected Golgi staining) and chief discoveries, but of the astonishing life that began with boyhood rebellions and rose to every triumph, including the Nobel Prize (with Camillo Golgi) in 1906. The 1989 MIT Press paperback has a foreword by W. Maxwell Cowan, who opines that Cajal's is one of only two pre-World War II autobiographies of biologists still worth reading: an "astonishingly frank and engaging account of one man's single-minded endeavor to understand the most complex of all biological issues, the organization and function of the nervous system." The book lists 288 scientific publications by Cajal, including many books.

The Principles of Psychology

By William James. Dover Publications pb, 2 vol., 1955 (Henry Holt & Co., 1890). $16.95/volume. 689 pp.

In his monumental "long course," James devoted fewer than 100 pages to the brain because little was known. "Chemical action must of course accompany brain activity," he writes at one point, "but little definite is known of its exact nature." Then he turned to "the Science of Mental Life" and never had such a persistent, discriminating eye been focused inward and what it saw reported by so careful and erudite a scientist. Stream of thought, consciousness of self, attention, conception, perception of time, memory: each aspect of mental life was analyzed, categorized, and conceptualized. Much remains valid—and not infrequently used as the starting point of discussions today—because James knew and honored the difference between observation and interpretation.



The Organization of Behavior: A Neuropsychological Theory

By Donald O. Hebb. (John Wiley, 1949). $50.00.

Hebb, a pioneering psychologist at the University of Montreal, is remembered for famous experiments in sensory deprivation but, most of all, for his statement of the principle that coactivation of neurons is required to strengthen the synaptic connection. This is cited in most accounts of learning theory and is called "Hebb's Rule" (although it probably preceded Hebb, Vernon Mountcastle suggests in his recent *Perceptual Neuroscience*). *The Organization of Behavior* was Hebb's culminating report to the world on his work and is still a classic.

—By the editors of *Cerebrum* ■

Great Literary Portrayals of Brain Disorders

By Marcia Clendenen and Dick Riley

Marcia Clendenen has been a psychotherapist in private practice for 25 years and is an instructor in psychology at Dominican College in New York.

Dick Riley is an author of fiction and nonfiction, including *The Bedside, Bathtub, and Armchair Companion to Sherlock Holmes* (Continuum Publication Group, 1998) written with Pam McAllister.

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"Nobody else suspected he was going crazy," reflects Billy Pilgrim in Kurt Vonnegut's *Slaughterhouse 5.* "Now he was in the hospital. The doctors agreed: He was going crazy."

As Billy gradually manifests the classic symptoms of full-blown posttraumatic stress disorder (PTSD), Vonnegut's novel takes us deep inside a disordered mind. If the best nonfiction, including "The Great Brain Books" (*Cerebrum*, Spring 1999), can inform and inspire, great fiction can recreate for us the experience of madness. With the generous help of scientists, scholars, and editors, we have culled a baker's dozen of the most compelling novels, short stories, and fictionalized memoirs of the past 200 years that create characters with what (at least in retrospect) we can identify as brain disorders. We particularly thank Richard Restak, M.D., for many helpful insights and suggestions relating to the literary selections and the brain disorders discussed in this article.

Some authors write from direct personal experience: Fyodor Dostoevsky of epilepsy, Sylvia Plath of depression, F. Scott Fitzgerald of alcoholism, and William Burroughs of heroin addiction. Others rely on observation, imaginative projection, and perhaps partial identification: Vonnegut's portrayal of posttraumatic stress in *Slaughterhouse 5* or Conrad Aiken's story of a child's withdrawal into an autistic state in "Silent Snow, Secret Snow."

Still others achieve unique insights through the eyes of schizophrenics (Timothy Findley's *Headhunter*) or the mentally retarded (Daniel Keyes's *Flowers for Algernon*), and even discover humor in the afflicted character (Charles Dickens's narcoleptic servant boy, Joe, in *The Pickwick Papers*, who "goes on errands fast asleep, and snores as he waits at table").

Ours is far from an exhaustive account of brain diseases in literature (Shakespeare alone could yield nearly as many), but these selections constitute a respectable cross section of popular

19th- and 20th-century fiction in which brain disease plays a prominent role.

Stories of characters who struggle with mental illnesses—from alcohol and drug addiction to depression and post-traumatic stress—continue to resonate with readers. Many of these works were best-sellers. The novels of Kurt Vonnegut and Sylvia Plath became icons of the antiwar and feminist movements; Kafka and Burroughs, while appealing to a narrower and more literary audience, still sell respectably; the works of Dickens and Dostoevsky are, of course, classics. The characters described here are indeed, as the poet C. Day Lewis terms it, going "mad in good company."

The works are discussed here in historical order, each author's understanding of a character's problems reflecting the era in which that author wrote. The recent extraordinary explosion of knowledge about the brain means that even a work as recent as Mark Vonnegut's *The Eden Express* (1975) includes what psychiatrists would now term a misdiagnosis (in this case, bipolar disorder is mistaken for schizophrenia). To put these works in a current clinical context, we have compared the characteristics and behavior of the characters to the symptoms described in the 1994 edition of the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders*, or DSM-IV, the standard descriptive and cataloging text for mental ailments.

The Pickwick Papers

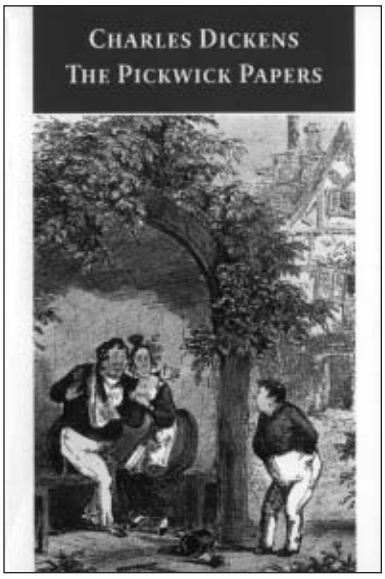
By Charles Dickens. Penguin USA pb, 2000 (1837). $11.00. 848 pp.

Among the most memorable of the many comic characters Dickens introduces in *The Pickwick Papers* is Joe, the narcoleptic servant of Mr. Tupman. Pickwick first meets Joe on the back of Tupman's carriage during an outdoor festival that includes a mock battle.

"On the box sat a fat and red-faced boy, in a state of somnolency" who, immediately after he got down to open the door of the carriage, "waddled to the same perch and fell fast asleep instantly...as if the roaring of cannon were his ordinary lullaby." Mr. Tupman has thoughtfully equipped the back of his carriage with a safety device for Joe, who, "if there had been a footboard instead, would have rolled off and killed himself in his very first nap."

As a servant, Joe has obvious drawbacks.

"Very extraordinary boy, that...does he always sleep in this way?" Mr. Pickwick wonders.



"Sleep," said the old gentleman, "he's always fast asleep. Goes on errands fast asleep, and snores as he waits at table."

Sent to find someone for Mr. Tupman, Joe bangs on the door of a room.

The object that presented itself to the eyes of the astonished clerk was a boy—a wonderfully fat boy—habited as a serving lad, standing upright on the mat, with his eyes closed as if in sleep. He had never seen such a fat boy, in or out of a traveling caravan....

"What's the matter?" inquired the clerk.

> The extraordinary boy replied not a word; but he nodded once, and seemed, to the clerk's imagination, to snore feebly.
>
> "What the devil did you knock in that way for?" inquired the clerk, angrily.
>
> "Because master said I wasn't to leave off knocking till they opened the door, for fear I should go to sleep," said the boy.

According to the DSM-IV, Joe's symptoms closely match those of narcolepsy: "repeated irresistible attacks of refreshing sleep." The element of irresistibility is critical to the syndrome, and the sufferer's sleep episodes are said to last 10 to 20 minutes but can go on for as long as an hour. Joe's ability to function may also be tied to what the DSM describes as "automatic behavior, in which the individual engages in activity without full awareness...individuals may drive, converse, or even work."

Despite Joe's faults, his employer seems to value him. Says Mr. Tupman, "I'm proud of that boy—wouldn't part with him on any account—he's a natural curiosity."

Perhaps the "natural curiosity" arises from the novelty of Joe's condition. According to the DSM-IV, narcolepsy—particularly in the extreme form exhibited by Joe—is rare; it would have occurred in as few as 3,600 of the approximately 18 million people in England and Wales at the midpoint of the 19th century.

The Idiot

By Fyodor Dostoevsky. Everyman's Library pb, 2002 (1869). $23.00. 672 pp.

As *The Idiot* opens, Prince Myshkin is returning to Russia from Switzerland, where he has been living for more than four years, for medical reasons. "His eyes were large and pale blue, and their intent gaze held at once something gentle and saturnine, filled as they were with that odd expression by which some people can detect epilepsy at a glance." Later, Dostoevsky describes Myshkin about to be attacked by a man with a knife:

> Then all at once everything seemed to open up before him: an extraordinary inner light flooded his soul. That instant lasted, perhaps, half a second, yet he clearly and consciously remembered the beginning, the first sound of a dreadful scream which burst from his chest of its own accord and which no effort of his could have suppressed. Then consciousness was extinguished instantly and total darkness came upon him.
>
> He had suffered an epileptic fit, the first for a very long time. As is well known, attacks of epilepsy, the notorious falling sickness, occur instantaneously. In that one instant the face suddenly becomes horribly contorted, especially the eyes. Spasms and convulsions rack the entire body and all the facial features. A frightful, unimaginable scream, quite unlike anything else, bursts from the chest.

The fit saves Myshkin's life. Unnerved by the sight of his convulsions, the attacker flees.

Myshkin's epilepsy is both a medical problem and a metaphor for the innocence that sets him apart: an otherworldliness that contrasts with the competitiveness and materialism of the people around him. This is consistent with the sense of transcendence that often affects people (like Dostoevsky himself) who have temporal lobe epilepsy:

> Amid the sadness, spiritual darkness and oppression, there were moments when

> his brain seemed to flare up momentarily and all his vital forces tense themselves at once in an extraordinary surge. The sensation of being alive and self-aware increased almost tenfold. ...His mind and heart were bathed in an extraordinary illumination...all his doubts and anxieties seemed to be instantly reconciled and resolved into a lofty serenity, filled with pure, harmonious gladness and hope...with the consciousness of the ultimate cause of all things.

Unfortunately, these moments "were merely the prelude to that final second (never more than a second) which marked the onset of the actual fit."

Born in 1821, Dostoevsky became linked with the forces of political reform in Russia. He and a group of friends were arrested for political activity, tried, and sentenced to death. In a dreadful charade, with Dostoevsky already on the scaffold, the sentence was commuted and he was sent to prison in Siberia. There he experienced his first epileptic seizure. Although he was a Russian nationalist, he left Russia for Europe in 1868 and there wrote *The Idiot* to help pay off his gambling debts. Dostoevsky's own epilepsy was particularly acute as he was writing the novel.

"A Hunger Artist"

By Franz Kafka, Twisted Spoon Press, 1996 (1924). $13.50. 88 pp.

"During these last decades the interest in professional fasting has markedly diminished," begins Franz Kafka in his short story "A Hunger Artist." He goes on to paint a world where at one time "the whole town took a lively interest in the hunger artist...everybody wanted to see him at least once a day" in his barred cage set up in some prominent place, a public production orchestrated by "the impresario":

> The longest period of fasting was set up by his impresario at forty days, beyond that he was not allowed to go, not even in great cities, and there was good reason for it, too. Experience had proved that for about forty days the interest of the public could be stimulated by a steadily increasing pressure of advertisement, but after that the town began to lose interest.

So frail would Kafka's hunger artist become by the end of his performance that he could not stand. He would have to be helped out of his cage and to a table upon which was laid "a carefully chosen invalid repast." The artist, "in a kind of half-fainting trance," would force himself to eat to the accompaniment of band music, after which "the spectators melted away, and no one had any cause to be dissatisfied with the proceedings, no one except the hunger artist himself." His dissatisfaction is not from the starvation, though, but from annoyance with the audience's failure to appreciate the deep nature of his art and with the rules that prevent him from taking his fast beyond 40 days.

We would not expect to find a great deal of clinical detail in "The Hunger Artist," which is really an extended metaphor, but Kafka is accurate in noting, through the reflections of bystanders at the performance, that the artist's "melancholy was probably caused by fasting." When this is pointed out to him, however, the artist reacts "with an outburst of fury and to the general alarm beg[ins] to shake the bars of his cage like a wild animal."

Those who willingly starve themselves are defined by the DSM-IV as having anorexia nervosa. There are two major types: patients who restrict what they eat and patients who engage in binge eating and then purging, either by vomiting or using laxatives. Certainly the hunger artist exhibits behaviors mentioned in the DSM, including "depressive symptoms such as depressed mood, social withdrawal, irritability, insomnia."

Anorexia is most prevalent among girls and young women, peaking in individuals

between 14 and 18 years of age. The disorder is serious; among patients admitted to university hospitals, long-term mortality is more than 10 percent Kafka's hunger artist, freed from the restraints imposed by his impresario, starves himself to death.

Mrs. Dalloway

By Virginia Woolf. Harvest Books, 1990 (1925). $12.00. 216 pp.

Mrs. Dalloway takes us through one day in the life of Clarissa Dalloway, an upper-class Englishwoman married to a government minister. Although beneath her serene exterior flow currents of conflict and unhappiness, Mrs. Dalloway's life is contrasted with the tragic story of another major character, Septimus Warren Smith.

The novel is set in 1923, five years after the end of World War I (the "Great War" to the English at the time). Smith had served in the war, and "developed manliness; he drew the attention, indeed the affection of his officer, Evans by name." Yet "when Evans was killed, just before the Armistice, in Italy, Septimus, far from showing any emotion or recognizing that here was the end of a friendship, congratulated himself upon feeling very little and very reasonably."

The effects of his experience creep up on him after the war, however. "For now that it was all over, truce signed, and the dead buried, he had, especially in the evening, these sudden thunder-claps of fear....There were moments of waking in the early morning. The bed was falling; he was falling."

His reaction becomes worse when he returns to England; even the literature that had once meant so much to him has lost its appeal. Reading Shakespeare, he discovers "the message hidden in the beauty of words. The secret signal which one generation passes, under disguise, to the next is loathing, hatred, despair."

A day in a London park overwhelms him. "A sparrow chirped Septimus, Septimus, four or five times over and went on, drawing its notes out, to sing fresh and piercingly in Greek words how there is no crime...from trees in the meadow of life beyond a river where the dead walk, how there is no death."

He hears people talking behind the bedroom walls, sees a woman's head in the middle of a fern, talks constantly of death and suicide. His doctor thinks Smith suffers only from obsessive introspection; his Italian wife is mystified and overwhelmed by his mental problems. "Now we will kill ourselves," he announces as they are standing by a river, "and he looked at it with a look which she had seen in his eyes...a look as if something fascinated him; and she felt he was going from her and she caught him by the arm." After contemplating suicide by knife, razor, and gas, Smith eventually throws himself out a window.

Given the lack of symptoms before his military service, and the stresses of combat, it seems obvious that Septimus Smith is suffering from "shell shock," the term then applied to post-traumatic stress disorder. The DSM lists "intense psychological distress," along with "markedly diminished interest in significant activities" and "detachment or estrangement from others" as part of that syndrome.

The vivid passages describing Smith's depression and hallucinations no doubt owe much to Virginia Woolf's own bouts with depression and perhaps schizophrenia. Woolf had two nervous breakdowns in her youth, and in 1913 attempted suicide. She was in and out of mental institutions for two years, but recovered and went back to writing. By the late 1920s, she had become a significant literary figure, though continually struggling with health problems, including debilitating headaches and insomnia. In 1941, feeling a return of the voices and delusions that had earlier so troubled her mind, she filled the pockets of her dress with rocks and walked into a river to drown.

"Silent Snow, Secret Snow"

By Conrad Aiken. The Creative Company, 1983 (1934). 48 pp. (Out of print. Used copies available online.)

In his short story "Silent Snow, Secret Snow," Conrad Aiken portrays a 12-year-old boy, Paul Haselman, slipping into an autistic state—a progression from apparent normality to a state of consciousness that excludes all contact with the world.

As Paul is overtaken by autism, we see the world through his eyes—the little girl who sits in front of him in school has "a funny little constellation of freckles in the back of her neck, exactly like the Big Dipper"—and through his ears: the postman's footsteps are closer and softer because of the secret snow that begins to fill the world. Although it is not winter, every day the snow accumulates, making that world more silent, more remote. Paul surrenders as though to a delicious secret that envelops his consciousness. His parents, though concerned, become increasingly peripheral. Paul sees his condition progressing and knows that he will lose one world as he is drawn into another.

He does not have conventional infantile autism, which strikes very young children, who are never symptom-free after the age of two. Aiken's evocation of the state seems accurate, however, especially Paul's inability to communicate or sustain relationships at even a minimal level.

The story ends with Paul's interrogation and examination by the family doctor in the presence of his parents. Paul avoids the doctor's eyes ("marked impairment in the use of multiple nonverbal behaviors such as eye-to-eye gaze" is one of the DSM's criteria for autism) or else stares, preoccupied with the light in his pupils. Finally he stands sideways, smiling at the secret snow filling the corners of the room. His father becomes "the brown slippers" with the "well-known punishment voice, resonant and cruel." His laughter horrifies his mother.

Paul flees to his room, where the snow encompasses him in a roar. His mother's efforts to pull him back fill him with loathing. He experiences them as cruel, and withdraws from her into the cold, remote, and peaceful snow—to sleep.

As a child, Aiken saw his father kill his mother and then commit suicide. He was raised by relatives, graduated from Harvard in 1910, and became a successful writer. It is easy to speculate that this exquisitely written account is his imaginative projection of an autistic state he may have begun to enter in the wake of his awful trauma—to shelter himself from his pain and the morbid curiosity of others.

While no traumatic event is mentioned in "Silent Snow, Secret Snow," the story could be describing a posttraumatic stress reaction in the form of an autistic state. The course of Aiken's life suggests that he did not withdraw from the world as Paul did, but his temptation to do so may well have become the realistic kernel of this haunting narrative.

Tender Is the Night

By F. Scott Fitzgerald. Scribner 1995 (1934). $12.00. 320 pp.

When Nicole and Dick Diver meet in *Tender Is the Night*, he is a young psychiatrist with a brilliant career and she is a beautiful 16-year-old girl deposited in a Swiss mental hospital by her wealthy father, who declares, "she is not right in the head."

To Nicole, all men are evil (she accuses Dick's valet of improper

advances, for example). She has been diagnosed as schizophrenic, but her doctor, sensing a falsity in her father, has his doubts about this diagnosis of "the young bird with wings crushed." He demands a return visit from her father who, confronted, confesses incest with Nicole. Her doctors take action to protect her from her father and release her to Dick Diver, with whom she has been corresponding (and creating a psychodynamic "father transference"). Dick restrains himself, at first, but then succumbs to his desire for her and they marry. The compromise in his professional ethics begins his decline; he is doomed to be the incestuous father figure in their marriage.

Nicole alternately clings, goes mad, and recovers. Dick blames and reproaches her, refuses to take responsibility for his own actions, and begins drinking. We observe the downward spiral and professional ruin of a man once full of promise.

Fitzgerald suffered from alcoholism; his wife, Zelda, was diagnosed as schizophrenic and hospitalized. Fitzgerald seems to want us to believe that Dick's drinking, although problematic, is his way of coping with problems outside his control, rather than (as defined by the DSM-IV) a serious, progressive disease in and of itself. Dick insults friends when he is inebriated. A patient accuses him of having alcohol on his breath, and his associate, Dr. Gregorious, asks him to take "a leave of abstinence." The DSM-IV criteria for diagnosis of substance abuse include "failure to fulfill major role obligations at work."

This is the death knell for Dick Diver professionally. His drinking increases, his problems multiply. Close friends become alienated, as in the DSM-IV description: "persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance." Beneath the surface of all Dick's drinking and partying is desperation. Nicole comes to see him as weak and flawed and leaves him for a man with whom she has no history of psychological transference. Dick is left to a life of small jobs in small towns, punctuated by scandals.

Tender Is the Night, published in 1934, was the last novel Fitzgerald completed. His life had taken a downward turn, personally and professionally, after publication of *The Great Gatsby* in 1925. He ended up in Hollywood, writing movie scripts.

Junky

By William S. Burroughs. Penguin USA pb, 2003 (1953). $14.00. 158 pp.

"Junk is not a kick. It is a way of life," says novelist William S. Burroughs in *Junky,* his "memoir of a life of addiction":

> The addict himself has a special blind spot as far as the progress of his habit is concerned. He generally does not realize that he is getting a habit at all....I have talked to many addicts and they all say they were surprised when they discovered they actually had the first habit. Many of them attributed their symptoms to some other cause.

Burroughs's plain language and matter-of-fact tone cast his recollections in an unsparing light:

> You become a narcotics addict because you do not have strong motivations in any other direction. Junk wins by default. I tried it as a matter of curiosity. I drifted along taking shots when I could score. I ended up hooked....You don't decide to be an addict. One morning you wake up sick and you're an addict.

Burroughs grew up in a middle-class family in the Midwest, graduated from college, drifted around Europe in the mid-1930s on the proceeds of a trust fund, and finally returned to the United States. He started using morphine stolen from a shipyard during World War II, then graduated to more and different drugs. His memoir omits few of the DSM-IV signs of the substance abuser,

including "failure to fulfill major role obligations at work, school, or home," not to mention "recurrent substance-related legal problems" and "continued substance use despite having persistent or recurrent...problems caused or exacerbated by the effects of the substance."

Much of *Junky* deals with the seamy side of hustling for the drug, scrapes with the law, and the trauma of repeated withdrawals from addiction:

> It is possible to detach yourself from most pain....From junk sickness there seems to be no escape. Junk sickness is the reverse side of junk kick....I was too weak to get out of bed. I could not lie still. In junk sickness, any conceivable line of action or inaction seems intolerable. A man might simply die because he could not stand to stay in his body.

Junky follows Burroughs through years of on-and-off addiction and "cures," including a session at the federal hospital at Lexington, Kentucky, which specialized in treating narcotics addiction. *Junky* was published in 1953 under the pseudonym William Lee.

Burroughs is regarded as a standard-bearer of the Beat movement. He went on to write *Naked Lunch* and other works, including *The Yage Letters*—a collection of correspondence between him and the Beat poet Allen Ginsberg, as Burroughs pursued in South America an Amazonian hallucinogen known as yage.

In the 1930s, Burroughs went through three years of psychoanalysis. "Analysis removed inhibitions and anxiety so that I could live the way I wanted to live," he wrote. "Much of my progress in analysis was accomplished in spite of my analyst.... I was more pleased with the results than he was."

The Bell Jar

By Sylvia Plath. Perennial pb, 2000 (1963). $12.95. 288 pp.

The Bell Jar is the story of Esther Greenwood, a young lady of respectable New England background but limited economic means, whose sojourn in Manhattan one summer during college is made possible by winning a contest sponsored by a fashion magazine. In Esther's opening words: "It was a queer, sultry summer, the summer they electrocuted the Rosenbergs, and I didn't know what I was doing in New York."

The novel follows Esther through her adventures in the New York City of the 1950s, dating experiences that leave her empty, her return home to the Boston suburbs to her widowed mother, and a long mental decline. In the aftermath of rejection from a writing program, she becomes too depressed to sleep or even read. Staring at her book, she begins to hallucinate:

> The letters grew barbs and rams' horns. I watched them separate, each from the other, and jiggle up and down in a silly way. Then they associated themselves in fantastic, untranslatable shapes, like Arabic or Chinese.

At the beach with friends, she feels her rigid exterior cracking. "I was afraid that any moment my control would snap, and I would start babbling about how I couldn't read and couldn't

write and how I must be just about the only person who had stayed awake for a solid month without dropping dead from exhaustion."

Esther fits many of the DSM criteria for depressive personality disorder, including "dejection, cheerlessness, joylessness" and "brooding and given to worry." She begins electroshock therapy as an outpatient, but her obsession with thoughts of death worsens. She contemplates suicide by opening her veins, but cannot go through with it; by drowning herself in the ocean, but she keeps bobbing to the surface; by hanging herself, but she is unable to find a way to do it effectively.

Finally, when her mother is out of the house, she discovers a bottle of sleeping pills that her mother has locked away. She pours herself a glass of water and retreats to the basement, where she starts swallowing the pills:

> At first nothing happened, but as I approached the bottom of the bottle, red and blue lights began to flash before my eyes. The bottle slid from my fingers and I lay down. The silence drew off, baring the pebbles and shells and the tatty wreckage of my life. Then, at the rim of vision, it gathered itself, and in one sweeping tide, rushed me to sleep.

This suicide attempt fails, too, but sets off a long round of hospitalizations and treatments, including insulin therapy and more electroshock.

The Bell Jar, originally published in England under the pseudonym Victoria Lucas, is thinly disguised autobiography. In 1953, Plath, a successful student at Smith College, spent part of the summer working for *Mademoiselle* magazine in Manhattan, returned to suburban Boston to a mental breakdown, then was hospitalized. She eventually returned to Smith, graduated summa cum laude, and won a Fulbright grant. In England, she married the British poet Ted Hughes, and began writing poems herself. She was separated from him, and living in a house in London where the Irish poet William Butler Yeats had once lived, when she killed herself in 1963.

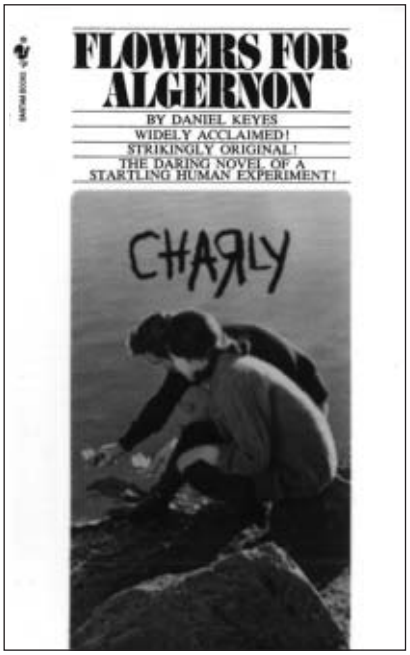
For all its grim subject matter, *The Bell Jar* is full of humor, particularly in its opening passages, and has been described as a female version of the adolescent rite-of-passage novel *A Catcher in the Rye*. Enormously popular, it has sold more than three million copies.

Flowers for Algernon

By Daniel Keyes. Skylark pb, 1984 (1966). $6.50. 224 pp.

Charlie Gordon is a 32-year-old mentally retarded man who becomes a genius, thanks to a sketchily described new treatment, only to have the process reverse itself. Charlie himself narrates his transformation from a bakery janitor with an intelligence quotient of 68 to a man with an "intelligence that can't really be calculated."

From the crude spelling and painful effort of his first journals, the reader follows him through an intellectual explosion that takes him well beyond the capabilities of the neurosurgeons who created his new mind. But the emotional isolation that he knew as a retarded man accompanies him in his new life, since his intelligence is so great that he has no one with whom he can communicate as an intellectual equal. Ironically, his brilliance also enables him to detect a flaw in the experimental method used to increase his IQ. He anticipates—and then lives through—a gradual decline back to his low level of intelligence.



> I want to be smart. My name is Charlie Gordon I werk in Donners bakery

where Mr Donner gives me 11 dollers a week and bred or cake if I want. I am 32 yeres old and next munth is my birthday. I tolld dr Strauss and perfesser Nemur I cant rite good but he says it don't matter he says I shud rite just like I talk....

The same thing happened when I tried to discuss Chaucer with an American literature specialist, questioned an Orientalist about the Trobriand Islanders, and tried to focus on the problems of automation-caused unemployment with a social psychologist who specialized in public opinion polls on adolescent behavior. They would always find excuses to slip away, afraid to reveal the narrowness of their knowledge....

Anyway I bet Im the frist dumb persen in the world who found some thing inportent for sience. I did somthing but I don't remembir what...

Flowers for Algernon (the name refers to a mouse that underwent the same experimental brain treatment) was originally published in 1959 as a short story in *The Magazine of Fantasy and Science Fiction*, and won a Hugo science fiction award. Widely anthologized, it was first adapted as a drama for the *U.S. Steel Hour* on television as *The Two Worlds of Charlie Gordon*, starring Cliff Robertson, then as a feature film for which Robertson won an Academy Award. It was adapted again for television in 1999.

An individual with an IQ of 68 would be classified under DSM 317, Mild Mental Retardation. "As a group, people with this level of mental retardation typically develop social and communication skills...have minimal impairment in sensorimotor areas...can acquire academic skills up to approximately the sixth-grade level...usually achieve social and vocational skills adequate for minimum self-support." The DSM-IV lists both biological and psychosocial factors as potential causes of mental retardation. These include genetic abnormalities; prenatal changes due to toxins; pregnancy problems such as fetal malnutrition; childhood trauma such as lead poisoning; and environmental influences, including deprivation of nurturance and of social, linguistic, and other stimulation.

Among other books by Daniel Keyes, who earned his undergraduate degree in psychology, is *The Minds of Billy Milligan*, a nonfiction book about a man with multiple personality disorder.

Slaughterhouse Five

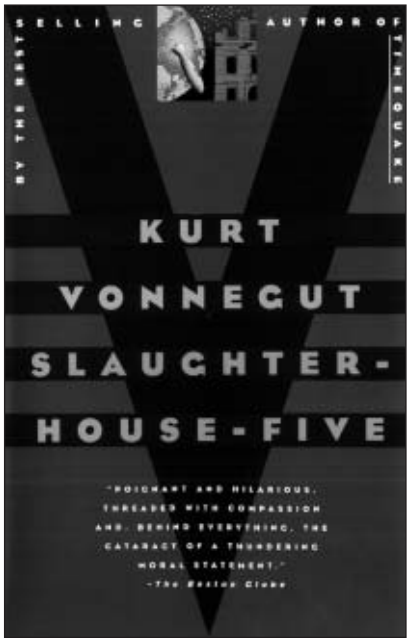
By Kurt Vonnegut. Dell pb, 1991 (1969). $7.50. 224 pp.

In World War II, Kurt Vonnegut served in the U.S. Army, was captured in the Battle of the Bulge, and was a prisoner of war in the German city of Dresden when the city was utterly destroyed from round-the-clock raids by British and American bombers. As many as 135,000 people may have died in the firebombing, a death toll worse than in Hiroshima.

This novel tells in a nonlinear narrative of the capture of a young soldier, Billy Pilgrim, and his survival in a meat locker deep below the place where the prisoners are billeted. This is *Schlachthof-funf*, or Slaughterhouse Five. The story also bounces back and forth between Billy's life after the war as an optometrist in upstate New York and (being as well a kind of science fiction) his kidnapping by aliens to the planet Tralfamadore.

Twice in the novel Billy Pilgrim finds himself hospitalized. The first time is after he has been separated from his unit, wandered for three days in the snow, been captured, nearly died in a freight car stuffed with other prisoners, and finally found himself in a prison camp where a group of English prisoners of war entertain their new companions with a stage show. "Billy...not only laughed—he shrieked. He went on shrieking until he was carried out of the shed and into another, where the hospital was....Billy was put to bed and tied down, and given a shot of morphine."

The second hospitalization comes several years after the war, as he contemplates a career



in which he has no interest and marriage to a rich young woman whom he finds repellent. "He knew he was going crazy when he heard himself proposing marriage to her." Unable to come to terms with witnessing "the greatest massacre in European history," Billy had committed himself "in the middle of his final year at the Ilium School of Optometry. Nobody else suspected he was going crazy. Everybody else thought he looked fine and was acting fine. Now he was in the hospital. The doctors agreed: He *was* going crazy."

While in the hospital, he befriends another veteran. "They both found life meaningless, partly because of what they had seen in the war....So they were trying to re-invent themselves and their universe."

"Recurrent and intrusive distressing recollections," a classic symptom of posttraumatic stress disorder (PTSD), according to the DSM-IV, could well describe this novel, although it is written in what Vonnegut describes as a "telegraphic schizophrenic manner" and with a tone of detached and saddened wonder. Billy's passivity certainly fits in with other DSM criteria for PTSD, such as "numbing of general responsiveness" and "markedly diminished interest or participation in significant activities," along with a feeling of "estrangement from others." Another indicator is a sense of "foreshortened future," in which one does not expect to have a normal career, marriage, or life span.

In the novel Billy believes in predestination: "he has seen his own death many times, has described it into a tape recorder. *I, Billy Pilgrim*, the tape begins, *will die, have died and always will die on February thirteenth, 1976*."

Slaughterhouse Five was published in 1969 and became, like Joseph Heller's *Catch-22,* an icon of the antiwar movement.

The Eden Express

By Mark Vonnegut. Seven Stories Press pb, 2002 (1975). $13.95. 240 pp.

This is an autobiographical account of Mark Vonnegut's descent into madness, diagnosed at the time (1970) as schizophrenia. His story is unsentimental, poignant, and brutally honest. He neither condemns nor excuses himself, his family, his friends, or the mental health practitioners he encounters.

In retrospect, Vonnegut realizes that he was always "different," a judgment with which all who knew him concurred. When he is called to take a physical for the draft for Vietnam, he describes going in "so hyped and furious" that he was classified 4F (undraftable), even without the usual letter from a psychiatrist. "My friends said I should get an Academy Award for my act."

Drug use was common in his circle at college, but Vonnegut, sensing his vulnerability, for the most part avoided hallucinogens. Adding to his sense of psychological distress was his newly famous counterculture father, Kurt Vonnegut, who had left his mother and moved in with a younger woman. Mark describes himself as "more and more desperately unhappy and self-conscious," imagining that strangers feel contempt, or more often compassion, for him. But he is always left with a feeling of loneliness.

Complicating his situation was the way the counterculture was challenging the established order during this period. Any action could be defined as political, and anything that opposed authority had merit. At the same time, "hippie" culture provided a safe, nurturing environment, along with permission to see madness as enlightenment.

To help find a purpose and a structure for his life, Mark decides to homestead in British Columbia with a group of friends. For some people in the 1970s, this was a social-political experiment. To Mark, however, it was a desperate attempt to forestall what he later determined to be the inevitable.

His first psychotic break occurs on a trip back East, where he beat a drug arrest, and consists of episodes of uncontrolled crying, shaking, and social blunders. The symptoms abate when he returns to the farm. He then takes a mescaline trip, ending up in a manic period in which he sees the farm as Eden. Filled with grandiosity, he stops sleeping and eating, writes long letters, and tries to work but loses all coordination. This combination of depressive and manic episodes would probably be attributed today to bipolar disorder (DSM 296.89) rather than schizophrenia—the diagnosis at the time.

Mark attempts to fend off a second break by smoking a great deal of marijuana, but eventually his fears grow and his symptoms worsen. The title *The Eden Express* comes from his feeling of hurtling out of control. "This train is bound for glory. The brakeman has resigned."

He stops being able to talk—only screams, gestures, fantasizes, and tries to kill himself. Exhausted by the 24-hour watch it takes to guard him, his friends reluctantly have him admitted to a mental hospital, where he hears voices, sees visions, and tries to strangle himself. He is treated with thorazine and electroshock.

When he was released from the hospital, Vonnegut adopted a life structure and regimen intended to keep himself balanced: consuming a high-protein diet, avoiding caffeine and recreational drugs, and taking high doses of vitamins and minerals. In fact, Vonnegut "went back to school to learn more about the biochemistry I was suddenly so enthusiastic about" and eventually became a physician.

The Accidental Tourist

By Anne Tyler. Ballentine Books pb, 2002 (1985). $14.95. 400 pp.

Macon Levy, in Anne Tyler's *The Accidental Tourist*, has suffered a profound loss. His 12-year-old son, Ethan, has been senselessly murdered in a holdup. Macon's reaction is simply to carry on as before. He creates a world of routines, rituals, and dependable habits that get him through each day and hold his grief at bay. His wife, Sarah, who is openly experiencing the pain of their loss, becomes more and more resentful and angry at his aloof, methodical exterior.

When Sarah announces she is leaving him, Macon's response is to pull the car over and "rub his knees with his palms." Sarah moves out, and Macon reacts by creating yet more rituals aimed at economy and efficiency. He washes his clothes by trampling them underfoot as he showers; he sews sheets together to form a seven-layer sleeping bag that provides clean sheets every night for a week. Instead of running the dishwasher, he deposits dirty dishes in the sink in water spiked with chlorine bleach, which he changes on alternate days.

Macon, who makes his living writing a series of "Accidental Tourist" books for businessmen who wish to be insulated from anything foreign or unknown, does question whether he has carried things too far with his "fondness for method." Had Sarah's messiness balanced his orderliness? He takes some comfort from knowing that he came from a family of methodical people—his sister and brothers all adhered to strict routines, as did their grandparents, who raised them. But Sarah saw their methodical behavior in a different light. "They have to have their six glasses of water every day. Their precious baked potatoes every night. They don't believe in ballpoint pens or electric typewriters or automatic transmissions. They don't believe in hello and goodbye."

The DSM-IV, category 300.3, describes obsessive-compulsive disorder as manifesting

repetitive behaviors that a person feels driven to perform, behaviors that are aimed—however unrealistically—at preventing or reducing distress or at forestalling some dreaded event or situation.

When he first met Sarah at a college mixer, Macon had reflected: how sought-after she was, yet it was she who approached him. He decided that the only way to get her was to play it cool, to withhold. Now he felt "locked inside the stand-offish self he'd assumed....He was frozen there."

On the night Ethan died, it was the chitchat in the car on the way to the morgue that he remembers. He flossed his teeth before going to bed. He began clearing out Ethan's possessions immediately, so they would not be wasted. It was a shock to him that others found this cold.

Now he is left asking himself: "I'm all alone; it's just me; it seems everyone's just...fled from me. I don't know, I've lost them, I'm left standing here saying, 'Where'd they go? Where is everybody?'"

The catalyst for change in his life is Muriel, a zany dog trainer. She is everything that Macon is not—unpredictable, exuberant, youthful. After spending time with her and her boy, Macon begins to realize "that what mattered was the pattern of her life; that although he did not love her he loved the surprise of her, and also the surprise of himself when he was with her." Muriel gives Macon a photo of herself as a toddler, showing "her spikey, pugnacious fierceness." It is that fierceness that dissolves his ossification. They are both scarred, he realizes. A "sorrow sweep[s] through him" and "his life regain[s] its old perils," as he falls in love with Muriel and her young son, Alexander.

Headhunter

By Timothy Findley. HarperCollins, 1993. (Out of print. Used copies available online.)

Lilah Kemp, a principal character in Timothy Findley's novel *Headhunter,* is a childless former librarian who walks the streets of Toronto pushing an empty baby carriage. She believes that she has the power to bring forth into real life the characters she finds in books. "I require some news of Kurtz," she thinks. "I have released him out of *Heart of Darkness*. He has disappeared and I am afraid. Kurtz, if he puts his mind to it, can destroy the world—and only I can prevent him."

The medical center where Lilah goes for psychiatric treatment includes a central mall:

> There was a swimming pool off to one side where—so it was believed—recreation therapists drowned their charges. And a basketball court where murderers were turned loose every day and allowed to kill one another. Out in the Mall itself, tables were provided for cannibals and other types of feeders to bring their cups of blood and paper plates of human entrails and to sit there feasting, day unto day, on one another.

Lilah, reared in an abusive home, apparently developed her worst symptoms later in life. "That had been before the onslaught of schizophrenia and its distortions—before the shadows of trees had begun to crash in her path and the vines had begun to crawl through the windows to steal the food from her table."

Findley describes how "Lilah...was subjected to methods considered to be advanced and innovative...forced confinement and massive doses of various neuroleptic drugs....The object of the confinement had been to separate Lilah from her 'imaginary' companions. The drugs were meant to eliminate these companions altogether."

But Lilah finds herself "deprived of her world of wonders....*No one understands what I*

have in here she said to her kitchen one day. *I am an open door through which the dead can come and go at will*."

According to the DSM-IV, schizophrenia manifests as a combination of delusions, hallucinations, disorganized speech (frequent derailment or incoherence), and grossly disorganized or catatonic behavior. Among the sufferers are people whose delusions are bizarre or whose hallucinations consist of a voice keeping up a running commentary on the person's behavior or thoughts, or two or more voices conversing with each other. Subtypes of schizophrenia include catatonic, disorganized (referring to disorganized speech and behavior, flat or inappropriate affect), and paranoid. The essential feature of the paranoid type, such as that from which Lilah suffers, is "the presence of prominent delusions or auditory hallucinations in the presence of relative preservation of cognitive functioning and affect; delusions are typically persecutory or grandiose, or both."

Paranoid schizophrenia often appears in adulthood; its victims, properly medicated and treated, can retain the ability to live independent lives, as indeed does Lilah Kemp.

Findley is a well-known Canadian writer. His interest in issues of mental health was obvious in the title of his first novel, published in 1967: *The Last of the Crazy People*.

OTHER INTERESTING PORTRAYALS OF CHARACTERS WITH BRAIN DISORDERS CAN BE FOUND IN THE FOLLOWING WORKS (IN HISTORICAL ORDER):

The Double, by Fyodor Dostoevsky (1846): schizophrenia
Crime and Punishment, by Fyodor Dostoevsky (1866): mania, epilepsy
The Gambler, by Fyodor Dostoevsky (1866): obsessive-compulsive disorder
War and Peace, by Leo Tolstoy (1869): stroke
Anna Karenina, by Leo Tolstoy (1877): depression and suicide
The Complete Sherlock Holmes, by Sir Arthur Conan Doyle (1887): drug addiction
The Yellow Wallpaper, by Charlotte Perkins (1892): depression
The Sound and the Fury, by William Faulkner (1929): mental retardation
Long Day's Journey into Night, by Eugene O'Neill (1941): addiction
Justine, by Lawrence Durrell (1953): borderline personality disorder
A Separate Peace, by John Knowles (1959): spinal cord injury
The Tin Drum, by Günter Grass (1959): autism
Last of the Crazy People, by Timothy Findley (1967): childhood delusions, postpartum depression
Sophie's Choice, by William Styron (1974): post-traumatic stress disorder and suicide
Hotel du Lac, by Anita Brookner (1984): depression
Forrest Gump, by Winston Groom (1994): mental retardation, spinal cord injury
Scar Tissue, by Michael Ignatieff (1994): Alzheimer's disease
Blindness, by Jose Saramago (1995): blindness
She's Come Undone, by Wally Lamb (1996): anorexia and bulimia

Tracing Shakespeare's Insights Through Modern Brain Science

By Paul M. Matthews M.D., and Jeffrey McQuain, Ph.D.

(Excerpted from *The Bard on the Brain: Understanding the Mind Through the Art of Shakespeare and the Science of Brain Imaging.* By Paul Matthews, M.D., and Jeffrey McQuain, Ph.D. Dana Press, Washington, DC, 2003. Reprinted with permission.)

Paul M. Matthews, M.D., director of brain imaging at Oxford University, says that William Shakespeare provided exceptional insights on the brain and the mind in his characters. Modern brain researchers just now have the imaging tools to prove these observations.

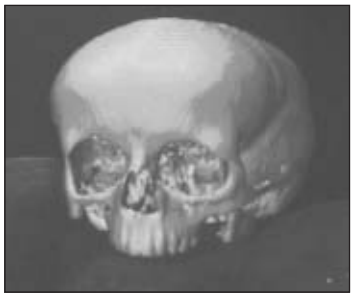
From the Introduction:

For the people of England, the Elizabethan period was a time of enormous expansion in many spheres of life. The broadening of intellectual horizons throughout Europe established the foundations for the period of enlightenment in the eighteenth century. It was a time of great economic and social change, during which England became a dominant European power. A key to this power was control of the seaways, by which explorations of the outside world proceeded ever more rapidly. And as new lands were being discovered, the nature of the European world was being redefined and the sense of human potential enlarged.

William Shakespeare both led and reflected his age. He developed the English language to an extent that no single writer has since. He mined the language of the rich and poor, rulers and the ruled, to develop more precise ways of expressing his thoughts and feelings. In doing so, he explored the inner world of man in a way that paralleled the journeys of the seafarers whose tales filled the taverns of England's ports….

What we appreciate as Shakespeare's genius derives from his keen insight into the human mind and from his obvious excitement in using this insight to experiment in drama. While his experiments were not designed and executed as those of modern brain scientists, the underlying goals had intriguing similarities. His laboratory was the theater, where he tested his words and refined them until they communicated powerfully and accurately. Like a modern brain scientist, he was testing hypotheses concerning the ways in which the human mind works. By using—and at the same time working to define—this complexity in his poetry and plays, he achieved his great art. In creating his enduring theater, Shakespeare also defines for us the uniqueness and wonder of the human mind.

Self reflection: Hamlet reveals the sensitivity of the brain to its own condition. (Daniel Travis, actor.)



The Shakespeare Theatre in the Nation's Capital joined Dr. Paul Matthews in bringing selections from *The Bard on the Brain* to life. Students in drama and biology can increase their knowledge of the brain by doing the same.

In attempting to understand the mind, brain scientists finally have the means to address questions that Shakespeare so eloquently put forward four centuries ago….

Minds and Brains

(Seeing the Man Through His Brain)
Extract from* Hamlet*, Act V, Sc. 1

Grasping the skull of a long-dead friend, Hamlet speaks what is perhaps the most misquoted line ever penned by Shakespeare: "Alas, poor Yorick, I knew him, Horatio" (not "I knew him well," as is so popularly believed). The Prince of Denmark's words come during a brief comic scene near the end of the play, when Hamlet meets a garrulous gravedigger. Hamlet does not yet know that his beloved Ophelia has drowned herself or that her grave is being prepared. When the gravedigger produces the skull of Yorick, once a jester to Hamlet's father, Hamlet fondly recalls the jester from his youth, now perhaps two decades past. Presaging the tragic news of Ophelia that is to follow, the skull reminds Hamlet that all of us must eventually die. Hamlet sees his former friend through his skull—a solid shell that can remain even after the brain is long decayed.

Hamlet: Alas, poor Yorick. I knew him, Horatio, a fellow of infinite jest, of most excellent fancy. He hath bore me on his back a thousand times, and now—how abhorred in my imagination it is. My gorge rises at it. Here hung those lips that I have kissed I know not how oft. Where be your gibes now, your gambols, your songs, your flashes of merriment, that were wont to set the table on a roar? Not one now to mock your own grinning? Quite chop-fallen? Now get you to my lady's chamber and tell her, let her paint an inch thick, to this favour she must come. Make her laugh at that.

Hamlet, 5.1

…Yorick's "most excellent fancy" must, of course, have arisen from the physical substance of his brain. A recurring theme in brain science (which also may have contributed to Shakespeare's beliefs concerning the brain) has been that the structure of the brain reflects its function in a rather direct way. People have even thought that the shape of the brain (which would be reflected in the shape of the inner surface of Yorick's skull) reflects an individual's personality, intellectual capacity, and moral character….

We do not now believe that character traits or brain functions can be localized in a simple way. Instead, it is felt that the brain processes information by means of complex networks of interactions between widely distributed regions of the brain—rather than solely in specific areas that might be reflected in local skull shape. Yet it is also clear that over the course of its development, the brain becomes regionally specialized for different functions. Perhaps one of the clearest examples of this is the way that regions specialized for processing language are highly lateralized to the left side of the brain in most people….

Language and Numbers

(A Subtle Voice)

Extract from* The Merchant of Venice, *Act IV, Sc. 1

Word choice is key to the poet's art. Novel words or turns of phrase are so striking to us that their novelty must influence the way in which the brain processes language. In The Merchant of Venice, *Portia speaks one of Shakespeare's most emotionally charged passages, which includes unexpected and novel word images. Dressed as a man, Portia enters a Venetian courtroom and passes herself off as Bathazar, a young doctor of laws from Rome. In the passage chosen here, Portia eloquently reminds the court of the "quality of mercy" that "droppeth" like rain and urges Shylock to be merciful toward the merchant Antonio. It is important to know that although Shylock remains unmoved by her impassioned arguments and demands that Antonio forfeit the promised pound of flesh, Portia's subtle voice eventually works its power and turns the tables on Shylock.*

Portia: The quality of mercy is not strain'd,
It droppeth as the gentle rain from heaven
Upon the place beneath: it is twice blest.
It blesseth him that gives and him that takes,
'Tis mightiest in the mightiest, it becomes
The throned monarch better than his crown.
His sceptre shows the force of temporal power,
The attribute to awe and majesty,
Wherein doth sit the dread and fear of kings:
But mercy is above this sceptred sway,
It is enthroned in the hearts of kings,
It is an attribute to God himself;
An earthly power doth then show likest God's
When mercy seasons justice. Therefore Jew,
Though justice be thy plea, consider this,
That, in the course of justice, none of us
Should see salvation: we do pray for mercy;
And that same prayer doth teach us all to render
The deeds of mercy. I have spoke thus much
To mitigate the justice of thy plea;
Which if thou follow, this strict court of Venice
Must needs give sentence 'gainst the merchant there.

The Merchant of Venice, 4.1

One aspect of great poetry such as that of Shakespeare is the way in which the words resonate in our minds. As we read, "The quality of mercy is not strain'd/It droppeth as the gentle rain from heaven/Upon the place beneath," the words arrest our attention because of the beauty and uniqueness of both the metaphor and the sound. Why is it that the novelty of Shakespeare's words and their combinations add so much to his poetry?

We respond to novelty in different ways than we respond to the over-familiar, and this is as true for words as it is for other inputs to the brain…. [B]rain scientists [have] used the sensitive technique of magnetoencephalography [MEG] to study the patterns and relative timing of activations in the brain during a task that involved making a simple decision….[T]he MEG method detects the very tiny changes in magnetic fields produced by electrical activity in neurons.

Drugs and the Brain

(A Celebration of Alcohol)
Extract from* Henry IV, *Sc. 3

In various ways, Shakespeare both censures and celebrates the effects of alcohol on the human brain and body. For its celebration, he speaks through Falstaff, one of his most memorable characters and a man resolutely committed to drinking. In Henry IV, Part II, *Falstaff recounts the benefits of alcohol. Left alone onstage by the sober Prince John, Falstaff comically considers that some wine would help mellow the too-serious prince. As this prose monologue continues, he singles out Prince Henry (or Harry), John's older brother and the heir to the throne, as an example of one who has improved as a result of the effects of alcohol (a popular form of which at the time was "sherris-sack," a type of fortified wine similar to modern sherry).*

Falstaff: Good faith, this same young sober-blooded boy doth not love me, nor a man cannot make him laugh; but that's no marvel, he drinks no wine. There's never none of these demure boys come to any proof; for thin drink doth so over-cool their blood, and making many fish meals, that they fall into a kind of male green-sickness; and then when they marry they get wenches. They are generally fools and cowards—which some of us should be too, but for inflammation. A good sherris-sack hath a twofold operation in it. It ascends me into the brain, dries me there all the foolish and dull and crudy vapours which environ it, makes it apprehensive, quick, forgetive, full of nimble, fiery, and delectable shapes, which delivered o'er to the voice, the tongue, which is the birth, becomes excellent wit. The second property of your excellent sherris is the warming of the blood, which before, cold and settled, left the liver white and pale, which is the badge of pusillanimity and cowardice; but the sherris warms it and makes it course from the inwards to the parts, extremes. It illumineth the face, which, as a beacon, gives warning to all the rest of this little kingdom, man, to arm; and then the vital commoners, and inland petty spirits, muster me all to their captain, the heart; who, great and puffed up with this retinue, doth any deed of courage; and this valour comes of sherris. So that skill in the weapon is nothing without sack, for that sets it a-work, and learning a mere hoard of gold kept by a devil, till sack commences it and sets it in act and use. Hereof comes it that Prince Harry is valiant; for the cold blood he did naturally inherit of his father he hath like lean, sterile, and bare land manured, husbanded, and tilled, with excellent endeavour of drinking good and good store of fertile sherris, that

> he is become very hot and valiant. If I had a thousand sons, the first human principle I would teach them should be to forswear thin potations, and to addict themselves to sack.
>
> *Henry IV, Part II, 4.3*

Falstaff is a rogue, a drunkard, and a coward. He is also the comic "life of the party" and deeply fond of his companions-in-carousing. But despite his rich good humor, one sees in him the tragic self-awareness of a life unfulfilled. His melancholy stems in part from recollections of slights, failures, and unmet expectations.

Falstaff has become enamored of the personality that he has generated for himself with the help of alcohol. His celebration of alcohol springs from the way it relieves him of self-doubt and banishes unpleasant memories. He needs to be freed from inhibitions arising from his own sense of unworthiness in order to enjoy himself. His celebration of alcohol is also interesting from a medical point of view because it both describes much that is true about this most common of drugs and includes myths that only a person "under the influence" (such as Falstaff) could propagate.

In trying to rationalize Prince John's dull seriousness, Falstaff concludes that part of the problem is that John simply "drinks no wine." Falstaff describes the effects of alcohol in reducing inhibition, claiming that "It ascends me into the brain, [and] dries me there all foolish and dull and crudy vapours," allowing his "excellent wit" to surface.

Alcohol of course has more general effects on the body. The "warming of the blood" that Falstaff refers to is not real but a feeling that comes from increased circulation due to alcohol-induced dilation of the small vessels of the skin. In consequence, it "illumineth the face, which, as a beacon, gives warning to all the rest of this little kingdom, man…"—the "warning" likely being simply that the drinker has had too much!

Falstaff describes alcohol from the standpoint of an unrepentant abuser of the drug. In fact, alcohol is a depressant of the nervous system. It makes speech appear "nimble" because it depresses brain functions responsible for self-monitoring and other processes that demand focused attention. This loss of effective self-monitoring underlies the partygoer's insistence that he can drive home safely, when everyone else can see that he is too drunk even to walk straight…

Sociopathic behavior: Richard III, in his own words, is "subtle, false, and treacherous" and lacks any sense of right or wrong. (Daniel Travis, actor.)

Decision and Action

(Motivation and Morality)

Extract from* Richard III*, Act I, Sc. 1

What motivates us to act (or not to act) is a central concern of Shakespeare's drama. Among the earliest of Shakespeare's history plays, Richard III *is also the only one of his plays to begin with a soliloquy by its title character. As the Duke of Gloucester and brother to King Edward IV, Richard makes his motivation all too clear in this introduc-*

tory speech. Punning on "sun" and "son" in the opening sentence, he goes on to boast of his immoral scheme to usurp the crown, excusing his evil intentions with his physical deformity. He has set his plan in motion by promoting a prophecy that someone with the initial G will murder Edward's heirs. As a result, the king orders the arrest of George, the Duke of Clarence, brother to both the king and Richard, and unwittingly aids his evil brother's rise to become Richard III.

Richard III: Now is the winter of our discontent
Made glorious summer by this son of York;
And all the clouds that lour'd upon our House
In the deep bosom of the ocean buried.
Now are our brows bound with victorious wreaths,
Our bruised arms hung up for monuments,
Our stern alarums chang'd to merry meetings,
Our dreadful marches to delightful measures.
Grim-visag'd War hath smooth'd his wrinkled front;
And now, instead of mounting barded steeds
To fright the souls of fearful adversaries,
He capers nimbly in a lady's chamber,
To the lascivious pleasing of a lute.
But I, that am not shap'd for sportive tricks
Nor made to court an amorous looking-glass;
I, that am rudely stamp'd, and want love's majesty
To strut before a wanton ambling nymph;
I, that am curtailed of this fair proportion,
Cheated of feature by dissembling nature,
Deform'd, unfinish'd, sent before my time
Into this breathing world scarce half made up—
And that so lamely and unfashionable
That dogs bark at me, as I halt by them—
Why, I, in this weak piping time of peace,
Have no delight to pass away the time,
Unless to spy my shadow in the sun,
And descant on mine own deformity.
And therefore, since I cannot prove a lover
To entertain these fair well-spoken days,
I am determined to prove a villain,
And hate the idle pleasures of these days.
Plots have I laid, inductions dangerous,
By drunken prophecies, libels, and dreams,
To set my brother Clarence and the King
In deadly hate, the one against the other;
And if King Edward be as true and just
As I am subtle, false, and treacherous,
This day should Clarence closely be mew'd up

About a prophecy, which says that 'G'
Of Edward's heirs the murderer shall be—
Dive, thoughts, down to my soul: here Clarence comes.

Richard III, 1.1

Richard III is particularly chilling as he describes his joint deformities of body and mind: "I, that am curtail'd of this fair proportion,/Cheated of feature by dissembling Nature,…I am determined to prove a villain." The horror of this passage is that a man could be so evil as to desire to harm others without specific cause. There is no motivation for revenge or power behind Richard's plan—he believes that he is "subtle, false, and treacherous" because to be so is quite simply in his nature.

Understanding the basis of moral action has been a challenge for Western literature since its beginnings in the great epics of the Iliad and the Odyssey. It is now becoming an important issue for modern brain science. We cannot help being fascinated by the enigma of Richard, who so clearly understands our moral universe and yet rejects its tenets. There is still no science that can explain the evil of Shakespeare's Richard, but brain scientists are beginning to define structures in the brain that are essential for aspects of moral and responsible behavior.

A critical aspect of moral behavior is the ability to forgo smaller, short-term gains in order to realize more distant but greater rewards. For example, a student learns to forgo the pleasures of a night out before examinations in order to achieve higher marks and the praise and new opportunities that arise from them. Patients who have suffered severe damage to the middle part of the frontal lobe such as Phineas Gage have a childlike impulsiveness that prevents them from acting "responsibly" in this way. Nonetheless, patients who damage their brains as adults, like Gage, are at least able to appreciate the concepts behind this strategy.

Recent studies by Hannah and Antonio Damasio and their group at the University of Iowa suggest that this may not be the case if damage to the same areas of the brain occurs early in development. They studied two young adults who had sustained damage to the front part of the brain (the orbitofrontal and medial frontal cortices) before 16 months of age, as shown in Figure 17 (overleaf). Both had a history of severe family and social problems arising from irresponsibility, an inability to follow orders, and lack of guilt or remorse for misdeeds. However, not only were these subjects impaired in their moral behavior, like those who suffer similar lesions as adults, but they also showed defects in their ability to perform social and moral reasoning in the abstract. With early damage to this area of the brain, they simply were unable to appreciate the rules. The cases were clearly different from that of Phineas Gage, who retained an ability to distinguish between right and wrong.

The power of music: Shakespeare recognizes the magic of music and dramatizes its potency in one of his later plays, *The Winter's Tale.*

Our Inner World

(Music as a Call to Life)

Extract from* The Winter's Tale, *Act V, Sc. 3

Music seems to have a magic all its own. Shakespeare recognizes this magic and dramatizes its potency in one of his later plays, The Winter's Tale*. Dramatic intensity is focused on the final scene of the play, in which music appears to bring a statue to life. At the beginning of the play, after the Sicilian king Leontes' jealous rage against her, his innocent wife, Hermione, wrongfully imprisoned for adultery, conspires to be reported dead. With this following the death of his only son, the lonely king repents his anger. Paulina, a faithful attendant of Hermione, then unveils a "statue" that proves to be a remarkably exact replica of the supposedly dead queen. In the scene that follows, after Paulina reawakens Leontes' faith in his wife, her demand for music acts as a seemingly magical call to life for the "statue."*

Paulina: Music, awake her; strike!

[Music.]

'Tis time; descend; be stone no more; approach;
Strike all that look upon with marvel. Come!
I'll fill your grave up: stir, nay, come away:
Bequeath to death your numbness; for from him
Dear life redeems you. You perceive she stirs:

[Hermione comes down.]

Start not; her actions shall be holy as
You hear my spell is lawful.

[to Leontes] Do not shun her
Until you see her die again; for then
You kill her double. Nay, present your hand:
When she was young you woo'd her; now, in age,
Is she become the suitor?

Leontes: O, she's warm!
If this be magic, let it be an art
Lawful as eating.

The Winter's Tale, 5.3

The image of music calling a statue to life is striking. Who among us has not felt the compulsion to tap, rock, or gyrate wildly to the stimulating beat of a popular band? Music can animate the emotions as well as the body. Just as a stern face can melt into a smile on hearing a lively tune, so Hermione's apparently stony form dissolves into soft flesh with the sound of the music. Even without words, music communicates directly in ways that Shakespeare often used.

Shakespeare's plays are full of music, and he very consciously employs its power to move his audience. Songs such as the one at the end of *Twelfth Night*—"When that I was and a little tiny boy/With hey, ho, the wind and the rain,/A foolish thing was but a toy,/For the rain it raineth every day"—provide an appropriate denouement, or rounding out of the action, at the close of an act. There also is often a real sense of music in the rhythm of Shakespeare's words and the timbre of their sounds.

Modern neuroscientists now appreciate that musical processing activates many parts of the brain. Research is being conducted in several laboratories to define precisely how music is perceived in the brain. Richard Frackowiak and his colleagues at the Functional Imaging Laboratory of University College in London are among those who performed some of the first neuroimaging studies of the effects of music on the brain. In their experiments using PET, they varied specific qualities of music for a group of listeners. By recording brain activity while changing pitch and rhythm independently, for example, the images shown here were generated. They demonstrate that processing of these specific musical elements is performed by large groups of nerve cells primarily found in the left side of the brain. There appears to be considerable overlap with areas of the brain that are used for language. For example, both language and rhythm activate the so-called superior temporal gyrus, the fold on the top of the lower lobe of the brain, and Broca's area, in the lower part of the front of the brain. This should probably not be surprising, as making sense of the sounds of words also must involve an appreciation of rhythm and pitch. One of the greatest difficulties with learning a foreign language, for instance, is appreciating the typical patterns of sounds that define words and sentences in that language.

In their studies of music, Frackowiak and his colleagues were surprised to find that variation of pitch discrimination primarily activated areas in the back of the brain that had previously been thought to be used primarily for visual perception. One possible explanation for this is that pitch decoding may involve a visual component. Mental imagery may be used in some way to encode patterns of relative pitch in music. If this is true, then when we speak colloquially of a musical pitch as being "higher" or "lower," it may be a reflection of a bias in the human brain for processing relationships in spatial terms.

Frackowiak's experiments also identified brain activity in the back part of the right side during judgments of timbre. This area (known as the right parietal lobe) is activated also (although obviously not exclusively) for tasks that demand thinking about spatial relations. Timbre may in some respects require a type of thinking analogous to spatial processing, because it involves understanding the relationships between different pure tones that make up the sound as a whole.

Together these observations illustrate how much of the brain is involved in the processing of music—suggesting how completely it can dominate our consciousness. Music truly calls the brain as a whole to life!

The Bard on the Brain:
Understanding the Mind Through the Art of Shakespeare and Science of Brain Imaging

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(For more information on *The Bard on the Brain: Understanding the Mind Through the Art of Shakespeare and Science of Brain Imaging*, see p. 116.)

A Note on Sources of Information on the Brain

The Dana Foundation provides many resources and offers directions to other sources to keep you informed of news on the cutting edge of brain research. For information on these resources and how you can get involved in the science that will shape the 21st century, refer to the indicated pages:

The Dana Alliance for Brain Initiatives, p. 111
Brain Awareness Week, p. 112
Radio and Television Documentaries, p. 113
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www.dana.org

An Internet Connection for News on the Brain and Brain Research

The Dana Web site provides brain information, news, and links to other brain-focused organizations. Visitors will find information on **www.dana.org** about the activities of the Dana Alliance for Brain Initiatives, including the Brain Awareness Week campaign and public radio and television series. The Brain Information and *BrainWeb* section of the site provides general information about the brain as well as current brain research. and serves as a gateway to brain information on the World Wide Web with links to validated sites specializing in more than 25 different brain disorders. The Dana Press section provides information about Dana Press books, subscription forms for free print

publications, and access to the online versions of these publications, as available. An educational feature aimed at children, parents, and teachers, called *Brainy Kids Online*, makes learning about the brain fun through interactive activities and child-oriented facts. Older adults and caregivers will find resources related to brain health, education, and general sources of information by clicking on *Brain Resources for Seniors*.

Excerpts from the Privacy Statement at www.dana.org:

How the Dana Foundation, a 50-year-old private philanthropy, protects your privacy:

We at Dana believe that anyone who visits our Web site has the right to remain anonymous. Accordingly, we do not collect any information about you without your informed consent. If you do not want us to know your identity or anything about your interests, you remain welcome to the information onscreen on the Dana site.

Dana does not sell, lend, rent, or give your name and address or any other personally identifiable information about you to anyone. If you supply us with any information, you may direct us to delete it at any time.

What about "cookies"? (These are the electronic observers sent by a Web server to store on your computer containing information about you so that others can track your interests or remember your instructions.) Because many people believe these devices can be a threat to their privacy, Dana does not use cookies at any time for any reason. We urge parents to tell their children never to give out names, addresses, or phone numbers, without permission, when using the Internet. Ours is the most privacy-protective policy we can devise while retaining the ability to respond to your requests.…

Our Guiding Privacy Principles:

1. *You have the right to remain anonymous and*
2. *You can rest assured that Dana will do nothing with information you send us beyond its specific purpose without your consent.*

About the Dana Foundation

The Dana Foundation is a private philanthropic organization with principal interests in science, health, and education. Charles A. Dana, a New York State legislator, industrialist, and philanthropist, was president of the Dana Foundation from 1950 to 1966 and actively shaped its programs and principles until his death in 1975.

As chairman of the Charles A. Dana Foundation (1978-2000) and of the Dana Alliance for Brain Initiatives (1993-2000), the late David Mahoney had a vision to communicate the hope and promise of brain research to as wide an audience as possible. Nobel laureate and Dana Alliance member Leon N. Cooper, Ph.D., has said: "David Mahoney mobilized public opinion in support of brain research and is, to a remarkable extent, responsible for public and congressional recognition of the importance of neuroscience research."

The Dana BrainWeb: Great Sites for Information on Brain Diseases and Disorders

It can be difficult to find resources helpful for your particular interest when searching for brain-related information on the Internet. The *Dana BrainWeb* can speed you to the precise information you need.

For each of 31 common brain diseases and disorders, the Dana Alliance for Brian Initiatives has selected, reviewed, and validated up to four sites that provide current information for the layperson, including descriptions of the diseases, FAQs (Frequently Asked Questions), background for talking with a physician, treatment options, support for families and caregivers, and sources of more information.

New sites are added quarterly to the *BrainWeb*, so check back often.

The Dana Alliance for Brain Initiatives

The Dana Alliance for Brain Initiatives was born out of a three-day meeting at Cold Spring Harbor Laboratory in 1992, in the early days of "The Decade of the Brain." There, 30 of the country's most eminent neuroscientists convened to debate the progress and promise of brain research. The meeting was organized by James D. Watson, Ph.D., director of the laboratory and Nobel laureate for his codiscovery of the structure of DNA, and David Mahoney, then-chairman of the Dana Foundation. Their vision was to establish a group of prominent neuroscientists who would commit themselves to translating the advances in brain research to the public, the ultimate beneficiary of these advances.

The assembled scientists debated how best to communicate the promise of neuroscience to the public in a way that would convey their knowledge and excitement. They were particularly concerned about recent decreases in federal funding for neuroscience research at the very time such research was beginning to yield breakthrough treatments for some of the most devastating neurological disorders.

"People want to know what you can do for them," Mahoney told the neuroscientists. "They want results that can benefit them." Only by convincing the public of the direct benefits of their work, Mahoney cautioned them, could they hope to receive the funding, public and private, that would accelerate their vital work.

By the end of the Cold Spring Harbor meeting, the group had vowed to change the landscape of public support for brain research. They developed a "Declaration of Objectives" setting forth 10 research goals that were both meaningful to the public and considered achievable by the end of the 1990s. These goals guided the Alliance's activities over the next several years.

A Global Force in Brain Research Advocacy

From those 30 founding members, the Dana Alliance has grown to include more than 200 neuroscientists, including ten Nobel laureates. Its members, all leaders in their field, represent a broad range of neuroscience disciplines, including neurology, neurobiology, neuropsychology, cognitive neuroscience, neuroimmunology, and virtually every subspecialty within neuroscience. Today, the Alliance is considered one of the most effective and respected forces in communicating science.

In 1997, leading scientific colleagues in Europe sought to make the mission global. After discussions in Europe with Mahoney and Dana Foundation Director William Safire, the European Dana Alliance for the Brain (EDAB) was created. EDAB's active membership has taken the message about the promise of brain research worldwide, firmly establishing that organization as another important international force in advocacy for brain science.

In August 2001, almost nine years after its formation, the Dana Alliance convened a follow-up meeting among 33 of its leading researchers to consider how the Alliance should direct its efforts over the next five to ten years. After reviewing the advances in brain research and technology, the Alliance announced a new research agenda for the next decade and recommitted itself to public communication.

Brain Awareness Week[sm]

Brain Awareness Week is an international campaign to raise public awareness of the benefits, promise, and progress of brain research. Begun by the Dana Alliance in 1996 as an effort involving 160 organizations in the United States, Brain Awareness Week has grown into a powerful global initiative with more than 1,400 partners in more than 50 countries.

During Brain Awareness Week, leading universities and research centers open their doors to the public. Brain researchers go into their local communities to convey the excitement of brain research. Across the country and around the world, patient-advocacy groups, government agencies, service organizations, hospitals, and K-12 schools deliver the message about the promise of brain science in creative and compelling programs. These activities range from interactive brain exhibits that show children and teenagers models of the human brain to 3-D video presentations of what happens inside the brain.

In support of Brain Awareness Week, the Dana Alliance provides partner organizations with Internet and print resources. The Alliance also coordinates partnerships and special events and in recent years has cosponsored educational exhibits with the National Institutes of Health to introduce middle-school children to the wonders of the brain. The Alliance coordinates Partners in Education, a coalition of national organizations dedicated to reaching out to the next generation of scientists by linking today's neuroscientists directly with students. Partners in Education works with universities and academic research centers to enhance existing science curricula and instill a sense of the excitement of brain science.

To learn about Brain Awareness Week, visit our Web site at www.dana.org/brainweek.

Radio and Television Documentaries

Gray Matters, the Dana Alliance's award-winning radio documentary series, has informed public radio audiences with in-depth reports on a wide range of fascinating brain topics since 1994. The series now includes 18 installments, with two to four new programs produced annually. Recent additions to the series include *Emotion and the Brain, Arts and the Brain*, *Sleep and the Brain*, and reports focused on specific brain disorders, including stroke, depression, Alzheimer's disease, and trauma. Transcripts of the programs are available on the Dana Web site, **www.dana.org**.

Programs and their hosts include:
Alcohol, Drugs, and the Brain—Pat Summerall
The Aging Brain—Samantha Eggar
Alzheimer's and the Brain—Diana Nyad
The Arts and the Brain—Richard Dreyfuss
Bioterrorism and the Brain—Garrick Utley
The Developing Brain—Judy Woodruff
Depression and the Brain—Mike Wallace
Emotions and the Brain—Garrick Utley
Memory and the Brain—Garrick Utley
Men, Women, and the Brain—Garrick Utley
Music and the Brain—Mandy Patinkin
Sleep and the Brain—Garrick Utley
Sports, Fitness, and the Brain—Frank Gifford
Stroke and the Brain—Ben Vereen, with Maya Angelou and Ray Bradbury
Stress and the Brain—Robert MacNeil
Surgery and the Brain—Garrick Utley
The Teenage Brain—Natalie Portman
Trauma and the Brain—Garrick Utley

To order cassette tapes, call 1-800-65BRAIN. To view more titles, listen to audio, and/or download transcripts at no cost, visit: **www.dana.org/books/radiotv**.

The Alliance reaches millions of television viewers through popular public television documentaries about the brain. More than 30 Alliance members recently participated in *The Secret Life of the Brain*, a five-part television series. A companion book copublished by the Dana Press, a Web site, a lecture series, and educational outreach brought the documentaries to an international audience.

Public Forums and Lectures

Dana Alliance members frequently donate their time to speak at public forums and symposia. In 2001 and 2002, the Alliance partnered with the AARP to make presentations to older Americans that focused on brain-aging topics such as brain fitness, memory loss and Alzheimer's disease, coping with depression, successful aging of the brain, and the effects of chronic health problems on the brain. In conjunction with the Smithsonian Associates, the Alliance sponsors an annual series of lectures in Washington, DC. Topics have included "Your Personality and Your Health," "The Fragile Power of Human Memory," "Creativity and Mood Disorders," and "The Dreaming Brain."

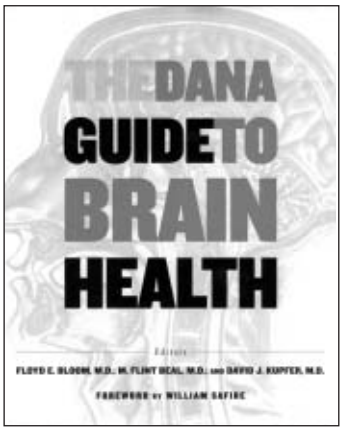
Growing public interest often results in overflow crowds for programs and forums on the brain and brain research.

Books from Dana Press

Dana Press, a division of the Dana Foundation, publishes health and popular science books about the brain for the general reader. It also publishes periodical and educational materials as well as informational materials on behalf of the Dana Foundation and the Dana Alliance for Brain Initiatives. Dana Press books are available wherever books are sold, or by logging onto: **www.dana.org/books/press**.

The Dana Guide to Brain Health

Edited by Floyd E. Bloom, M.D., M. Flint Beal, and David J. Kupfer, M.D.
Foreword by William Safire



The Dana Guide to Brain Health is the first major family medical guide about brain health. This easy-to-understand, 768-page book provides up-to-date information on how the brain works, in addition to a comprehensive description of 72 psychiatric and neurological disorders, and their diagnosis and treatment. Filled with informative diagrams, charts, drawings, and sidebars, this important new book includes

- New insights on the brain's development from infancy to old age.
- An overview of the incredible diversity of the brain's physical and emotional functions.
- Invaluable information on understanding and coping with almost any brain or nervous system disorder.

Three of the world's leading experts, in collaboration with more than 100 of America's most distinguished scientists and medical professionals, explain the

latest science in a reader-friendly format full of easy-to-understand illustrations and useful advice.

"I have long wanted a reference on the brain to which I could refer the educated lay reader who has questions arising either from curiosity about the most fascinating of topics, or, as is often the case, from the illness of a friend or family member. This guide serves the purpose ideally well. The information is accurate as it is accessible and has been assembled by leaders in the field."
—Steven E. Hyman, M.D., Provost, Harvard University; Prof. of Neurobiology, Harvard Medical School; Former Director, National Institute of Mental Health

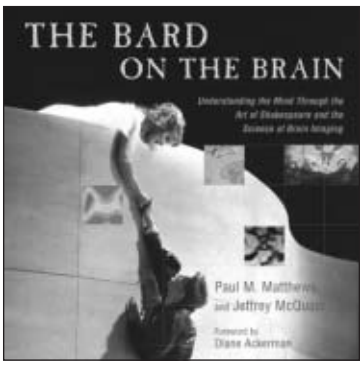
"…Covering an array of topics, the [Dana Guide to Brain Health] *includes detailed information that goes beyond encyclopedia-type entries about medical testing, childhood development, autism, cerebral palsy, and treatments for these and other diseases. The writing is clear and accessible….Patients newly diagnosed with brain-related ailments will find this an invaluable resource."* —Publisher's Weekly

"[A]n irreproachably comprehensive look at the state of current neuroscience on how the brain works when it is normal and how it works when things go wrong."—The Boston Globe

Floyd E. Bloom, M.D., is chairman of the Department of Neuropharmacology at The Scripps Research Institute in California, president of the AAAS, and former editor-in-chief of the journal *Science.* **M. Flint Beal, M.D.**, is neurologist in chief of the New York-Presbyterian Hospital and chairman of the Department of Neurology and Neuroscience at the Weill Medical College of Cornell University. **David J. Kupfer, M.D.**, is the Thomas Detre Professor and chairman of psychiatry at the University of Pittsburgh School of Medicine.

768 pages, 16 pages of full-color illustrations, 200 black and white drawings, charts, and sidebars, 7¼ x 9¼, ISBN 0-7432-0397-6, cloth, $45.00. Published by The Free Press. Editorial preparation by Dana Press.

The Bard on the Brain: Understanding the Mind Through the Art of Shakespeare and



the Science of Brain Imaging

By Paul M. Matthews, M.D., and Jeffrey McQuain, Ph.D.
Foreword by Diane Ackerman

This beautiful full-color book is a completely original adventure in exploring the human mind through the great works of Shakespeare. The director of the University of Oxford's Centre for Functional Magnetic Resonance Imaging of the Brain joins a Shakespeare scholar to show us the center-stage role of the brain in famous scenes from the Bard's plays. In stunning modern brain scans and clear, plain English, you'll discover how uncannily Shakespeare perceived the brain at work in his characters' thoughts and actions and see the living brain as it mirrors human experiences the Bard created 400 years ago.

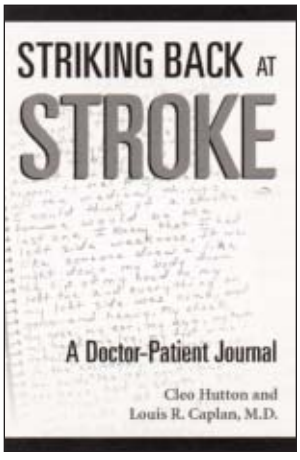
"For anyone intrigued by the inscrutability of the human mind, The Bard on the Brain *is a remarkable journey into the mysterious labyrinth of the brain and its interaction with the world around us, and our guide is none other than our greatest dramatist and poet, William Shakespeare."* —Harry Hamlin, actor

"No one who is genuinely interested in the workings of the brain can afford to ignore William Shakespeare who, through his unparalleled genius in the use of language, gave us significant insights into the workings of the brain. Here, at last, is a compelling and beautifully illustrated book that unites the study of the brain to that of Shakespeare in a thrilling read."—Prof. Semir Zeki, University College of London and Institute of Neuroesthetics, author of *Inner Vision: An Exploration of Art and the Brain*

248 pages, 100 full-color illustrations, 9 x 9, ISBN 0-9723830-2-6, cloth, $35.00. A Dana Press book.

Striking Back at Stroke: A Doctor-Patient Journal

By Cleo Hutton and Louis R. Caplan, M.D.



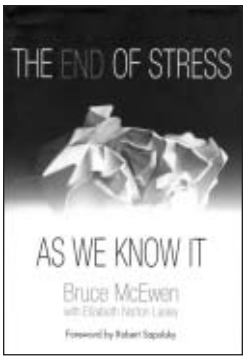
Striking Back at Stroke is an autobiographical account of a stroke survivor, detailing her hard-won success rebuilding a life in ruins and overcoming difficulties she never imagined confronting. Cleo Hutton's account of her experiences is interwoven with medical and scientific commentary by the leading expert in the field, Louis Caplan, M.D., who explains Hutton's case in terms of what scientists and doctors have come to know about strokes. Both authors give valuable advice about home care, emotional support, and physical recovery from the frontlines of the battle against stroke.

"…[S]hould provide reassurance to lay readers that they are getting the medical facts they need to know about stroke. It will take you by the hand to help you cope with a stroke. For the health professional, it will remind you of the day-to-day trials and tribulations and ultimately successes of the patients you care for and inspire you in your

clinical care and research endeavors."—Jordan Grafman, Ph.D., chief, Cognitive Neuroscience Section, National Institute of Neurological Disorders and Stroke
ISBN 0-9723830-1-8, cloth, $27.00. A Dana Press book.

The End of Stress As We Know It

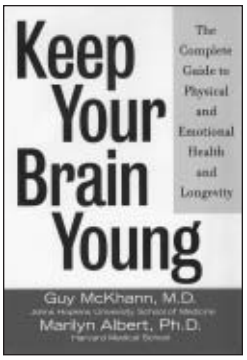
By Bruce McEwen, Ph.D., with Elizabeth N. Lasley
Foreword by Robert Sapolsky, Ph.D.



A world authority on the subject of stress provides readers with the gold standard in understanding how our bodies work under stress and why we have the power to avoid its debilitating effects. Bruce McEwen, Ph.D., provides here unshakeable evidence of how mind and body work together for good or ill when challenged by life's events.
ISBN 0-309-07640-4, cloth, $27.95. Co-published by Dana Press and Joseph Henry Press.

Keep Your Brain Young: The Complete Guide to Physical and Emotional Health and Longevity

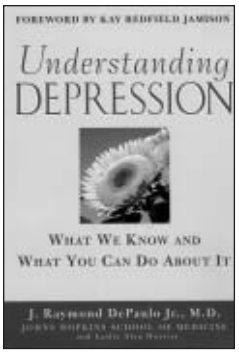
By Guy McKhann, M.D., and Marilyn Albert, Ph.D.
Foreword by Kay Redfield Jamison, Ph.D.



Two of the most highly regarded experts on the brain in aging bring us the first truly useful advice book for living with your brain in the second half of life. The authors discuss every aspect of aging—changes in memory, nutrition, mood, sleep, and sex, as well as problems that creep up in alcohol use, vision, hearing, and movement and balance. The authors' frankness also provides what we need to know about Alzheimer's and Parkinson's diseases, tremors, stroke, and other common disorders.
ISBN 0-471-43028-5, paper, $15.95; ISBN 0-471-40792-5, cloth, $24.95.
Co-published by Dana Press and John Wiley & Sons, Inc.

Understanding Depression: What We Know and What You Can Do About It

By J. Raymond DePaulo, Jr., M.D., with Leslie Alan Horvitz



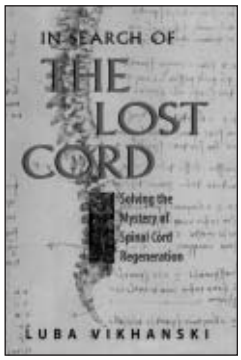
This tour de force from one of America's leading experts on depression gives the general reader the latest and best information about an illness one in five Americans will experience at some time in life. Dr. DePaulo explains what depression is, who gets it and why, what happens in the brain, the troubles that come with the illness, and the treatments that work—or don't.
ISBN 0-471-430307, paper, $14.95; ISBN 0-471-39552-8, cloth, $24.95
Co-published by Dana Press and John Wiley & Sons, Inc.

A Good Start in Life: Understanding Your Child's Brain and Behavior

By Norbert Herschkowitz, M.D., and Elinore Chapman Herschkowitz, M.A.
Foreword by Jerome Kagan, Ph.D.

The renowned neuroscientist-clinician, Dr. Norbert Herschkowitz, and educator-writer Elinore Chapman Herschkowitz, distill decades of studying infants and children into an enchanting exploration of how brain development shapes a child's personality and behavior from birth to age six.

ISBN 0-309-07639-0, cloth, $22.95. Co-published by Dana Press and Joseph Henry Press.

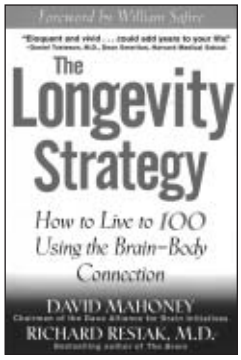


In Search of the Lost Cord: Solving the Mystery of Spinal Regeneration

By Luba Vikhanski

A riveting account of courage and conviction, as top scientists and young acolytes fight their way toward vital advances in the understanding and treatment of spinal cord injury. Written by the award-winning science journalist, Luba Vikhanski.

ISBN 0-309-07437-1, cloth, $27.95. Co-published by Dana Press and Joseph Henry Press.

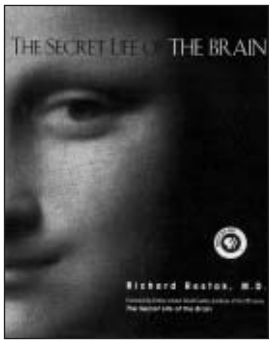


The Longevity Strategy: How to Live to 100 Using the Brain—Body Connection

By David Mahoney and Richard Restak, M.D.
Foreword by William Safire

A successful CEO and a leading brain expert reveal how the discoveries of brain research—together with personal actions—will make a longer life not just worthwhile, but a genuine gift.

ISBN 0-471-32794-8, paper, $14.95; ISBN 0-471-24867-3, cloth, $22.95.
Co-published by Dana Press and John Wiley & Sons, Inc.



The Secret Life of the Brain

By Richard Restak, M.D.

A visually beautiful, thoroughly satisfying exploration of recent discoveries about the brain and their human impact, *The Secret Life of the Brain* unfolds the story of the brain as, unseen and usually unnoticed, it develops and changes throughout our life span. Companion book to the 2002 PBS series *The Secret Life of the Brain.*

ISBN 0-309-07435-5, cloth, $35.00. Co-published by Dana Press and Joseph Henry Press.

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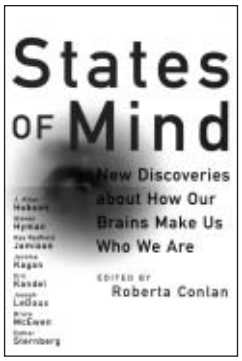

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"Stumbling on Gold: Two Smart Alecks in Cambridge" (Book Excerpt: James Watson and DNA: Making a Scientific Revolution by Victor K. McElheny)

Watson and Crick—the simple conjoining of the two names says it all. The 1953 scientific coup by two brash, brilliant young men began a revolution

that swept through biological science, medicine, psychiatry, behavioral science, technology, philosophy, ethics, and public policy. As we mark the 50th anniversary of the improbably exact "guess" that penetrated the structure of DNA, a veteran science journalist weaves together first-hand accounts to recreate a science legend in the making.

"From the Gene to the Brain: 1953–2003"
By ***Samuel H. Barondes***
Some 50 percent of our genes carry the codes for development, growth, and change in our brains. Small wonder, then, that molecular biology's power to penetrate and manipulate the genetic basis of life is transforming brain science. Neurobiologist Barondes shows how DNA technology has driven the pace of research on brain diseases, development of drugs for treating mental illness, and our concept of human nature and behavior.

Other Articles:

"The Telltale Hand: How Writing Reveals the Damaged Brain"
By ***Marc J. Seifer***
The handwriting sample appears clear and well formed, but we can see unnatural breaks between letters, false starts, and misaligned letters, characteristic of writing by people who have had their right and left brain *hemispheres* surgically split to control severe epilepsy. Handwriting is, in fact, brain writing, a complex process that engages areas of the brain from the cerebral cortex to the spinal cord. When this process is affected by disease or trauma, handwriting is altered in specific ways that provide an intriguing, often underestimated window on the brain.

"Brainsick: A Physician's Journey to the Brink"
By ***Leon E. Rosenberg***
"I have the typical risk profile for a suicide victim, if one can use such a banal expression for so terrible an action," writes Rosenberg. How could a brilliant physician—a noted researcher, medical school dean, and head of pharmaceutical research for an international drug company—miss decades of the telltale signs and symptoms of bipolar disorder until the day when a disordered brain trumped reason, the caring of family, and the power of modern medicine? Is there a road to recovery? "There are some things I have come to know and need to tell," writes Rosenberg.

"Patients Have Been Too Patient with Basic Research"
By ***Ralph M. Steinman*** and ***Maia Szalavitz***
Steinman has devoted his long career to pioneering studies of immunology. Basic research of this kind has been hugely productive, he says, but its potential benefits for treating serious illnesses are taking too long to reach patients. We are failing to maintain a crucial transmission belt between basic research and clinical applications: the physician-scientist. We must take immediate and effective steps to reverse this trend, because our lives "may one day depend upon the progress of medicine."

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"Worried Sick"
The End of Stress as We Know It
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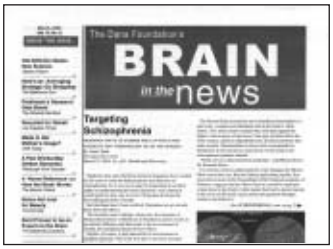

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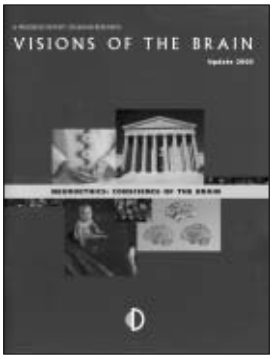

Visions of the Brain: A Progress Report on Brain Research

Published annually since 1995, *Visions of the Brain: A Progress Report on Brain Research* is the signature publication of the Dana Alliance for Brain Initiatives. The European Dana Alliance for the Brain also translates, augments, and distributes the report in three languages—English, French, and German—throughout Europe.

Visions of the Brain describes and interprets the important advances of the previous year in these areas of research:

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- Stem Cells and Neurogenesis
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- Neuroimmunological Disorders
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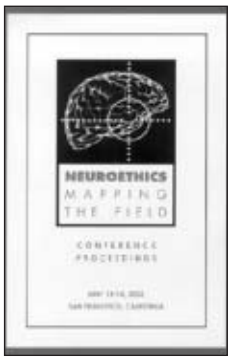

Neuroethics: Mapping the Field Conference Proceedings

Edited by Steven J. Marcus

More than 150 neuroscientists, bioethicists, doctors of psychiatry and psychology, philosophers, and professors of law and public policy came together in San Francisco in 2002 to participate in a landmark conference, *Neuroethics: Mapping the Field*. Neuroethics may be defined as the study of the moral and ethical questions involved in applying new brain-related scientific findings, such as genetics, brain imaging, disease diagnosis, and prediction, and how the medical, insurance, and governmental leaders will face them. Embracing their task, the participants took part in lively discussions, the transcripts of which have been organized into this proceedings book. It allows the reader to see what the experts think the future holds for this emerging field. Topics include the themes of enhancement and free will, and the promise and peril of technology.

367 pages, 40 black-and-white photos, 10 black-and-white illustrations. Available free by mail or online.

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This practical resource is directed to those interested in creating, maintaining, or upgrading arts-centered schools. Eighteen essays by artists and educators highlight best practices and offer approaches from their own varied experiences in the development of arts-centered schools. The *Handbook* was designed to guide organizations in essential issues, including curriculum and development, governance, funding, assessment, and community participation. Appendices offer valuable resource information.

This publication is available free to schools, school boards, arts agencies, artists who consult with schools, and organizations interested in arts and education.

In addition to the essays, there is a prolegomenon from William Safire, chairman of the Dana Foundation, and an opening commentary from Janet Eilber, principal arts consultant to the Dana Foundation.

164 pages, 3 color illustrations, 10 black-and-white illustrations. Available free by mail or online.

A Glossary of Key Brain Science Terms

(Italicized terms are defined within this glossary.)

adrenal glands: Located on top of each kidney, these two glands are involved in the body's response to stress and help regulate growth, blood glucose levels, and the body's metabolic rate. They receive signals from the brain and secrete several different *hormones* in response, including *cortisol* and *adrenaline*.

adrenaline: Also called epinephrine, this *hormone* is secreted by the *adrenal glands* in response to stress and other challenges to the body. The release of adrenaline causes a number of changes throughout the body, including the metabolism of carbohydrates, to supply the body's energy demands.

allele: One of the variant forms of a *gene* at a particular location on a chromosome. Differing alleles produce variation in inherited characteristics such as hair color or blood type. In an individual, one form of the allele (the *dominant* one) may be expressed if one copy is present, while a *recessive* allele will show only where both copies are present.

amino acid: One of a group of 20 different kinds of small molecules that contain nitrogen as well as carbon, hydrogen, and oxygen that link together in folded chains to form proteins. Often referred to as the "building blocks" of proteins.

amino acid neurotransmitters: The most prevalent *neurotransmitters* in the brain, these include glutamate and aspartate, which have excitatory actions, and glycine and gamma-amino butyric acid (GABA), which have inhibitory actions.

amygdala: Part of the brain's *limbic system,* this primitive brain structure lies deep in the center of the brain and is involved in emotional reactions such as anger, as well as emotionally charged *memories.* It also influences behavior such as feeding, sexual interest, and the immediate "fight or flight" reaction to stress, to help ensure that the body's needs are met.

amyloid-b (Ab) protein: A naturally occurring protein in brain cells. Tangles of this protein form the plaques that are the hallmark of Alzheimer's disease and are thought by many researchers to cause the disease itself.

animal model: A scientific technique that relies on laboratory animals (usually mice or rats) to mimic specific behavioral traits or symptoms of a human disease. Many of the most promising advances in treating brain disorders have come from research on animal models.

astrocyte: Cell that delivers "fuel" to the *neurons* from the blood, removes waste from the *neuron,* and modulates the activity of the *neuron.*

auditory cortex: Part of the brain's *temporal lobe* (see Figure 3, p. 136.), this is the area of the brain responsible for hearing. Nerve fibers extending from the inner ear carry nerve impulses generated by sounds into the auditory cortex for interpretation.

autonomic nervous system: Part of the *central nervous system* that controls functions of internal organs (e.g., blood pressure, respiration, intestinal function, urinary bladder control, perspiration, body temperature). Its actions are mainly involuntary.

axon: A long, single nerve fiber that transmits messages, via chemical and electrical impulses, from the body of the *neuron* to *dendrites* of other neurons, or directly to body tissues such as muscles. (See Figure 4, p. 137.)

basal ganglia: Structure below the cortex involved in motor, *cognitive,* and emotional functions.

brain imaging: Refers to various techniques, such as *magnetic resonance imaging (MRI)* and *positron emission tomography (PET)*, that enable scientists to capture images of brain tissue and structure and to reveal what parts of the brain are associated with various behaviors or activities.

brain stem: A primitive part of the brain that connects the brain to the *spinal cord.* The brain stem controls functions basic to the survival of all animals, such as heart rate, breathing, digestive processes, and sleeping. (See Figure 1, p. 134.)

central nervous system: The brain and *spinal cord* constitute the central nervous system and are part of the broader nervous system, which also includes the *peripheral nervous system.*

central sulcus: The primary groove in the brain's *cerebrum,* which separates the *frontal lobe* in the front of the brain from the *parietal* and *occipital* lobes in the rear of the brain. (See Figure 3, p. 136.)

cerebellum: A brain structure located at the top of the *brain stem* (See Figure 1, p. 134.) that coordinates the brain's instructions for skilled, repetitive movements and helps maintain balance and posture. Recent research also suggests the cerebellum may play a role, along with the *cerebrum,* in higher *cognitive* processes.

cerebrum (also called cerebral cortex): The largest brain structure in humans, accounting for about two-thirds of the brain's mass and positioned over and around most other brain structures. (See Figure 2, p. 135.) The cerebrum is divided into left and right *hemispheres,* as well as specific areas called lobes that are associated with specialized functions.

cognition: A general term that includes thinking, perceiving, recognizing, conceiving, judging, sensing, reasoning, and imagining. Also, cognitive, an adjective pertaining to cognition, as in cognitive processes.

Computed Tomography (CT or CAT): An x-ray technique introduced in the early 1970s that enables scientists to take cross-sectional images of the body and brain. CT uses an x-ray beam passed through the body to collect information about tissue density, then applies sophisticated computer and mathematical formulas to create an anatomical image from that data.

consciousness: The state of being aware of one's feelings and what is happening around one; the totality of one's thoughts, feelings, and impressions about the world around us. The search for the basis of consciousness in the activity and structures of the brain is one of the most intriguing areas of modern *neuroscience.*

cortisol: A steroid *hormone* produced by the *adrenal glands* that controls how the body uses fat, protein, carbohydrates, and minerals and helps reduce inflammation. Cortisol is released in the body's stress response; brain scientists have found that prolonged exposure to cortisol has damaging effects on the brain.

CT scan (also called CAT scan): See *computed tomography.*

dementia: General mental deterioration from a previously normal state of *cognitive* function due to disease or psychological factors (not to be confused with mental retardation, or developmental disability). Alzheimer's disease is one form of dementia.

dendrite: Short nerve fibers that project from a nerve cell, generally receiving messages from the *axons* of other *neurons* and relaying them to the cell's nucleus. (See Figure 4, p. 137.)

dependence: In reference to drug or alcohol addiction, dependence describes a state marked by uncontrolled, compulsive drug use, in which the brain's "pleasure pathways"—networks of *neurons* that use the *neurotransmitter dopamine*—physically change, leading to drug dependency. (Also see *psychological dependence*.)

depression: A mood or affective disorder often characterized by disruptions in one or more of the brain's *neurotransmitter* systems, including those related to *serotonin* and *dopamine*. Clinical depression is a serious condition that can be effectively treated with medications and/or behavioral therapy.

DNA (deoxyribonucleic acid): The material from which the 46 chromosomes in each cell's nucleus is formed. DNA contains the codes for the body's approximately 30,000 *genes,* governing all aspects of cell growth and inheritance. DNA has a *double-helix* structure—two intertwined strands resembling a spiraling ladder.

dominant: A *gene* that almost always results in a specific physical characteristic, for example a disease, even though the patient's *genome* possesses only

one copy. With a dominant *gene,* the chance of passing on the *gene* (and therefore the trait or disease) to children is 50-50 in each pregnancy.

dopamine: A *neurotransmitter* involved in the brain's reward, or pleasure, system and in the control of body movement. Some addictive drugs increase brain levels of dopamine, causing the "high" associated with illicit drug use. Virtually all addictive substances, from nicotine to alcohol to heroin and crack cocaine, affect the dopamine system in one way or another.

double helix: The structural arrangement of *DNA,* which looks something like an immensely long ladder twisted into a helix, or coil. The sides of the "ladder" are formed by a backbone of sugar and phosphate molecules, and the "rungs" consist of nucleotide bases joined weakly in the middle by hydrogen bonds.

endocrine system: A body system composed of several different glands and organs that secrete *hormones.*

endorphins: *Hormones* produced by the brain in response to pain or stress to blunt the sensation of pain. *Narcotic* drugs such as morphine imitate the actions of the body's natural endorphins.

enzyme: A protein that encourages a biochemical reaction, usually speeding it up. Organisms could not function if they had no enzymes.

frontal lobe: The front part of the brain's *cerebrum*, beneath the forehead. (See Figure 3, p. 136.) This area of the brain is associated with higher *cognitive* processes, such as decision-making, reasoning, and planning.

functional magnetic resonance imaging (fMRI): A *brain imaging* technique based on conventional *MRI,* but which uses sophisticated computer programs to create images that show which areas of the brain are functioning during certain tasks, behaviors, or thoughts.

gene: The basic unit of inheritance. A distinct section of *DNA* in a cell's chromosome that contains the codes for producing specific proteins involved in brain and body function. Gene defects (genetic *mutations*) are thought to cause many brain disorders.

gene expression: The process by which proteins are made from the instructions encoded in *DNA*.

gene mapping: Determining the relative positions of *genes* on a chromosome and the distance between them.

genome: The complete genetic map for an organism. In humans, this includes about 30,000 *genes* whose codes are written in our *DNA*, the spiraling chain of proteins that makes up the 46 chromosomes in each cell. More than 15,000 *genes* relate to functions of the brain.

glial cells: The supporting cells of the *central nervous system.* Though probably not involved directly in the transmission of nerve signals, glial cells protect and nourish the *neurons*.

glucose: A natural sugar that is carried in the blood and is the principal source of energy for the cells of the brain and body. *PET* imaging techniques measure brain activity by measuring increases in the brain's *metabolism* of glucose during specific mental tasks a person performs.

gray matter: The parts of the brain and spinal cord made up primarily of groups of *neuron* cell bodies (as opposed to *white matter*, which is composed mainly of *myelinated* nerve fibers).

gyrus: The ridges on the brain's outer surface. Plural is *gyri*.

hemisphere: In brain science, refers to the two halves of brain (the left and right hemispheres), which are separated by a deep groove, or fissure, down the center. Some major, specific brain functions are located in one or the other hemisphere.

hippocampus: A primitive brain structure located deep in the brain (see Figure 2, p. 135) that is involved in *memory* and learning.

hormone: A chemical released by the body's *endocrine* glands (including the *adrenal glands*), as well as by some tissues. Hormones act on *receptors* in other parts of the body to influence body functions or behavior.

hypothalamus: A small structure located at the base of the brain, where signals from the brain and the body's *hormonal* system interact.

interneuronal: Between *neurons,* as in interneuronal communication.

ions: Atoms or groups of atoms carrying a negative or positive charge of electricity. When a nerve impulse is fired, ions flow through channels in the membrane of a nerve cell, changing the charge in that local area of the cell to positive from its resting, negatively charged state. This sets off a chain reaction of positive charges that carries the nerve impulse along the cell's *axon* to the *synapse*, where it releases *neurotransmitters* into the *synaptic cleft*. (See Figures 5 and 6, pp. 138, 139.)

lesion: An injury or surgical incision to body tissue. Much of what has been learned about the functions of various brain structures or pathways has resulted from lesion studies, in which scientists observe the behavior of persons who have suffered injury to a distinct area of the brain or analyze the behavior resulting from a lesion made in the brain of a laboratory animal.

limbic system: A term for a group of brain structures that has probably changed little throughout evolution and is located in the inner brain, encircling the top of the *brain stem.* The limbic structures play a complex role in emotions, instincts, and behavioral drives.

magnetic resonance imaging (MRI): A brain imaging technique that uses intensely powerful magnets (some as much as 80,000 times the magnetic field of the Earth) to create sharp anatomical images of the brain or body. During an MRI scan, the person is placed inside a scanner, where the strong magnetic field causes the millions of atoms in the body to line up in a particular fashion (just as the needle of a compass lines up in the Earth's magnetic field). The machine then sends out pulses of radio waves, which cause the atoms to release radio signals. The pattern of signals provides information about the number of particular atoms present and their chemical environment. Sophisticated computer programs are then used to reconstruct the data into images of anatomical structure. MRI is also used to measure brain activity. (See *functional MRI.*)

melatonin: A *hormone* that is secreted by the pineal gland in the brain in response to the daily light-dark cycle, influencing the body's sleep-wake cycle and possibly affecting sexual development.

memory: A complex brain function that involves integrated systems of *neurons* in diverse brain areas, each of which handles individual memory-related tasks. Memory can be categorized into two distinct types, each with its own corresponding brain areas. Memory about people, places, and things is referred to as explicit or declarative memory and seems to be centered in the *hippocampus* and *temporal lobe*. (See Figures 2 and 3, pp. 135, 136.) Memory about motor skills and perceptual strategies is known as implicit, or procedural memory and seems to involve the *cerebellum*, the *amygdala* (see Figures 2 and 3, pp. 135, 136.), and specific pathways related to the particular skill (e.g., riding a bicycle would involve the *motor cortex*, etc.).

metabolize: To break down or build up biochemical elements in the body, effecting a change in body tissue. Brain cells metabolize *glucose,* a blood sugar, to derive energy for transmitting nerve impulses.

molecular biology: The study of the structure and function of cells at the level of the molecules from which they are comprised and how these molecules influence behavior and disease processes. Molecular biology has emerged as a scientific discipline only in the last couple of decades, due to advances in genetics and sophisticated technologies that have made it possible to "split" cells and study their internal structures.

motor cortex: The part of the brain's *cerebrum*, just to the front of the *central sulcus* in the *frontal lobe* (see Figure 3, p. 136), that is involved in movement and muscle coordination. Scientists have identified specific spots in the motor cortex that control movement in specific parts of the body, the so-called "motor map."

MRI: See *magnetic resonance imaging,* and/or *functional magnetic resonance imaging.*

mutation: A permanent structural alteration in *DNA.* In most cases, DNA changes either have no effect or cause harm, but occasionally a mutation can improve an organism's chance of surviving and passing the beneficial change on to its descendants.

myelin: The fatty substance that sheaths most nerve cell *axons*, helping to insulate and protect the nerve fiber and helping to speed up the transmission of nerve impulses. (See Figure 4, p. 137.)

narcotic: A synthetic chemical compound that mimics the action of the body's natural *endorphins, hormones* secreted to counteract pain. Narcotic drugs have a valid and useful role in the management of pain but may lead to physical *dependence* in susceptible individuals if used for long periods.

neuron: Nerve cell. The basic units of the *central nervous system*, neurons are responsible for the transmission of nerve impulses. (See Figures 4 and 5, pp. 137, 138.) Unlike any other cell in the body, neurons consist of a central cell body as well as several threadlike "arms" called *axons* and *dendrites*, which transmit nerve impulses. Scientists estimate there are more than 100 billion neurons in the brain.

neuroscience: The study of the brain and nervous systems, including their structure, function, and disorders. Neuroscience as a discipline has emerged only in the last couple of decades.

neurotransmitter: A chemical that acts as a messenger between *neurons* and is released into the *synaptic cleft* when a nerve impulse reaches the end of an *axon.* (See Figures 5 and 6, pp. 138, 139.) Several dozen neurotransmitters have been identified in the brain so far, each with specific, often complex roles in brain function and human behavior.

nurture: In science, refers to the influence of environmental factors, such as the experiences one is exposed to in early life, in human development. The term is often used in the context of "nature versus nurture," which relates to the interplay of "nature" (genetic or inherited, predetermined influences) and environmental, or experiential, forces.

occipital lobe: A part of the brain's *cerebrum*, located at the rear of the brain, above the *cerebellum.* (See Figure 3, p. 136.) The occipital lobe is primarily concerned with vision and encompasses the *visual cortex.*

olfactory: Pertaining to the sense of smell. When stimulated by an odor, olfactory receptor cells in the nose send nerve impulses to the brain's olfactory bulbs, which in turn transmit the impulses to olfactory centers in the brain for interpretation.

opiate: A naturally occurring chemical that has specific actions in the brain, influencing the "pleasure pathways" of the *dopamine* system by locking onto specialized opiate *receptors* in certain *neurons*.

pain receptors: Specialized nerve fibers in the skin and on the surfaces of internal organs, which detect painful stimuli and send signals to the brain.

parietal lobe: The area of the brain's *cerebrum* located just behind the *central sulcus.* (See Figure 3, p. 136.) It is concerned primarily with the reception and processing of sensory information from the body and is also involved in map interpretation and spatial orientation (recognizing one's position in space vis-a-vis other objects or places).

peripheral nervous system: The nervous system outside the brain and *spinal cord*.

PET: See *positron emission tomography.*

physical dependence: See *dependence.*

pituitary gland: An *endocrine* organ closely linked with the *hypothalamus*. The pituitary gland is composed of two lobes and secretes a number of *hormones* that regulate the activity of the other *endocrine* organs in the body.

plasticity: In *neuroscience,* refers to the brain's capacity to change and adapt in response to developmental forces, learning processes, or aging, or in response to an injury in a distinct area of the brain.

positron emission tomography (PET): A brain imaging technique that measures changes in brain metabolism to create three-dimensional images of brain activity. In a PET scan, a radioactive "marker" that emits, or releases, positrons (parts of an atom that release gamma radiation) is injected into the bloodstream. Detectors outside of the head can sense these "positron emissions," which are then reconstructed using sophisticated computer programs to create "tomographs," or computer images. Since blood flow and *metabolism* increase in brain regions at work, those areas have higher concentrations of the marker, and researchers are able to see which brain regions are activated during certain tasks or exposure to sensory stimuli.

postsynaptic cell: The *neuron* on the receiving end of a nerve impulse transmitted from another *neuron*. (See Figure 5, p. 138.)

prefrontal cortex: The area of the *cerebrum* located in the forward part of the *frontal lobe* (see Figure 3, p. 136.), which is thought to control higher *cognitive* processes such as planning, reasoning, and "social cognition"—a complex skill involving the ability to assess social situations in light of previous experience and personal knowledge and interact appropriately with others. The prefrontal cortex is thought to be the most recently evolved area of the brain.

premotor cortex: The area of the *cerebrum* located between the *prefrontal cortex* and the *motor cortex,* in the *frontal lobe.* (See Figure 3, p. 136.) It is involved in the planning and execution of movements.

presynaptic cell: In *synaptic transmission,* the *neuron* that sends a nerve impulse across the *synaptic cleft* to another *neuron*. (See Figure 5, p. 138.)

psychiatry: A medical specialty dealing with the diagnosis and treatment of mental disorders. (Contrast with *psychology*.)

psychoactive drug: A class of pharmaceutical medications that acts on the brain's pleasure and mood-regulating systems and can help control the symptoms of some neurological and *psychiatric* disorders, such as schizophrenia or obsessive-compulsive disorder.

psychological dependence: In the science of addiction, refers to what was once considered the psychological or behavioral aspects of addiction (such as craving a cigarette after a meal). Brain scientists now understand that psychological factors are central to addictive disorders and are often the most difficult to treat. (Also see *dependence*.)

psychology: An academic or scientific field of study concerned with the behavior of humans and animals and related mental processes. (Contrast to *psychiatry*.)

quadrillion: A number represented by 1 with 15 zeros (1,000,000,000,000,000). Scientists estimate that there are about 1 quadrillion *synaptic* connections among the *neurons* in the *central nervous system,* an estimate based on the belief that there are at least 100 billion (100,000,000,000) *neurons*, and that each *neuron* makes as many as 10,000 connections.

receptors: Molecules on the surfaces of *neurons* whose structures precisely match those of chemical messengers (such as *neurotransmitters* or *hormones*) released during *synaptic transmission*. The chemicals attach themselves to the receptors, in lock-and-key fashion, to activate the receiving cell structure (usually a *dendrite* or cell body). (See Figures 5 and 6, pp. 138, 139.)

recessive: A genetic trait or disease that appears only in patients who have received two copies of a *mutant gene,* one from each parent.

reuptake: A process by which released *neurotransmitters* are absorbed for subsequent reuse.

ribonucleic acid: A chemical similar to a single strand of *DNA.* The sugar is ribose, not deoxyribose, hence RNA. In RNA, the letter U, which stands for uracil, is substituted for T in the genetic code. RNA delivers *DNA's* genetic message to the cytoplasm of a cell, where proteins are made.

serotonin: A *neurotransmitter* believed to play many roles, including, but not limited to, temperature regulation, sensory perception, and the onset of sleep. *Neurons* using serotonin as a transmitter are found in the brain and in the gut. A number of antidepressant drugs are targeted to brain serotonin systems.

spinal cord: The "other half" of the *central nervous system* (with the brain). The spinal cord is a cable that descends from the *brain stem* to the lower back. It consists of an inner core of *gray matter* surrounded by *white matter*. (See Figure 1, p. 134.)

stem cells: Undifferentiated cells that can grow into heart cells, kidney cells, or other cells of the body. Originally thought to be found only in embryos, stem cells in the brain have unexpectedly been discovered in adults. Researchers have shown on research animals that stem cells can be transplanted into various regions of the brain, where they develop into both *neurons* and *glia*.

sulcus: The shallower grooves on the brain's *cerebrum* (deeper grooves are called fissures). Plural is *sulci*.

synapse: The junction where an *axon* approaches another *neuron* or its extension (a *dendrite*); the point at which nerve-to-nerve communication occurs. Nerve impulses traveling down the axon reach the synapse and release *neurotransmitters* into the *synaptic cleft*, the tiny gap between *neurons*. (See Figures 5 and 6, pp. 138, 139.)

synaptic transmission: The process of cell-to-cell communication in the *central nervous system* (see Figures 5 and 6, pp. 138, 139), whereby one *neuron* sends a chemical signal across the *synaptic cleft* to another *neuron*.

temporal lobes: The parts of the *cerebrum* that are located on either side of the head, roughly beneath the temples in humans. These areas are involved in hearing, language, *memory* storage, and emotion. (See Figure 3, p. 136.)

thalamus: A brain structure located at the top of the *brain stem*, the thalamus acts as a two-way relay station, sorting, processing, and directing signals from the *spinal cord* and mid-brain structures to the *cerebrum*, and from the *cerebrum* down. (See Figure 2, p. 135.)

visual cortex: The area of the *cerebrum* that is specialized for vision. It lies primarily in the *occipital lobe* (see Figure 3, p. 136) at the rear of the brain, and is connected to the eyes by the optic nerves.

white matter: Brain or *spinal cord* tissue consisting primarily of the *myelin*-covered *axons* that extend from nerve cell bodies in the *gray matter* of the *central nervous system*.

SOURCES:

Stedman's Medical Dictionary, 24th edition. Williams & Wilkins; Baltimore (1982).

Clayman C, ed., *The Human Body: An Illustrated Guide to Its Structure, Function, and Disorders.* Dorling Kindersley; New York (1995).

Posner MI, Raichle ME. *Images of Mind*. Scientific American Library; New York (1994).

Webster's New World Dictionary, 3rd College Edition. Simon & Schuster; New York (1991).

National Institute of Drug Abuse (NIDA); *Mind Over Matter Teachers Guide, Introduction and Background* (from the NIDA Web site).

National Human Genome Research Institute (NIH), www.nhgri.nih.gov.

Howard Hughes Medical Institute, *Blazing a Genetic Trail,* www.hhmi.org.

Society for Neuroscience, *Brain Facts, Fourth Edition,* Washington, DC (2002).

Maps of the Brain

Figure 1

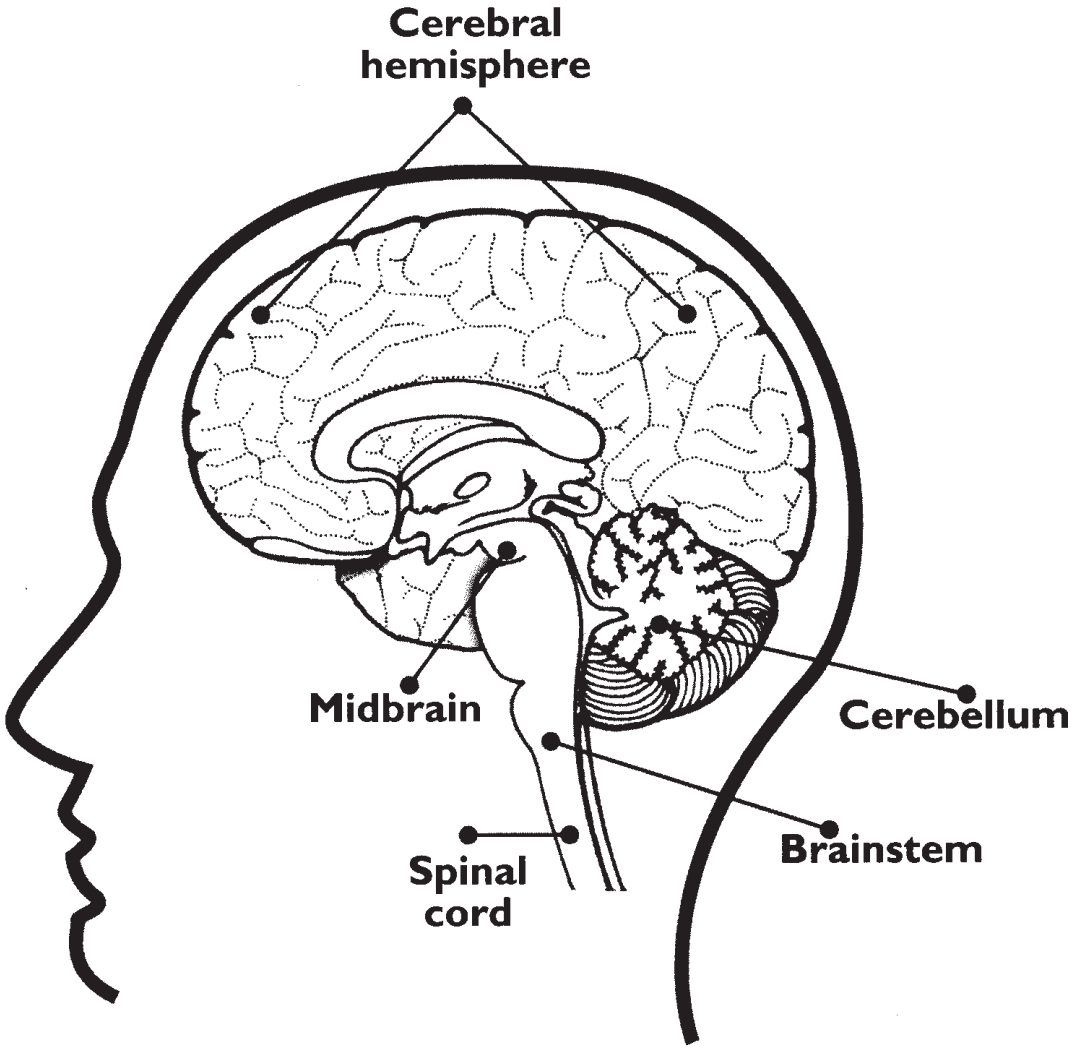


Figure 2

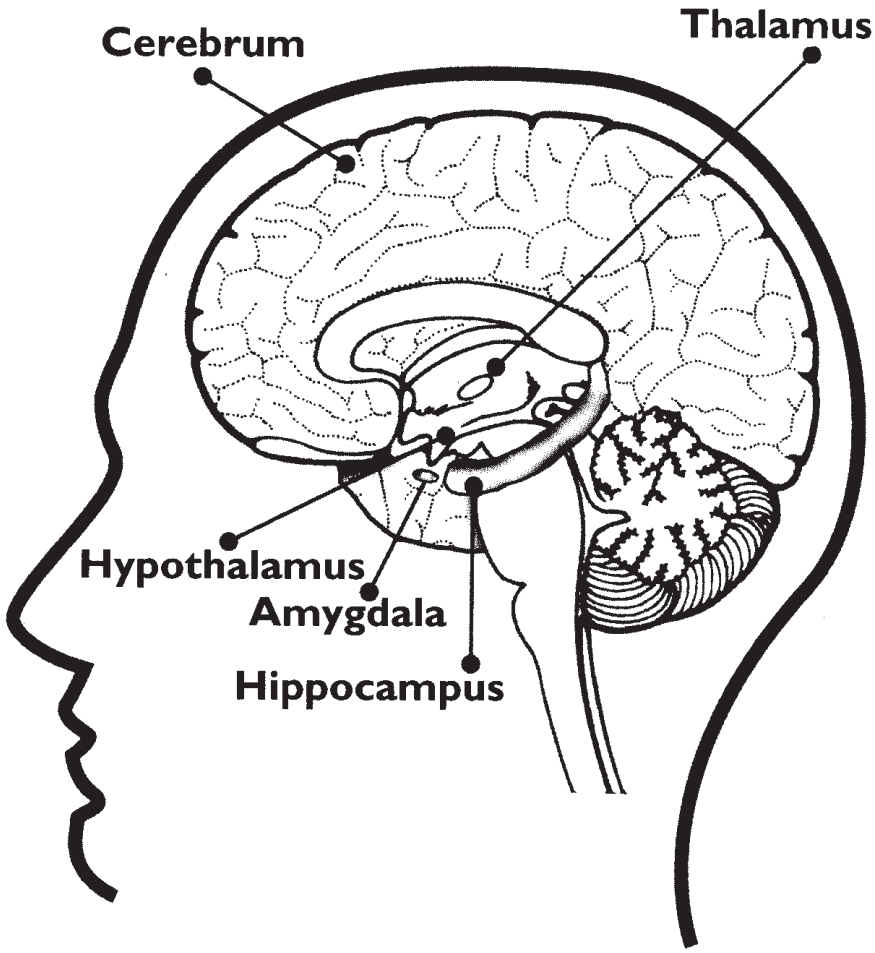


Figure 3

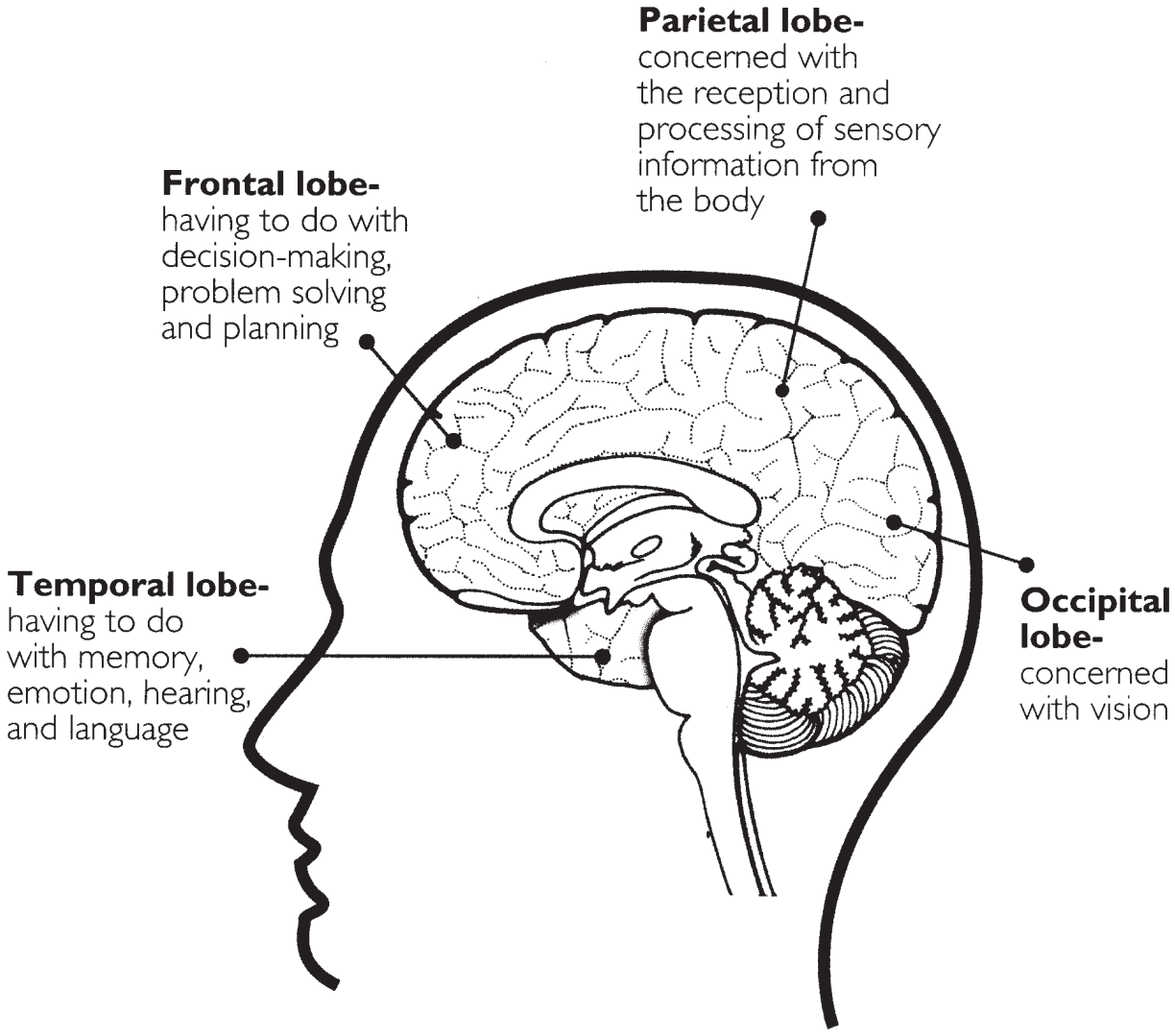

Parietal lobe-
concerned with
the reception and
processing of sensory
information from
the body
Frontal lobe-
having to do with
decision-making,
problem solving
and planning
Temporal lobe-
having to do
with memory,
emotion, hearing,
and language
Occipital
lobe-
concerned
with vision

Figure 4

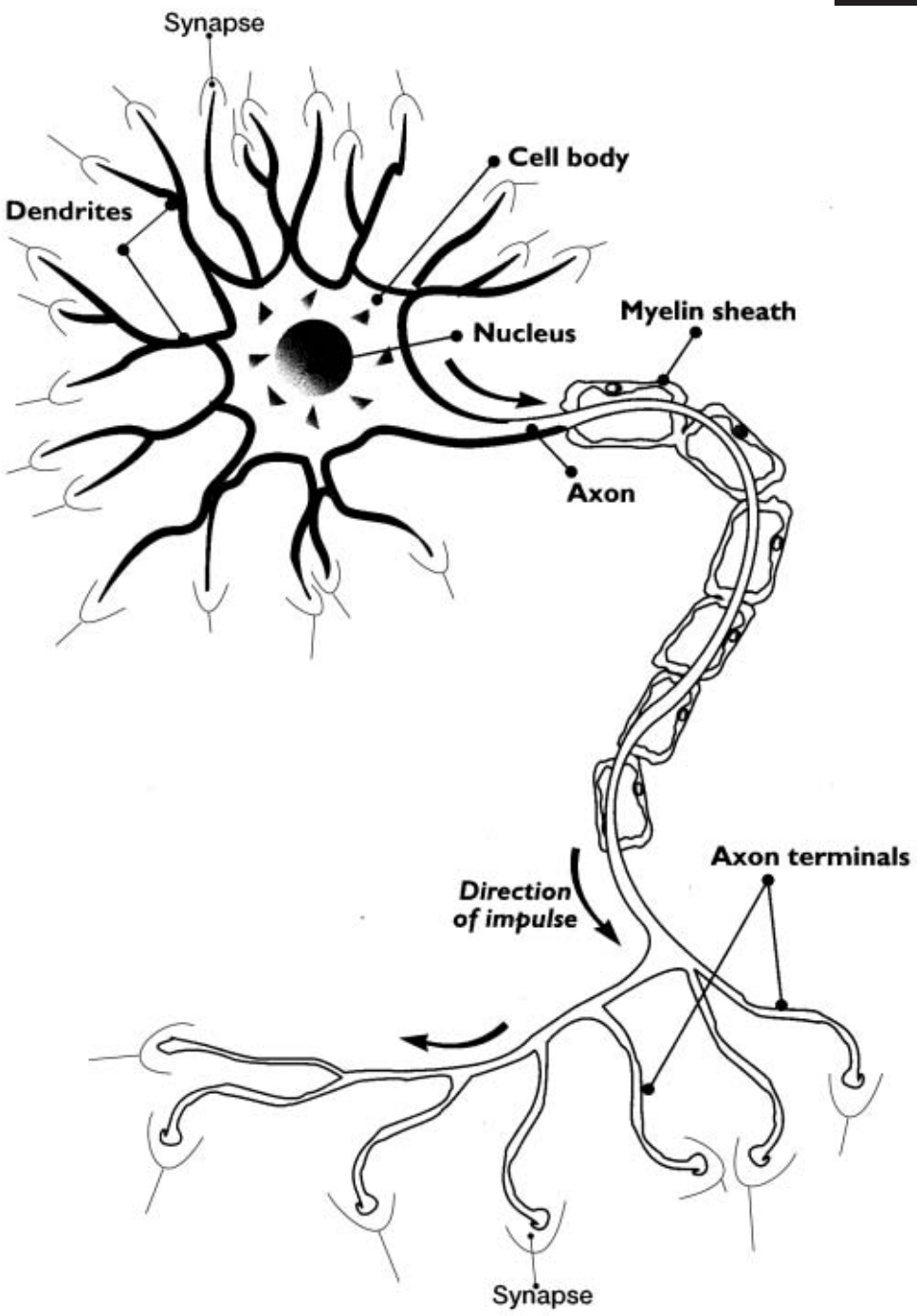

Synapse
Cell body
Dendrites
Myelin sheath
Nucleus
Axon
Axon terminals
Direction of impulse
Synapse

Figure 5

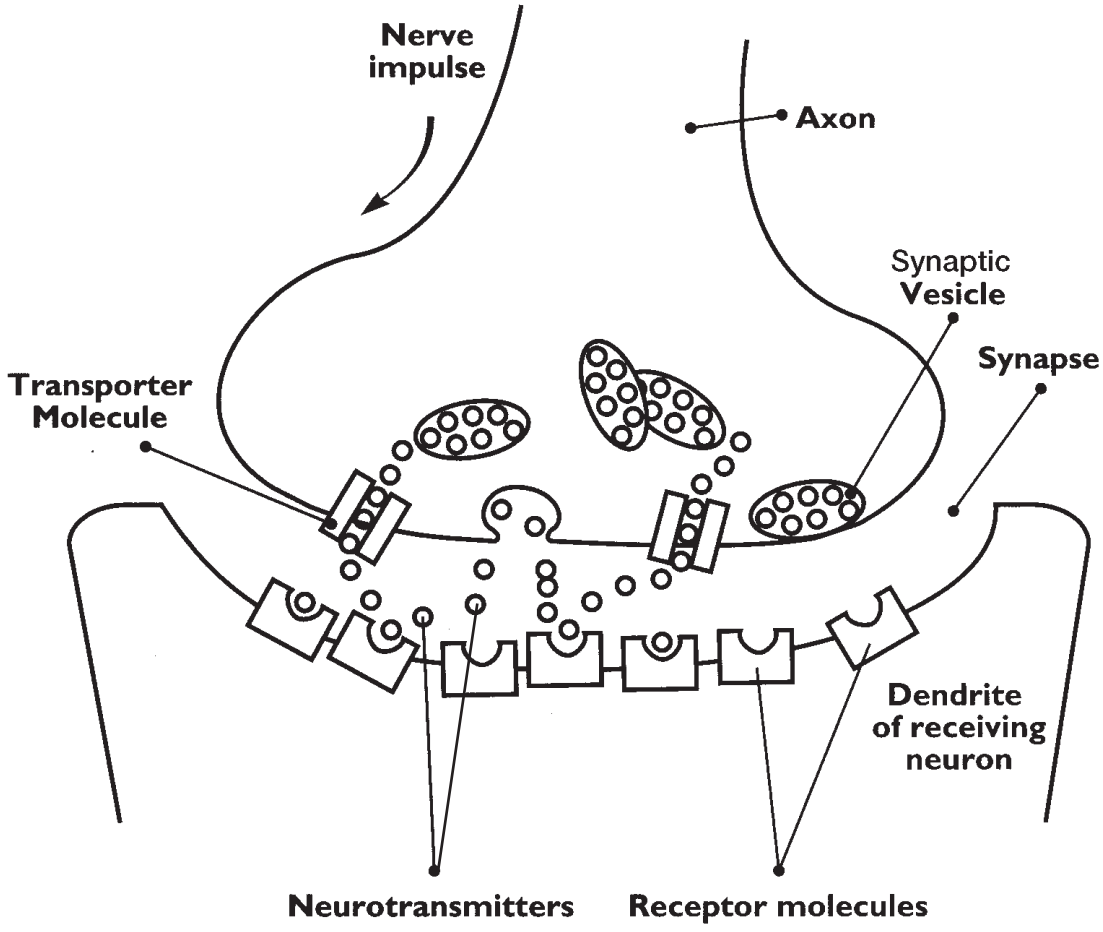
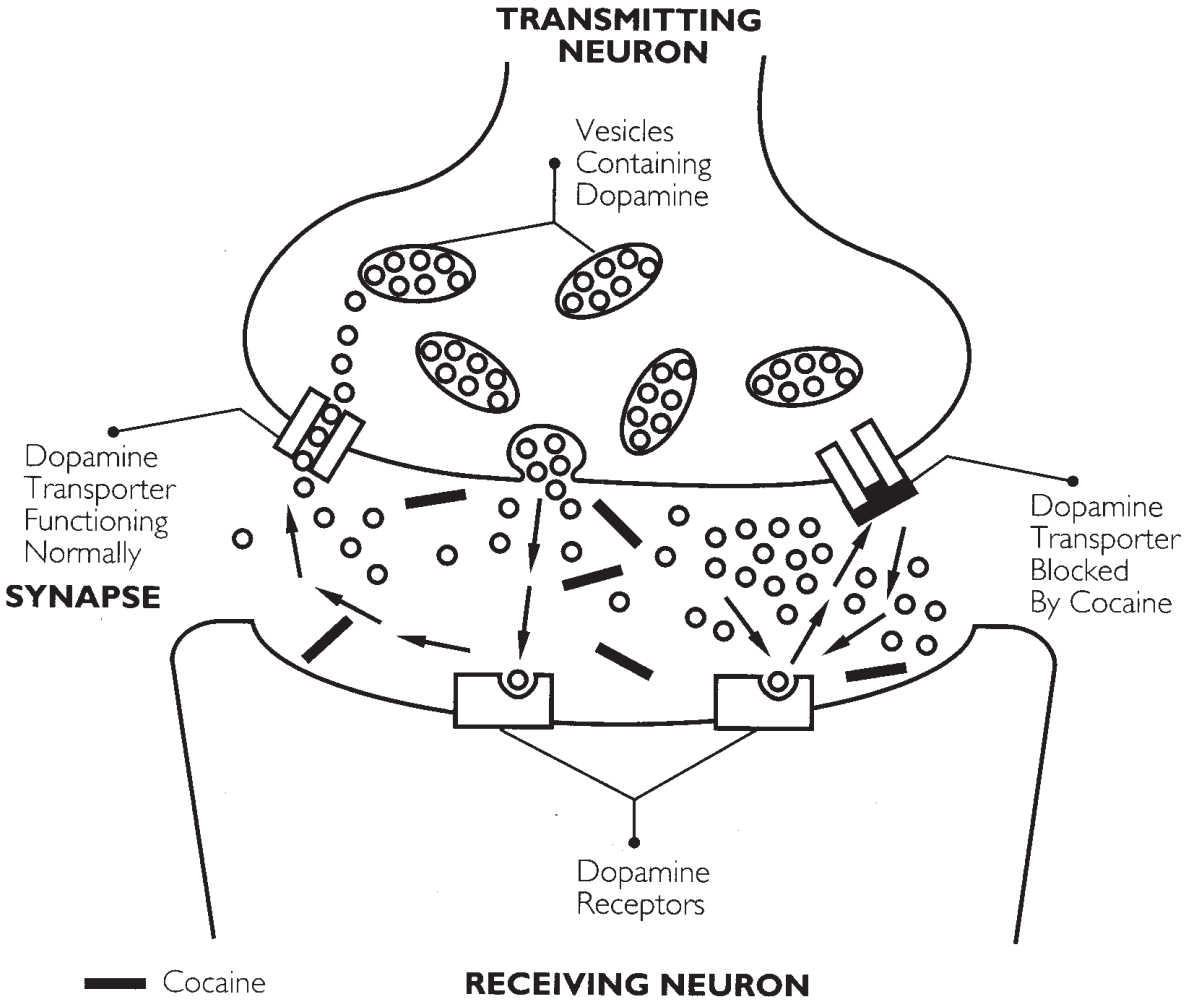

Nerve impulse
Axon
Synaptic Vesicle
Synapse
Transporter Molecule
Dendrite of receiving neuron
Neurotransmitters
Receptor molecules

Figure 6


TRANSMITTING NEURON
Vesicles Containing Dopamine
Dopamine Transporter Functioning Normally
SYNAPSE
Dopamine Transporter Blocked By Cocaine
Dopamine Receptors
Cocaine
RECEIVING NEURON

Resources on the Web

■ GENERAL INFORMATION/SUPPORT

AARP: www.aarp.org

American Academy of Neurology: www.aan.com

American Association of Suicidology: www.suicidology.org

American Psychiatric Association: www.psych.org

American Psychological Association: www.apa.org

American Self-Help Clearinghouse: www.selfhelpgroups.org

American Society for Adolescent Psychiatry: www.adolpsych.org

Children of Aging Parents: www.caps4caregivers.org

Easter Seals: www.easter-seals.org

Family Caregiver Alliance: www.caregiver.org

Federation of Families for Children's Mental Health: www.ffcmh.org

Genetic Alliance: www.geneticalliance.org

Harvard Brain Tissue Resource Center: www.brainbank.mclean.org

National Alliance for the Mentally Ill (NAMI): www.nami.org

National Mental Health Association: www.nmha.org

National Organization for Rare Disorders: www.rarediseases.org

Well Spouse Foundation: www.wellspouse.org

■ GOVERNMENT RESOURCES

Anxiety Disorder Education Program Library: www.nimh.nih.gov

Centers for Disease Control and Prevention: www.cdc.gov

Eldercare Locator: www.eldercare.gov

National Cancer Institute at NIH: www.cancer.gov

National Center for Complementary and Alternative Medicine: Information Clearinghouse: www.nccam.nih.gov

National Eye Institute: www.nei.nih.gov

National Heart, Lung and Blood Institute: www.nhlbi.nih.gov

National Institute on Aging: www.nih.gov/nia

National Institute on Alcohol Abuse and Alcoholism: www.niaaa.nih.gov

National Institute of Allergy and Infectious Diseases: www.niaid.nih.gov

National Institute of Child Health and Human Development: www.nichd.nih.gov

National Institute on Deafness and Other Communication Disorders: www.nidcd.nih.gov

National Institute on Drug Abuse (NIDA): www.nida.nih.gov

National Institute of Mental Health: www.nimh.nih.gov

National Institute of Neurological Disorders and Stroke: Office of Communications and Public Liaison: www.ninds.nih.gov

Office of Rare Diseases at NIH: www.rarediseases.info.nih.gov

■ ACOUSTIC NEUROMA

Acoustic Neuroma Association: www.anausa.org

■ AGENESIS CORPUS CALLOSUM

The ACC Network: University of Maine: E-mail: um-acc@maine.edu

■ AGING-RELATED DISEASES

Alliance for Aging Research: www.agingresearch.org

National Council on Aging: www.ncoa.org

■ AIDS DEMENTIA

CDC National Prevention Information Network: www.cdcnpin.org

Gay Men's Health Crisis (GMHC): www.gmhc.org

■ ALCOHOL AND DRUG ABUSE

(See also: Drug Abuse)

Al-Anon Family Groups Headquarters, Inc.: www.al-anon.alateen.org

Alcoholics Anonymous: AA World Services, Inc.: www.aa.org

American Society of Addiction Medicine: www.asam.org

Betty Ford Center at Eisenhower: www.bettyfordcenter.org

National Clearinghouse for Alcohol & Drug Abuse Information: www.health.org

National Council on Alcoholism and Drug Dependence (NCADD): www.ncadd.org

Recovery, Inc.: www.recovery-inc.org

■ ALZHEIMER'S DISEASE

Alzheimer's Association: www.alz.org

Alzheimer's Disease Education and Referral Center: National Institute on Aging: www.alzheimers.org

Alzheimer's Research Forum: www.alzforum.org

■ AMYOTROPHIC LATERAL SCLEROSIS (ALS or LOU GEHRIG'S DISEASE)

The ALS Association: www.alsa.org

Les Turner ALS Foundation: www.lesturnerals.org

■ ANGELMAN SYNDROME

(See: Rare Disorders)

■ ANOREXIA/BULIMIA (See: Eating Disorders)

■ ANXIETY DISORDERS

Anxiety Disorders Association of America: www.adaa.org

Freedom From Fear: www.freedomfromfear.org

National Anxiety Foundation: www.lexington-on-line.com/naf.html

■ APHASIA

National Aphasia Association: www.aphasia.org

■ ART/MUSIC THERAPY

National Coalition of Creative Arts Therapies Associations (NCCATA), c/o American Music Therapy Association: www.ncata.com

■ ATAXIA AND ATAXIA-TELANGIECTASIA

A-T Children's Project: www.atcp.org

National Ataxia Foundation: www.ataxia.org

■ ATTENTION DEFICIT/HYPERACTIVITY DISORDER (ADHD)

(See also: Learning Disabilities)

Children and Adults With Attention Deficit/Hyperactivity Disorder (CHADD): www.chadd.org

National ADD Association: www.add.org

■ AUTISM

Autism Genetic Resource Exchange: www.agre.org

Autism Society of America: www.autism-society.org

Cure Autism Now Foundation: www.cureautismnow.org

National Alliance for Autism Research: www.naar.org

National Center on Birth Defects and Developmental Disabilities: Centers for Disease Control and Prevention: www.cdc.gov/ncbddd/dd/ddautism.htm

■ AUTOIMMUNE DISEASES

(See: Neuroimmunological Disorders)

■ BACK PAIN (See: Pain (Chronic); Spine-Related Injury)

■ BATTEN DISEASE

Batten Disease Support and Research Association: www.bdsra.org

■ BEHAVIOR THERAPY

Association for Advancement of Behavior Therapy (AABT): www.aabt.org

■ BEHCET'S DISEASE

American Behcet's Disease Association: www.behcets.com

■ BENIGN ESSENTIAL BLEPHAROSPASM

Benign Essential Blepharospasm Research Foundation: www.blepharospasm.org

■ BIRTH DEFECTS

Birth Defect Research for Children: www.birthdefects.org

March of Dimes Birth Defects Foundation: www.marchofdimes.com

National Center on Birth Defects and Developmental Disabilities: www.cdc.gov/ncbddd/hot.htm

■ BLINDNESS/VISION IMPAIRMENT

Helen Keller National Center for Deaf/Blind Youth and Adults: www.helenkeller.org/national

Lighthouse International: www.lighthouse.org

Prevent Blindness America: www.preventblindness.org

Research to Prevent Blindness: www.rpbusa.org

■ BORDERLINE PERSONALITY DISORDER

Treatment and Research Advancements National Association for Personality Disorders: www.tara4bpd.org

■ BRAIN INJURY/PREVENTION

Brain Injury Association of America/Family HelpLine: www.biausa.org

Brain Injury Services: www.braininjurysvcs.org

Brain Trauma Foundation: www.braintrauma.org

Head Injury Hotline: www.headinjury.com

Think First Foundation: www.thinkfirst.org

■ BRAIN TUMOR (See also: Pediatric Brain Tumor; Pituitary Disorders)

American Brain Tumor Association: www.abta.org

The Brain Tumor Society: www.tbts.org

Dana-Farber Cancer Institute: www.dana-farber.net

The Healing Exchange BRAIN TRUST: www.braintrust.org

National Brain Tumor Foundation: www.braintumor.org

■ CEREBRAL PALSY

UCP National (United Cerebral Palsy)/United Cerebral Palsy Research and Educational Foundation: www.ucp.org

■ CHARCOT-MARIE-TOOTH DISEASE

Charcot-Marie-Tooth Association: www.charcot-marie-tooth.org

■ CHIARI MALFORMATION

(See: Spina Bifida; Syringomyelia)

■ COMA (See also: Brain Injury/Prevention)

Coma Recovery Association: www.comarecovery.org

■ CONCUSSION (See: Brain Injury/Prevention)

■ DEAFNESS/HEARING LOSS

Alexander Graham Bell Association for the Deaf and Hard of Hearing: www.agbell.org

American Society for Deaf Children: www.deafchildren.org

Better Hearing Institute: www.betterhearing.org

Cochlear Implant Association International: www.cici.org

Laurent Clerc National Deaf Education Center at Gallaudet University: http://clerccenter.gallaudet.edu/ (For ages 0-21)

National Cued Speech Association: www.cuedspeech.org

Self Help for Hard of Hearing People: www.shhh.org

■ DEJERINE-SOTTAS DISEASE
(See: Muscular Dystrophy)

■ DEPRESSION/MANIC DEPRESSION

Depression and Bi-Polar Support Alliance (formerly National Depressive and Manic-Depressive Association): www.dbsalliance.org

Depression and Related Affective Disorders Association (DRADA): www.drada.org

National Alliance for Research on Schizophrenia and Depression (NARSAD): www.narsad.org

National Foundation for Depressive Illness: www.depression.org

On Our Own: E-mail: ONOUROWN@aol.com

■ DISABILITY AND REHABILITATION
(See also: Spinal Cord Injury)

Disabled Sports USA: www.dsusa.org

The George Washington University HEATH Resource Center: www.heath.gwu.edu

Goodwill Industries International: www.goodwill.org

National Information Center for Children and Youth With Disabilities: www.nichcy.org

■ DIZZINESS (See: Vestibular Disorders)

■ DOWN SYNDROME

National Down Syndrome Society: www.ndss.org

■ DRUG ABUSE
(See also: Alcohol and Drug Abuse)

Do It Now Foundation: www.doitnow.org

National Families in Action: www.nationalfamilies.org

■ DYSAUTONOMIA

The Dysautonomia Foundation: www.familialdysautonomia.org

■ DYSLEXIA (See also: Learning Disabilities)

The International Dyslexia Association: www.interdys.org

■ DYSTONIA (See also: Tardive Dyskinesia/Tardive Dystonia)

Dystonia Medical Research Foundation: www.dystonia-foundation.org

■ EATING DISORDERS

National Association of Anorexia Nervosa and Associated Disorders: www.anad.org

National Eating Disorders Association (formerly Anorexia Nervosa and Related Eating Disorders (ANRED) and American Anorexia/Bulimia Association): www.nationaleatingdisorders.org

■ ENCEPHALITIS, RASMUSSEN'S
(See: Neuroimmunological Disorders)

■ EPILEPSY

Epilepsy Foundation: www.efa.org

■ ESSENTIAL TREMOR/FAMILIAL TREMOR

International Essential Tremor Foundation: www.essentialtremor.org

■ FETAL ALCOHOL SYNDROME

National Institute of Child Health and Human Development: (See Government Resources)

National Organization on Fetal Alcohol Syndrome: www.nofas.org

■ FRAGILE X SYNDROME

FRAXA Research Foundation: www.fraxa.org

■ FRIEDREICH'S ATAXIA

(See: Muscular Dystrophy)

■ GAUCHER DISEASE

National Gaucher Foundation: www.gaucherdisease.org

■ GUILLAIN-BARRE SYNDROME

Guillain-Barre Syndrome Foundation International: www.gbsfi.com

■ HEADACHE

American Council for Headache Education: www.achenet.org

Association for Applied Psychophysiology and Biofeedback: www.aapb.org

National Headache Foundation: www.headaches.org

■ HEAD INJURY/TRAUMA

(See: Brain Injury/Prevention; Coma)

■ HUNTINGTON'S DISEASE

Hereditary Disease Foundation: www.hdfoundation.org

Huntington's Disease Society of America: www.hdsa.org

■ HYDROCEPHALUS

Guardians of Hydrocephalus Research Foundation: http://ghrf.homestead.com/ghrf.html

Hydrocephalus Association: www.hydroassoc.org

National Hydrocephalus Foundation: www.nhfonline.org

■ JOSEPH DISEASES (See: Rare Disorders)

■ JOUBERT SYNDROME

Joubert Syndrome Foundation: www.joubertfoundation.com

■ LEARNING DISABILITIES

The International Dyslexia Association: www.interdys.org

Learning Disabilities Association of America: www.ldaamerica.org

National Center for Learning Disabilities: www.ld.org

■ LEIGH'S DISEASE (See: Rare Disorders)

■ LEUKODYSTROPHY

United Leukodystrophy Foundation: www.ulf.org

■ LOWE SYNDROME

Lowe Syndrome Association: www.lowesyndrome.org

■ LUPUS

Lupus Foundation of America: www.lupus.org

■ MACHADO-JOSEPH DISEASES

(See: Rare Disorders)

■ MEIGE SYNDROME

(See: Benign Essential Blepharospasm)

■ MENTAL RETARDATION

The Arc of the United States: www.thearc.org

■ MOEBIUS SYNDROME

(See: Rare Disorders)

■ MULTIPLE SCLEROSIS

Multiple Sclerosis Association of America: www.msaa.com

Multiple Sclerosis Foundation: www.msfacts.org

National Multiple Sclerosis Society: www.nmss.org

■ MUSCULAR DYSTROPHY

Muscular Dystrophy Association: www.mdausa.org

■ MYASTHENIA GRAVIS

(See also: Muscular Dystrophy)

Myasthenia Gravis Foundation of America: www.myasthenia.org

■ MYOSITIS **(See also: Muscular Dystrophy)**

Myositis Association of America: www.myositis.org

■ NARCOLEPSY **(See also: Sleep Disorders)**

Narcolepsy Network: www.narcolepsynetwork.org

■ NEIMANN-PICK DISEASE **(See: Rare Disorders)**

■ NEUROFIBROMATOSIS

National Neurofibromatosis Foundation: www.nf.org

Neurofibromatosis, Inc.: www.nfinc.org

■ NEUROIMMUNOLOGICAL DISORDERS **(See also: Multiple Sclerosis; Myasthenia Gravis)**

American Autoimmune RelatedDiseases Association: www.aarda.org

Institute for Brain and Immune Disorders: www.mmrfweb.org

■ NEUROMUSCULAR DISEASES **(See also: Polio/Post-Polio Syndrome; Charcot-Marie-Tooth Syndrome; Muscular Dystrophy)**

International Ventilator Users Network/Gazette International Networking Institute (GINI): www.post-polio.org

■ NEUROVASCULAR DISEASES **(See: Stroke; Epilepsy; Brain Tumor)**

■ OBSESSIVE-COMPULSIVE DISORDER (OCD)

Obsessive-Compulsive Foundation: www.ocfoundation.org

Trichotillomania Learning Center: www.trich.org

■ PAIN (CHRONIC)

American Chronic Pain Association: www.theacpa.org

American Pain Foundation: www.painfoundation.org

National Chronic Pain Outreach Association: www.chronicpain.org

■ PANIC DISORDERS **(See: Anxiety Disorders)**

■ PARALYSIS **(See: Spinal Cord Injury; Disability and Rehabilitation)**

■ PARKINSON'S DISEASE

American Parkinson's Disease Association: www.apdaparkinson.com

The Parkinson Foundation: www.pdf.org

Parkinson's Action Network: www.parkinsonsaction.org

The Parkinson's Institute: www.parkinsonsinstitute.org

■ PEDIATRIC BRAIN TUMOR

Brain Tumor Foundation for Children: www.btfcgainc.org

The Childhood Brain Tumor Foundation: www.childhoodbraintumor.org

Children's Brain Tumor Foundation: www.cbtf.org

Dana-Farber Cancer Institute: www.dana-farber.net

Pediatric Brain Tumor Foundation of the United States: www.pbtfus.org

■ PEDIATRIC STROKE **(See also: Stroke; Epilepsy; Cerebral Palsy)**

Pediatric Stroke Network: www.pediatricstrokenetwork.com

■ PITUITARY DISORDERS
(See also: Brain Tumor)
Pituitary Network Association: www.pituitary.org

■ POLIO/POST-POLIO SYNDROME
International Polio Network/Gazette International Networking Institute (GINI): www.post-polio.org
Post-Polio Syndrome Bibliography: E-mail: ppsbib7@aol.com

■ POSTPARTUM DEPRESSION
Depression After Delivery: www.depressionafterdelivery.com

■ POST-TRAUMATIC STRESS DISORDER
National Center for Post-Traumatic Stress Disorder: www.ncptsd.org

■ PRADER-WILLI SYNDROME
Prader-Willi Syndrome Association USA: www.pwsausa.org

■ PROGRESSIVE SUPRANUCLEAR PALSY
Society for Progressive Supranuclear Palsy: www.psp.org

■ PSEUDOTUMOR CEREBRI
(See: Rare Disorders)

■ RARE DISORDERS
National Organization for Rare Disorders (NORD): www.rarediseases.org

■ REFLEX SYMPATHETIC DYSTROPHY SYNDROME (RSDS)
RSDS Association: www.rsds.org

■ RESTLESS LEGS SYNDROME
RLS Foundation: www.rls.org

■ RETT SYNDROME
International Rett Syndrome Association: www.rettsyndrome.org

■ REYE'S SYNDROME
National Reye's Syndrome Foundation: www.reyessyndrome.org

■ SCHIZOPHRENIA
National Alliance for the Mentally Ill (NAMI): www.nami.org
National Alliance for Research on Schizophrenia and Depression: (NARSAD): www.narsad.org

■ SHY-DRAGER SYNDROME
Shy-Drager Syndrome/Multiple System Atrophy Support Group: www.shy-drager.com

■ SJOGREN'S SYNDROME
Sjogren's Syndrome Foundation: www.sjogrens.org

■ SLEEP DISORDERS (See also: Narcolepsy)
American Academy of Sleep Medicine: www.aasmnet.org
American Sleep Apnea Association: www.sleepapnea.org
National Sleep Foundation: www.sleepfoundation.org

■ SMELL AND TASTE (CHEMOSENSORY) DISORDERS (See Government Resources: National Institute on Deafness and Other Communication Disorders)

■ SOTOS SYNDROME
Sotos Syndrome Support Association: www.well.com/user/ssa/

■ SPASMODIC DYSPHONIA
National Spasmodic Dysphonia Association: www.dysphonia.org

■ SPASMODIC TORTICOLLIS
National Spasmodic Torticollis Association: www.torticollis.org

SPINA BIFIDA

Spina Bifida Association of America: www.sbaa.org

SPINAL CORD INJURY (See also: Disability and Rehabilitation)

Kent Waldrep National Paralysis Foundation: www.spinalvictory.org

National Spinal Cord Injury Association: www.spinalcord.org

Paralyzed Veterans of America: www.pva.org

Spinal Cord Injury Network International: www.spinalcordinjury.org

SPINAL MUSCULAR ATROPHY (See also: Muscular Dystrophy)

Families of Spinal Muscular Atrophy: www.curesma.com

SPINE-RELATED INJURY/BACK PAIN

North American Spine Society: www.spine.org

STROKE

American Stroke Association (A Division of the American Heart Association): www.strokeassociation.org

National Stroke Association: www.stroke.org

STURGE-WEBER DISEASE

The Sturge-Weber Foundation: www.sturge-weber.com

STUTTERING

National Stuttering Association: www.nsastutter.org

Stuttering Foundation of America: www.stutteringhelp.org

SYRINGOMYELIA

American Syringomyelia Alliance Project: www.asap.org

TARDIVE DYSKINESIA/TARDIVE DYSTONIA

Tardive Dyskinesia/Tardive Dystonia National Association: Voice: (206) 522-3166

TAY-SACHS DISEASE

Late Onset Tay-Sachs Foundation: www.lotsf.org

National Tay-Sachs and Allied Diseases Association: www.ntsad.org

TINNITUS

American Tinnitus Association: www.ata.org

Better Hearing Institute

TOURETTE SYNDROME

Tourette Syndrome Association: www.tsa-usa.org

TRIGEMINAL NEURALGIA

Trigeminal Neuralgia Association: www.tna-support.org

TUBEROUS SCLEROSIS

National Tuberous Sclerosis Association: www.tsalliance.org

VESTIBULAR DISORDERS

Vestibular Disorders Association: www.vestibular.org

VON HIPPEL-LINDAU SYNDROME

Von Hippel-Lindau (VHL) Syndrome Family Alliance: www.vhl.org

WILLIAMS SYNDROME

Williams Syndrome Association: www.williams-syndrome.org

WILSON'S DISEASE

Wilson's Disease Association International: www.wilsonsdisease.org

■ FOR FURTHER INFORMATION

These organizations focus primarily on research, professional support, and/or advocacy. They may, however, be able to provide information or assistance to the public on a limited basis.

Abraham Low Institute
(847) 441-0445; lowinsinstitute@aol.com

Acoustical Society of America
(516) 576-2360; asa@aip.org

American Academy of Addiction Psychiatry
(913) 262-6161; info@aap.org

American Academy of Anti-Aging Medicine
(773) 528-4333; A4M@worldhealth.net

American Academy of Child and Adolescent Psychiatry (202) 966-7300

American Academy of Pediatrics
(847) 434-4000; Kidsdocs@aap.org

American Association for Geriatric Psychiatry
(301) 654-7850; main@aagponline.org

American College of Medical Genetics
(301) 530-7127; acmg@faseb.org

American College of Mental Health Administration
(412) 820-0670; LawHel@aol.com

American College of Neuropsychopharmacology
(615) 322-2075; acnp@acnp.org

American Epilepsy Society
(860) 586-7505; Info@aesnet.org

American Federation for Aging Research
(888) 582-2327; info@afar.org

American Laryngological Association
(617) 355-6417; cfuentes@bu.edu

American Managed Behavioral Healthcare Association (202) 756-7308

American Methadone Treatment Association
(212) 566-5555

American Neurological Association
(952) 545-6284; lindawilkerson@msn.com

American Occupational Therapy Association
(301) 652-2682

American Society of Neuroradiology
(630) 574-0220

American Spinal Injury Association
(404) 335-9772

Americans for Medical Progress
(703) 836-9595

Association for Repetitive Motion Syndromes
(303) 369-0803; arms@lightspeed.net

Children's Brain Diseases Foundation
(415) 566-5404

Christopher Reeve Paralysis Foundation
(800) 225-0292

Coordinated Campaign for Learning Disabilities
(888) 478-6463

Foundation for Human Potential
(847) 853-9881

Foundation for Spinal Cord Injury Prevention
(800) 342-0330

The Gerontological Society of America
(202) 842-1275

John Douglas French Alzheimer's Foundation
(310) 445-4650

Judge David L. Bazelon Center for Mental Health Law
(202) 223-0409; materials@bazelon.org

Mental Illness Research Association
(800) 896-6472; info@miraresearch.org

National Center for the Study of Wilson's Disease
(212) 523-8717

National Council on Spinal Cord Injury
(617) 542-1661

National Foundation for Brain Research
(202) 293-5453

National Office on Disability
(202) 293-5960; ability@nod.org

Pilot International Foundation
(478) 743-7403

The Task Force on Science, Health Care, and the Economy
(617) 542-1661

ZERO TO THREE
(202) 638-1144; info@zerotothree.org

(For more information on *The Dana Guide to Brain Health,* see p. 114.)

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The Dana Sourcebook of Brain Science
Resources for Secondary and Post-Secondary Teachers and Students
Third Edition

David Balog, Editor

Contributors:

Murray Goldstein, D.O., M.P.H., Editorial Advisor
Uri Treisman, Ph.D., Charles A. Dana Center, University of Texas, Austin, Editorial Advisor
Brenda Patoine, Contributing Writer
Gerard Teachman, Ph.D., Mental Illness Research Association, Education Advisor
David Alpay, student, University of Toronto, Contributing Writer

Jane Nevins, Editor-in-Chief
Walter Donway, Director
Cynthia A. Read, Associate Director

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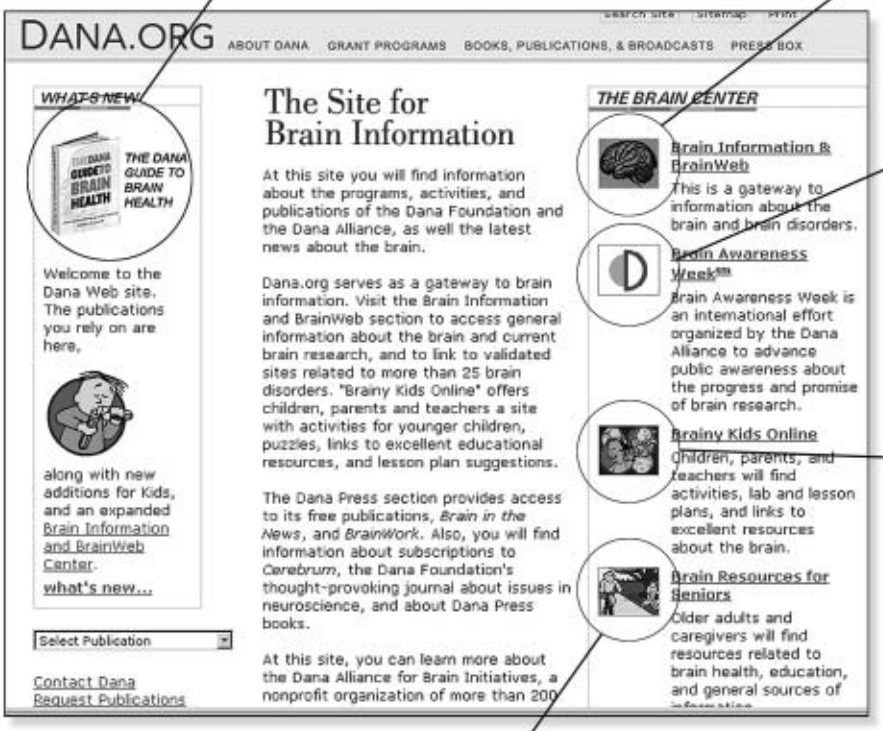
www.dana.org

THE SITE FOR BRAIN INFORMATION

At this site you will find information about the programs, activities, and publications of the **Dana Foundation** and the **Dana Alliance**, as well the latest news about the brain.

Dana Press
Check out the latest books and periodicals.

Brain Information & BrainWeb
This is a gateway to information about the brain and brain disorders.



Brain Awareness Week℠
Brain Awareness Week is an international effort organized by the Dana Alliance to advance public awareness about the progress and promise of brain research.

Brainy Kids Online
Children, parents, and teachers will find activities, lab and lesson plans, and links to excellent resources about the brain.

New!

Brain Resources for Seniors
Older adults and caregivers will find resources related to brain health, education, and general sources of information.

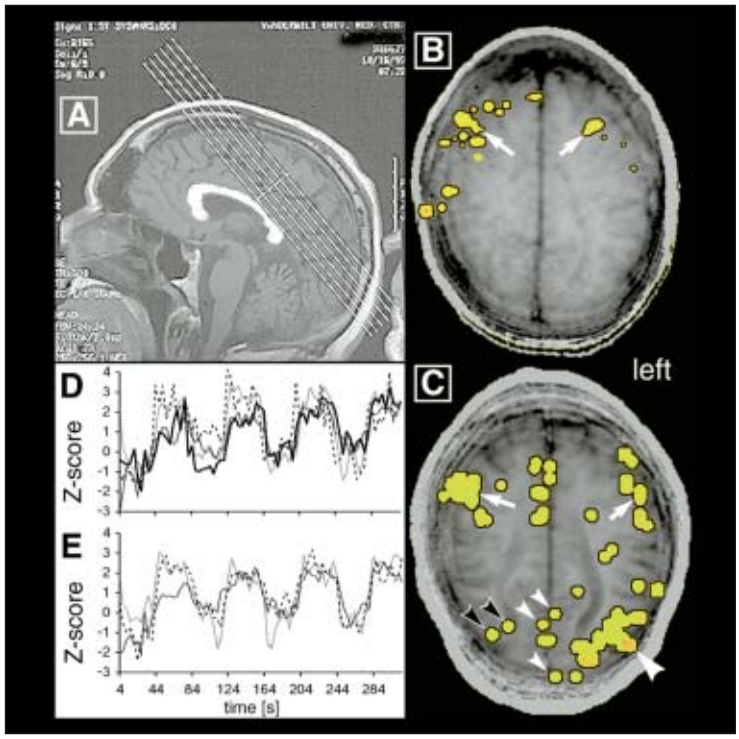
The Dana Foundation is a private philanthropic organization with interests in science, health, and education.

Credits:

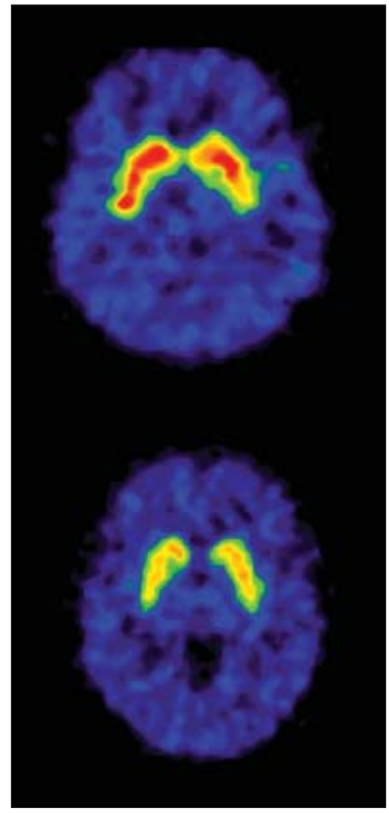
Cover: Marcus E. Raichle, M.D., Washington University School of Medicine, St. Louis, Department of Radiology and Neurology; *Inside front cover:* Clockwise, from top, Burke/Triolo/Brand X Pictures/Picture Quest, G.K. and Vicki Hart/Brand X Pictures/Picture Quest, Marcus E. Raichle, Washington University School of Medicine, St. Louis, Alvis Upitis/Brand X Pictures/Picture Quest. *pp. 20–21:* Eileen Whalen, except for neuron artwork on *p. 21* provided by National Institute on Drug Abuse; *pp. 26–39:* The Dana Alliance for Brain Initiatives and Dana Press; *p. 41:* University of Rochester; *p. 43:* (top) Max-Planck Institute, (bottom) Cold Spring Harbor Laboratory; *p. 45:* (l) University of Bristol, (r) J. Rehg/Zuma Images; *pp. 49–62:* Eileen Whalen; *p. 68:* (top to bottom) W.H. Freeman, W.H. Freeman, Simon & Schuster, Inc.; *p. 70:* (l-r) Appleton & Lange, Scientific American Library; *p. 71:* Scientific American Library; *p. 72:* Dana Press and John Wiley & Sons, Inc.; *p. 73:* Scientific American Library, Basic Books; *p. 75:* Basic Books; *p. 77:* G.P. Putnam's Sons; *p. 78:* HarperPerrenial; *p. 80:* (l-r) Alfred A. Knopf, Society for Neuroscience; *p. 81:* MIT Press; *p. 82:* Princeton University Press; *p. 86:* Penguin USA; *p. 87:* Random House, Inc.; *p. 90:* Simon & Schuster, Inc.; *p. 92:* Harper Perennial; *p. 93:* Skylark Press; *p. 95:* Dell Publishing Co.; *pp. 99–100, 103, 106:* Max Taylor Photography; *p. 109*: The Dana Foundation; *p. 111:* The Dana Foundation, The Dana Alliance for Brain Initiatives; *p. 114* (top) Adoramo, Co., (bottom) The Free Press; *p. 116:* Dana Press; *p. 117:* (top to bottom) Dana Press and Joseph Henry Press; Dana Press and John Wiley & Sons, Inc.; Dana Press and John Wiley & Sons, Inc.; *p. 118:* (top to bottom) Dana Press and Joseph Henry Press; Dana Press and Joseph Henry Press; Dana Press and John Wiley & Sons, Inc.; Dana Press and Joseph Henry Press. *p. 119:* (top to bottom) Dana Press and John Wiley & Sons, Inc.; Dana Press; *p. 121:* Dana Press; *p. 122:* (all) Dana Press; *p. 123:* (all) Dana Press; *Inside back cover:* Clockwise, from top, Peter Melzer, Vanderbilt Kennedy Center for Research in Human Development; Visualizing Addiction Project, Center for Image Processing in Education, Tucson, Arizona; David Miller, Vanderbilt Center for Molecular Neuroscience; Randy Blakely and Sally Shroeter, Vanderbilt Center for Molecular Neuroscience.

Credits for brain imaging timeline: (right, clockwise from top) Cajal drawing from the Cajal Museum, Madrid; CT and MRI images courtesy of Marcus Raichle, M.D., Washington University School of Medicine, St. Louis; PET photograph courtesy of Laboratory of Neurosciences, National Institute of Aging, Bethesda, MD; fMRI image courtesy of B.J. Casey, University of Pittsburgh Medical Center, Pittsburgh. Artwork coordinated by Dana Press Director of Production Randy Talley.

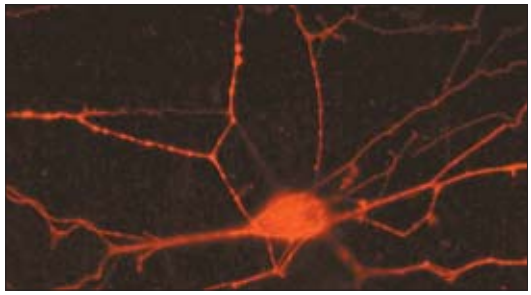
Design: Eileen Whalen



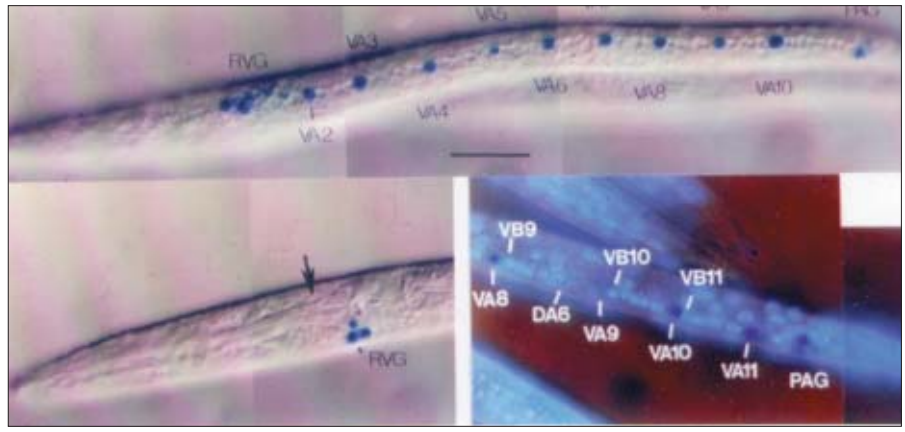
Does the brain reorganize itself?
These images suggest how the brain can reorganize itself to perform specific functions. The lines in image **A** represent the area of the brain examined by functional magnetic resonance imaging in two subjects: In image **B**, a sighted person reads a one-syllable word by touch in Braille. In image **C**, a person with severe visual disability reads the same word in Braille. In the visually-disabled person, additional brain activity occurs in the parietal, temporal, and occipital lobes—areas that process visual information in sighted people—suggesting that the brain of the visually-impaired person has reorganized its sensory pathways. The graphs represented by **D** and **E** plot the data of the experiment.



Positron emission tomography (PET) images reveal the effects of drug addiction.
The images show dopamine receptor levels of a control subject (top) and a methamphetamine abuser (bottom). Chronic abuse of drugs such as methamphetamine appears to damage the brain's dopamine system, which regulates the ability to sense pleasure.



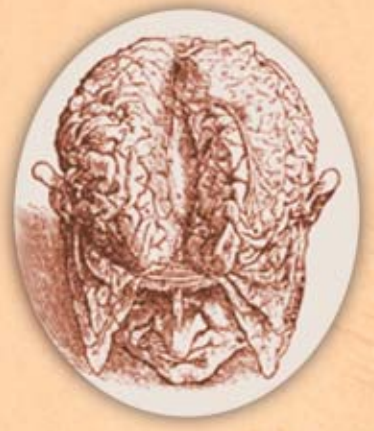
One in 100 billion—and a quadrillion connections.
Here is an image of a single neuron taken from a rat brain, isolated in culture. The cell body is represented by the large red area; the neuron's axon sprouts from the left of the cell body. Other lines represent dendrites connecting to other neurons. Scientists estimate that there are more than 100 billion neurons in the human brain, and that there are about 1 quadrillion (1 with 15 zeroes) connections between neurons.

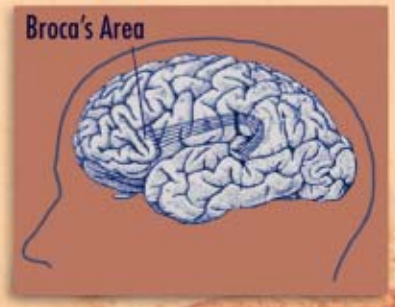


A tiny worm with great potential to help explain the human nervous system.
The worm *C. elegans,* shown here, was the first multicellular animal to have its complete genetic code mapped. The blue dots in this image mark synapses that permit motor movement. As in vertebrates, including humans, the *C. elegans* nervous system relies on neurotransmitters such as dopamine and serotonin, and it shares other basic chemical structures as well. The 2002 Nobel Prize in Physiology or Medicine honored three scientists who used *C. elegans* as an experimental model system to study genetic regulation of organ development and controlled elimination of cells (programmed cell-death).

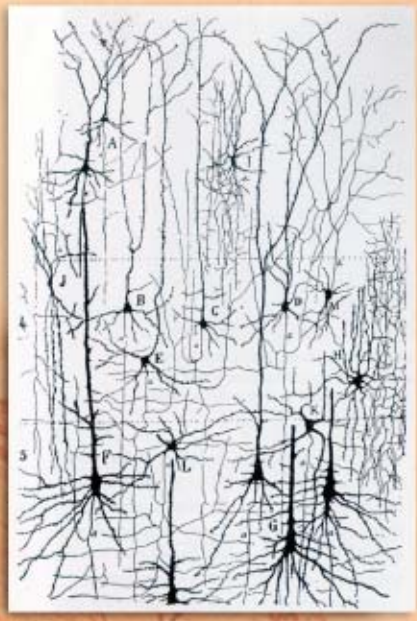
BRAIN IMAGING TIMELINE

1543: Artists in the painter Titian's studio sketched detailed drawings of the brains of cadavers. This sketch appeared in a book by Dutch anatomist Andreas Vesalius, which revolutionized the study of anatomy.

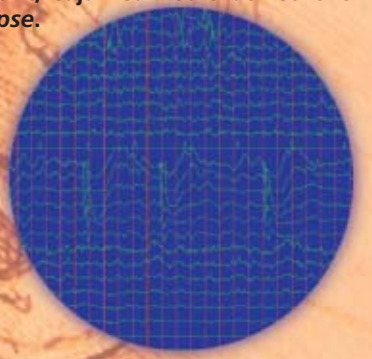




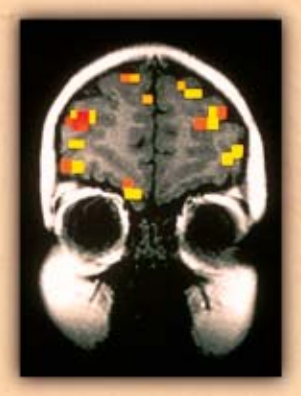
1861: French surgeon Paul Broca identified the speech center in the brain through autopsies.



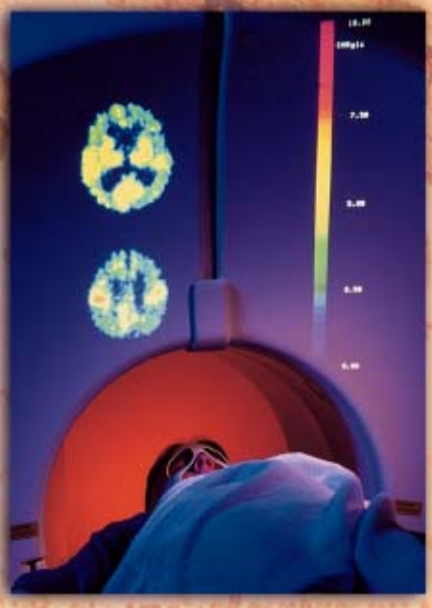
1911: Santiago Ramon y Cajal's drawings and staining methods advanced those of Camillo Golgi for visualizing neurons, dendrites, and axons. Cajal promoted the "neuron theory," the fundamental principle of modern neuroscience which holds that neurons are the basic unit of the central nervous system. More important, Cajal realized that neurons communicate across a small gap, or *synapse*.

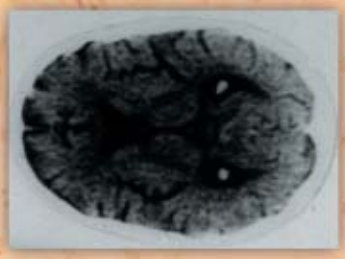


1929: *Electroencephalogram (EEG)* introduced; measures and records minute wavelike electrical signals produced by neurons as they "fire."

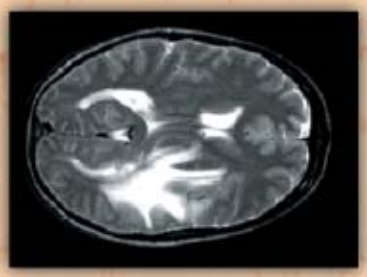


1992: *Functional magnetic resonance imaging* (fMRI) introduced; used to map brain activity by detecting variations in the response of hydrogen atoms when oxygen is present in the blood.





1973: First *computed tomography* (CT) camera; produces a composite image of the brain with a scanner that revolves around the skull, taking thousands of x-rays.



1977: First *magnetic resonance imaging* (MRI) camera; produces images by subjecting the patient's head to a strong magnetic field, followed by several pulses of radio waves, producing three-dimensional computer-generated images.

1975: First *positron emission tomography* (PET) camera; uses the principle that blood is rushed to busy areas of the brain to deliver oxygen and nutrients to the neurons. Patients are injected with radioactive glucose, then scanned for the rays emitted as the solution metabolizes, highlighting neuronal activity.

1489: *Background: Sketch of the brain by Leonardo da Vinci.*