INSIDE THE BRAIN

REVOLUTIONARY DISCOVERIES OF HOW THE MIND WORKS

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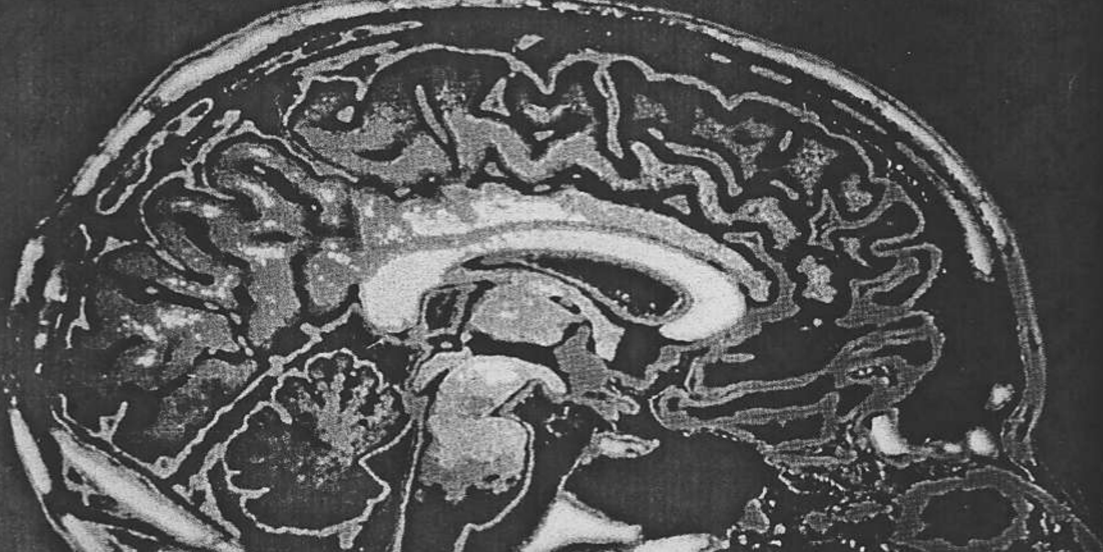


Based on the Pulitzer Prize-winning series that is profoundly changing our understanding of early childhood development.

1 Revealing the Secrets of the Brain

Seeing stars, it dreams of eternity. Hearing birds, it makes music. Smelling flowers, it is enraptured. Touching tools, it transforms the earth. But deprived of these sensory experiences, the human brain withers and dies.

Scientists long have wondered how the brain can do all the things that make one person a poet, another a builder or musician, and still another a criminal or social dropout. Until recently, medical researchers never thought they could understand the brain's inner workings. They could see that a child who is loved and given stimulating experiences usually turns out to be a bright, affable person, while an abused child often becomes an abuser. But no one knew what happened inside the brain that made one person a success and another antisocial.

Researchers were resigned to measuring what went into the brain and studying what came out. The brain simply was considered the "black box." But now many secrets are being revealed.

Two of the most surprising and profound discoveries are that the brain uses the outside world to shape itself and that it goes through crucial periods in which brain cells must have certain kinds of stimulation to develop such powers as vision, language, smell, muscle control, and reasoning.

The new discoveries are overturning the old concept of a static brain, a self-contained unit that slowly begins the process of learning from a preset, unchangeable set of rules, like a tape recorder that stores whatever words it happens to hear.

Now, thanks to a recent revolution in molecular biology and new imaging techniques, researchers believe that genes, the chemical blueprints of life, establish the framework of the brain, but then the environment takes over and provides the customized finishing touches. They work in tandem. The genes provide the building blocks, and the environment acts like an on-the-job foreman, providing instructions for final construction.

These discoveries are changing the way we think about thinking and are illuminating the biological causes of behavior.

"Within a broad range set by one's genes, there is now increasing understanding that the environment can affect where you are within that range," said Dr. Frederick Goodwin, former director of the National Institute of Mental Health. "You can't make a 70 IQ person into a 120 IQ person, but you can change their IQ measure in different ways, perhaps as much as 20 points up or down, based on their environment."

The discovery that the outside world is indeed the brain's real food is intriguing. The brain gobbles up its external environment in bits and chunks through its sensory system: vision, hearing, smell, touch, and taste. Then the digested world is reassembled in the form of trillions of connections between brain cells that are constantly growing or dying, or becoming stronger or weaker, depending on the richness of the banquet.

"Just as the digestive system can adapt to many types of diet, the brain adapts to many types of experiences," says Felton Earls, professor of human behavior and development at the Harvard School of Public Health and professor of child psychiatry at the Harvard Medical School.

How a newborn learns either English or Hindi or adjusts to being raised in Sweden or Ghana or to eating a diet of beef and potatoes or raw fish and seaweed are all due to the brain's great flexibility.

"All infants require milk before they can eat solids," Earls said. "Is there an equivalent state of affairs for the brain? The answer is clearly an affirmative one. It requires stimulation: touch, holding, sound, and vision."

Several recent animal experiments have demonstrated how brain cells can rearrange their 500 trillion or so connections in response to the stimuli they are being fed.

- Vision. Magrinka Sur of the Massachusetts Institute of Technology converted brain cells that interpret sounds into cells that can process visual images by reconnecting them to the stimuli coming in through the eyes. The experiment demonstrated the interchangeability of brain cells in early development.
- Touch. When monkeys were allowed to use only one finger to perform a task, neuroscientist Michael Merzenich of the University of California at San Francisco found that the brain cells that had been committed to the now-useless fingers switched their function to other parts of the hand. Amazingly, even mature brain cells can perform totally new tasks.
- Smell. Eager to learn from the moment of birth, an infant first bonds with its mother through its sense of smell. Michael Leon of the University of Southern California discovered that within seconds of the first time a newborn smells its mother's body, indelible networks rapidly form in its brain.
- Sound. Without proper stimulation, the connections that allow brain cells to process sound, and thus language, become scrambled. They don't form the neat columns of cells that are so characteristic of the brain's architecture. According to Martha Pierson of the Baylor College of Medicine in Houston, such scrambling may cause childhood seizures, epilepsy, and language disorders. Pierson's remarkable experiment showed how experience, or the lack of it, can physically change the brain and cause mental disorders.

"It's just phenomenal how much experience determines how our brains get put together," Pierson, a neurobiologist, said. "If you fail to learn the proper fundamentals at an early age, then you are in big trouble. You can't suddenly learn to learn when you haven't first laid down the basic brain wiring. . . . That's why early education is so important, why Head Start is so important," she said, referring to the federally funded program for preschoolers.

Essentially, a human comes equipped with a brain for all places and all ages. It takes in stride TV, the transition from horses and buggies to jets, and moon travel in a single lifetime.

But what the brain can do depends on whether or not it is used. It is the ultimate use-it-or-lose-it machine, and it is eager to learn new skills. The ability to form abstract thoughts, for instance, is now seen as a consequence of the brain's learning to read.

"A thousand years ago in medieval England most people did not think abstractly," said Dr. Bruce Perry, a Baylor College of Medicine neuropsychiatrist. "The majority of people viewed the world very concretely. When we look back now and think about how superstitious they were and all that kind of stuff, it's not that dissimilar from the way eight- or nine-year-old children today think about things and view the world.

"In the same way that we evolved a certain cognitive abstract capability as a function of our capacity to read, there is every reason to believe that there are other untapped abstract capabilities of our brains that are not being developed by our traditional educational system."

In their quest to learn how the brain works, scientists have found that the three-pound, walnut-shaped mass of gray matter goes through four major structural changes: in fetal development, after birth, between four and twelve, and during the years thereafter.

Starting from a few cells at the tip of an embryo, brain cells multiply at an astounding rate: About 200 billion are created in several months. Their job is to get in touch with the body that is developing around them and they compete to succeed. Half of the brain cells die off by the twentieth week of fetal life because they fail to connect to some part of the awakening body.

This overproduction of brain cells is important: It is evolution's way of making sure there are enough cells to handle the development of new skills, just as brain cells did in past generations to develop upright walking and language.

During the winnowing-down phase, the brain is organized into more than forty different physical "maps," which broadly govern such things as vision, language, muscle movement, and hearing. How these maps are organized is influenced by electrochemical signals coming into the brain from all parts of the body, and by hormones. Sex hormones are especially potent because they can physically shape a male or female brain and influence its skills, favoring such things as language in females and spatial abilities—mathematical concepts, for example—in males.

Alcohol and drug abuse can interfere with growing brain cells, jamming their genetic performance and increasing the risk of mental disorders. Alcohol-induced birth defects, for instance, are the leading known preventable cause of mental retardation in the United States, affecting 1 in every 800 to 1,500 newborns.

Long thought to be a clean slate to which information could be added at any time, the brain is now seen as a super-sponge that is most absorbent from birth to about the age of twelve. Thus, the brain can reorganize itself with particular ease early in life during crucial learning periods, when connections between brain cells are being made and broken down at an enormous rate. Information flows easily into the brain through "windows" that are open for only a short duration. These windows of development occur in phases from birth to age twelve when the brain is most actively learning from its environment. It is during this period, and especially the first three years, that the foundations for thinking, language, vision, attitudes, aptitudes, and other characteristics are laid down. Then the windows close, and much of the fundamental architecture of the brain is completed.

"A kind of irreversibility sets in," Harvard's Earls said. "There is this shaping process that goes on early, and then at the end of this process, be that age two, three, or four, you have essentially designed a brain that probably is not going to change very much more."

That's not to say that all is lost if this early learning period is not optimized. Using the tools left over from shaping brain cells and their connections, the brain gives its owner a big second chance which runs to about age twelve. Even after that the brain never stops learning. There is, however, a price to pay. Instead of being easy, learning becomes harder later on, as any adult who has tried to learn a foreign language knows. For a child, foreign languages are picked up easily.

The brain learns and remembers throughout life by employing the same processes it uses to shape itself in the first place: constantly changing its network of trillions of connections between cells as a result of stimuli from its environment.

One of the most striking examples of this ability to change was shown recently by Bruce McEwen of Rockefeller University. During the four-day reproductive cycle of a female rat, he found, new connections are created and old ones are destroyed as hormones prepare their brains for pregnancy and later to care for their pups.

"People hear that and say, 'My God, that's amazing!' and these are neuroscientists," he said. "A lot of people are surprised at the rapidity with which connections can be made and broken down in the brain. It especially comes as a big surprise to people who take a more psychological view and separate the mind from the brain. They are part and parcel of the same thing. It doesn't degrade your ability to talk about higher cognitive function [when you] realize that there's a brain under there that's doing the work."

Surprisingly, almost anything can cause physical changes in the brain: Sounds, sights, smells, touch—like little carpenters—all can quickly change the architecture of the brain, and sometimes they can turn into vandals.

"The new thing is that the brain is very dynamic," said Dr. Robert Post, chief of the National Institute of Mental Health's biological psychiatry branch. "At any point in this process you have all these potentials for either good or bad stimulation to get in there and set the microstructure of the brain."

Post and his colleagues were startled to find that outside stimulation can permanently alter the function of brain cell genes. Stress and drugs like cocaine, for instance, can produce biochemical changes that directly affect the function of some key brain-cell genes, in effect laying down permanent, maladaptive behavior patterns.

Faced with the new evidence about how the brain develops and functions, many scientists are concluding that society is wasting a tremendous amount of the brain power of its young, and creating a lot of unnecessary problems—including crime, aggression, and depression—later on in their lives.

"We are underinvested in our children," said Frederick Goodwin. "We spend seven times more per capita on the elderly than we do on children. Now that we have better concepts of the plasticity of the brain, it is obvious we are wasting a tremendous resource."

Understanding the role of the environment in altering brain plasticity has opened the door to prevention. "The question now is if we can identify the kids who are the most vulnerable to being damaged by their environment and get the plasticity of the nervous system working for us to prevent such damage," Goodwin said.

Recent research shows that proper stimulation affects such brain functions as:

- Language. Children whose mothers talk to them frequently have better language skills than do the children of mothers who seldom talk to them. After about age twelve the ability to learn new languages declines rapidly.

- Vision. Lack of visual stimulation at birth will cause those brain cells designed to interpret vision to dry up or be diverted to other tasks, making perfectly healthy eyes permanently unable to see. This discovery has saved the sight of thousands of infants born with vision-blocking cataracts, which are now removed as quickly after birth as possible.

- Brain power. Mice and rats raised in enriched environments, with toys and playmates, have billions more connections between brain cells than similar mice raised alone in empty cages. Pioneering studies also show that the IQs of children born into poverty, or of those who were premature at birth, can be significantly raised by exposure to toys, words, proper parenting, and other stimuli.

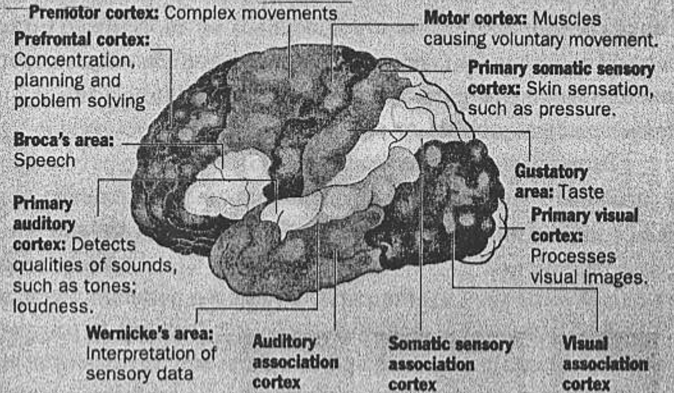
- Aggression. Early exposure to violence, stress, and other environmental pressures can cause the brain to run on a fast track, increasing the risk of impulsive actions and high blood pressure.

- Emotions. Animals exposed to unpredictable stresses while still in the womb develop anxious personalities. After birth, a little extra

THE BRAIN: HOW IT WORKS AND DEVELOPS

New discoveries are changing old concepts of how the brain develops and works. Two of the most surprising discoveries indicate that the brain uses the outside world to shape itself, and that it goes through critical periods in which brain cells require specific types of stimulation to develop such powers as vision, language, smell, muscle control, and reasoning. A related discovery is that the brain has the ability to change rapidly as it physically reshapes itself into a kind of biological map of the outside world. Researchers now believe that genes establish the framework of the brain, but the external environment provides the customized finishing touches.

Mapping the cerebrum Areas and their known functions



THE GROWING BRAIN

Major structural developments

- **Fetal development:** Billions of brain cells are formed in the first months of fetal life. Half of them die as hormones and other stimuli eliminate and organize them to form the brain's basic scaffolding, e.g. male or female.
- **After birth:** Trillions of brain cell connections are established and form the brain's physical "maps" that govern such things as vision, language, and hearing.
- **Age 4 to 10:** New learning reorganizes and reinforces connections between brain cells. New connections are formed as new things are learned.
- **After age 10:** Still able to undergo physical changes, the brain learns and remembers throughout life.

ASSOCIATION AREAS:

Areas that further interpret information received by primary areas.

Example: The primary auditory cortex detects simple sounds such as pitch and volume, while the auditory association cortex analyzes that information and enables recognition of whole sounds, such as spoken words.

Sources: *ABC's of the Human Body*, American Medical Association, *The Human Body*.

Chicago Tribune/Steve Little, Terry Volpp

mothering has the opposite effect, instilling in them confidence and the urge to explore.

- Touch. Premature infants whose sensory systems are activated by being held and cuddled are more mentally alert and physically stronger than those who are routinely isolated in incubators.
- Education. The best time to learn foreign languages, math, music, and other subjects is between one and about twelve years of age, yet these years are usually put on pause, given over to youngsters to "enjoy their childhood."

"The aspects of brain development most closely tied to human behavior can be affected for better or worse by the care we give our children," said Yale University neurobiologist Martha Constantine-Paton. Such knowledge provides the moral and social imperative to prevent or cure brain damage caused by the lack of proper environmental stimulation during the brain's crucial periods of development in fetal life and childhood.

"Legislative and educational efforts aimed at nurturing the developing brain through these critical periods could be instituted in the immediate future if the collective public conscience realized that the actual structure of the brain can be adversely affected by neglect," she added.

What can parents do to ensure that the brains of their children develop properly?

"If you want to significantly influence a child's ability to think and to acquire knowledge, the early childhood years are very critical," said neurobiologist Peter Huttenlocher, whose studies helped open the door to understanding the brain's plasticity.

Rockefeller University's McEwen says: "The most important thing is to realize that the brain is growing and changing all the time. It feeds on stimulation and it is never too late to feed it."

2 Mental Workouts and Brain Power

Counting the grains of sand on Oak Street Beach would have been easier, but then University of Chicago neurobiologist Peter Huttenlocher wouldn't have discovered a key to unlocking one of the brain's deepest secrets. Peering into the lens of a new, powerful electron microscope, Huttenlocher was counting for the first time the connections between brain cells—the tiny, numerous linkages that make the brain a thinking organ.

The brain samples, which had been removed during autopsies on fetuses, deceased babies, and elderly people, contained more than 70,000 cells each, even though they were only the size of a pinhead. As he focused on one sample and then another, Huttenlocher was astonished by the sharply increasing number of brain-cell connections; he later compared the sight to watching the slow-motion frames of an explosion.

A sample from a twenty-eight-week-old fetus totaled 124 million connections between cells; the sample from a newborn, 253 million; and the sample from an eight month old—an amazing 572 million connections, findings that defied conventional scientific wisdom.

"It was a strange thing to see," he said. "The number of connections kept going up and up and up and then they started to go down." Brain connections, he soon learned, start to fizzle toward the end of the first year of life, stabilizing at 354 million per speck of brain tissue by age twelve.

By the time he was done with his census, Huttenlocher not only stunned neuroscientists with his demonstration of how fast the brain initially develops, he also provided a glimpse of the brain's raw power

to create a powerful learning machine. "I stumbled on the whole thing," said Huttenlocher, who launched the census about a decade ago. "It was something that nobody expected. It took quite a long time until people began to accept that this really happens."

Huttenlocher's pioneering census was the first hint of something that has evolved into accepted scientific fact today: The brain is not a static organ; it is a constantly changing mass of cell connections that are deeply affected by experience and hold the key to human intelligence.

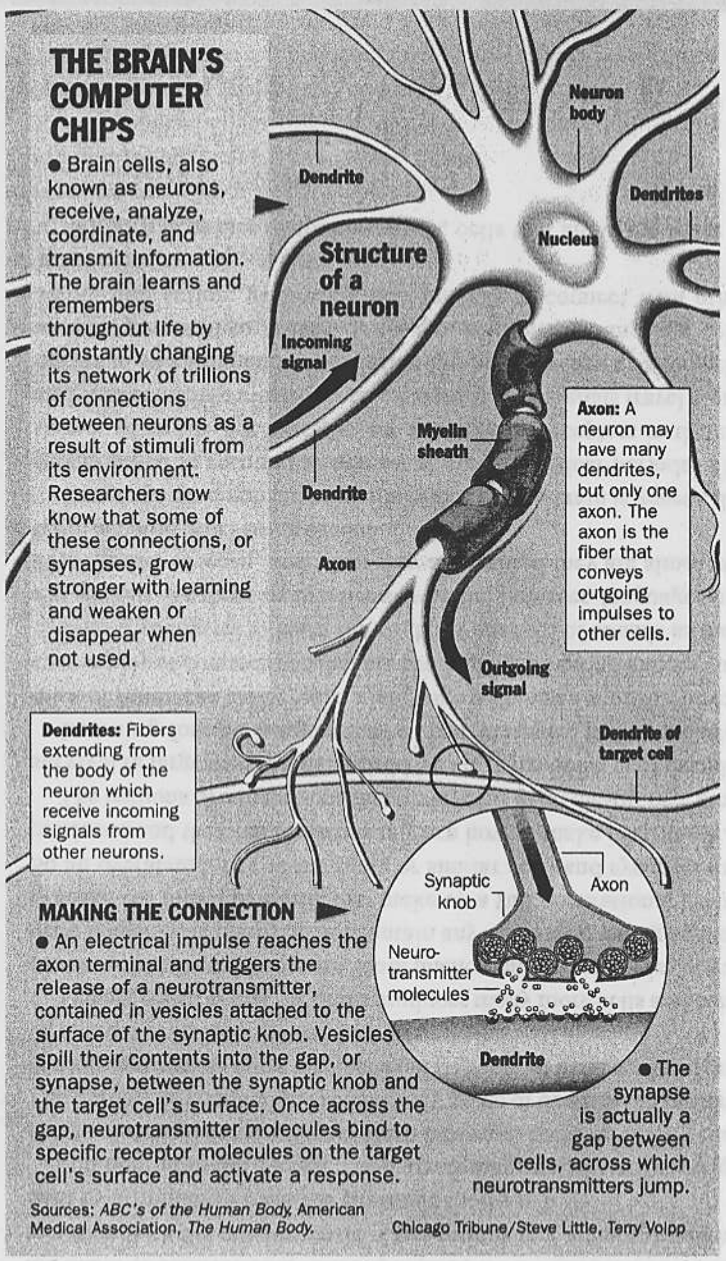
By probing further into Huttenlocher's insights, scientists have since developed measurable biological explanations for imprinting, bonding, and other critical periods of learning that parents, educators, and scientists could only guess at before.

At the University of Illinois at Champaign-Urbana, for example, William T. Greenough, a psychologist and cell biologist, found that rats raised in enriched environments with toys and other animals to play with had measurably more connections between brain cells and were better learners than those raised in less stimulating surroundings.

Scientists also are zeroing in on the idea that aggression, violence, and crime are rooted in the brain's biological reactions to violent and stressful experiences. The genesis for these insights dates back decades to when scientists, puzzled by the mysteries of learning problems and physical disabilities, began looking to the brain for some answers. No one suspected that the brain was as changeable as science now knows it to be.

The first brain cell, or neuron, is thought to have appeared in animals about 500 million years ago. Able to form flexible connections with other cells to send and receive electrochemical messages, the neuron marked a crucial leap in evolution, second only to that of the DNA molecule that appeared some three billion years earlier. Just as DNA gave birth to life in all its forms, the neuron made possible complex functions and, eventually, creative thought.

Scientists discovered that the power of a brain grows in direct relationship with the number of cells it has. "Our brains are built from the same molecular bricks as the other species, but we have a different building, a new architectural structure with more bricks," said



neurobiologist Pasko Rakic of Yale University. "The secret is in the total number of brain cells and the number of connections between them."

A fruit fly has 100,000 brain cells, a mouse 5 million, and a monkey, man's closest relative in the animal kingdom, 10 billion. Each is equipped with the brain power it needs to live in a particular environmental niche, evolution's way of finding a home for everything.

But nature overshoots its mark with humans. In only thirty-six hours of embryonic development, the human brain makes ten times more cells than a monkey's. Having 100 billion cells puts the human brain into a class by itself. That kind of computing power allows us to leapfrog into new realms: self-awareness, language, making associations, and abstract thinking. We can remember the past and anticipate the future so as to better guide ourselves in the present.

That is what is generally called consciousness. With less capacity, other animals are locked in the present, forced to depend on instinct.

During fetal development the human brain goes wild, producing twice the number of cells it will eventually keep. Before birth about half of these cells are killed off when they fail to find a job to perform.

Brain cells compete to connect to some part of the body. Those cells that fail to hook up do not get the proper feedback, which includes chemicals that nourish and maintain brain cells. Left without such nourishment or a sense of direction, they perish.

In their struggle to survive, brain cells send out cables known as axons. Axons search for the right brain cells to connect with, bypassing cells that emit "no trespassing" chemical signals and hooking up with those that put out a chemical welcome mat. Once axons find cells that are on their same wavelength, they sprout dendritic connections. Cells that fire together will wire together, setting down cables that connect the brain to itself and to the developing body. These cables act like intercity telephone trunk lines. The next step, which starts immediately after birth, is to string telephone lines from the cables to every house in the city, the individual brain cells.

About halfway through fetal life, when some brain cells start to die and a unique brain takes shape, sex differences and temperament begin to emerge, says Harvard University child psychiatrist Felton Earls.

After birth, another wild spurt of growth occurs as the brain races to make the connections that Huttenlocher measured between all of its cells, a profusion that happens so fast that it would be easier to count the drops of water in a rainstorm. Then another massive die-off occurs as half of the connections disappear by puberty. This time the death of connections, called synapses, is caused by a lack of interaction with the outside world. Connections that are not strengthened by stimulation from the environment die off.

Left behind in the average brain are as many as 500 trillion wiggling conduits that are ready to flash messages between brain cells. The number of connections could easily go up or down by 25 percent or more, depending upon whether a child grows up in an enriched environment or in an impoverished one.

The net effect is that the brain produces many more cells and connections than it could ever use. Both phenomena are examples of genetic frugality. Humans do not contain anywhere near enough genes to make the individual cells that make up a fully operational brain. So an overabundance of the same or similar cells and synapses are produced and then the brain has to learn how to make itself work.

The trillions of connections that survive the great die-off owe their survival in large part to what a child learns in his or her first decade.

Learning foreign languages is a clear example. Before puberty most children can easily learn a language without an accent. The excess supply of connections that are available to be called into service enables a youngster to learn the slightest nuances of sounds as they are spoken. As these connections dwindle, however, languages become harder to learn, and when they are learned they are almost always accompanied by an accent.

Language development helps illustrate how the brain is genetically programmed to respond to stimuli at certain critical periods. The sounds of words, for example, are received by receptors in the ear and converted into electrochemical signals. The signals travel along nerves to specific parts of the infant brain where they awaken cells to their potential to process language. Millions of language cells swing into action, generating new tendrils to connect with other brain cells.

Without exposure to spoken words, cells that allow the brain to construct meaningful sentences do not develop properly. They die on the vine or their function is usurped by more aggressive cells in other parts of the brain. In the process, their owner is cheated of the brain's full potential to use language, as has been shown by children who grow up alone in the wild.

Appropriate early stimulation is likewise crucial for the development of vision and other sensory functions. Scientists now believe that everything else that the brain regulates—learning, memory, emotions, physiological responses like reaction to stress and high blood pressure—are molded in early development when the brain changes the most.

In adulthood, the brain finally settles down but it is not idle. It will keep building and destroying connections and strengthening and weakening established ones for the rest of its life as it adjusts to the continuous changes in its environment.

"The fetal brain and the developing brain are very different structures from the adult brain, and the developing brain of a baby is really not a small version of an adult brain," said Carla J. Shatz, a neurobiologist at the University of California at Berkeley. "That takes people by surprise," she said. "They always think the brain just gets bigger."

William Greenough found that he could quickly increase the number of connections in animal brains by 25 percent simply by exposing the animals to an enriched environment. "What we know from animals suggests that the harder you use your brain, whether it's thinking or exercising, the more in shape it's going to be," Greenough said.

And that's exactly what seems to be happening in the human brain. Scientists at the University of California at Los Angeles recently found in autopsy studies that the brains of university graduates who remained mentally active had up to 40 percent more connections than the brains of high school dropouts.

"This is the human equivalent of the animals exposed to enriched environments having smarter brains," said UCLA neuroscientist Bob Jacobs. "We found that as you go up the educational ladder there is a dramatic increase in dendritic material."

Dendrites sprout from brain cells like tree branches. Studded along the branches like leaves are junctions called synapses, which connect to other brain cells. Just as leaves receive light from the sun to enable a tree to grow, synapses receive information from other brain cells to increase the brain's power to think.

But education alone is no guarantee of a better brain, the UCLA scientists found. Unless the brain is continuously challenged, it loses some of the connections that grew out of a college experience. The brains of university graduates who led mentally inactive lives had fewer connections than those of graduates who never stopped letting the light in. "The bottom line is that you have to use it or you lose it," Jacobs said.

An unanticipated bonus of an educated brain is that it may be better protected against Alzheimer's disease, scientists are finding. With more connections serving as front-line defenses, "educated" brains can better withstand the destructive attacks of Alzheimer's.

The power of experience to shape the brain struck like a thunderbolt in the 1960s and 1970s, and it took many years for scientists to believe it. It started with a landmark series of experiments at Harvard Medical School in which Torsten Wiesel and David Hubel sewed shut one eye of newborn kittens to test the effects of sensory deprivation. When the eyes that had been stitched closed were opened a few weeks later, the eyes were not able to see. But, surprisingly, the eyes that had remained open could actually see better than normal eyes.

Something strange had happened. The brain cells that normally would have been committed to processing visual stimulation from the closed eye had failed to learn that task. But they had gone off to help the other eye, and no amount of visual coaxing could get them back.

Wiesel and Hubel had made two important discoveries for which they won a Nobel Prize. They showed that sensory experience is essential for teaching brain cells their jobs, and after a certain critical period, brain cells lose the opportunity to learn those jobs.

That failure to learn is well known in real life. Even if a person's brain is perfect, if it does not process visual experiences by the age of two, the person will not be able to see, and if it does not hear words by age ten, the person will never learn a language.

"These are very important insights," said Wiesel, who is now president of Rockefeller University. "There is a very important time in a child's life, beginning at birth, when he should be living in an enriched environment—visual, auditory, language, and so on—because that lays the foundation for development later in life."

What was true for the cats was also true for humans. Babies born with cataracts, clouded lenses that prevented visual experiences from reaching the brain, also grew up blind because the brain cells that would normally process vision were called to duty elsewhere.

Based on the discoveries of Wiesel and Hubel, surgeons abandoned their practice of waiting until a child was several years old before removing cataracts. They began removing cataracts early, thereby preventing blindness by allowing visual experiences to reach the brain.

On a more fundamental level, Wiesel and Hubel showed what brain cells really are up to. The brain, it seems, is the ultimate reductionist. It reduces the world to its elemental parts—photons of light, molecules of smell, sound waves, vibrations of touch—which send electrochemical signals to individual brain cells that store information about lines, movements, colors, smells, and other sensory inputs.

Wiesel and Hubel discovered this when they implanted tiny electrodes into cells of the visual cortex of cats and monkeys. One set of cells recognized perpendicular lines. Another set of cells next to them recognized only lines slanted at a one o'clock angle; the next set recognized lines at two o'clock, and so on.

As a data-storage strategy, it was brilliant. A countless number of images could be disassembled into their parts and stored in specialized brain cells. One cell then could be used many times to recall similar lines found in a building, book, or car. With hundreds of trillions of connections to work with, the brain can establish flexible circuits between groups of cells that capture the various parts of an experience, whether it be a face, sunset, smell, or meal.

Thus, there are no pictures stored in the brain, as was once thought. There are patterns of connections, as changeable as they are numerous, that, when triggered, can reassemble the molecular parts that make up a memory. Each brain cell has the capacity to store frag-

PATH OF THE MIND'S EYE

The brain and the eye work together to process images by converting them into specialized electrochemical signals, then storing these components in the visual cortex for future recall.

From eye to brain

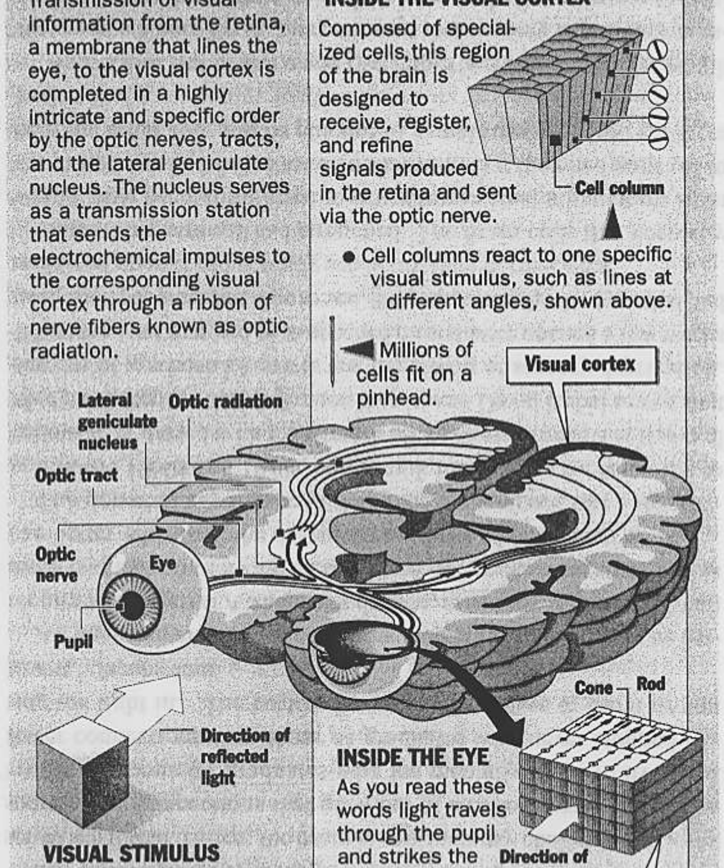
Transmission of visual information from the retina, a membrane that lines the eye, to the visual cortex is completed in a highly intricate and specific order by the optic nerves, tracts, and the lateral geniculate nucleus. The nucleus serves as a transmission station that sends the electrochemical impulses to the corresponding visual cortex through a ribbon of nerve fibers known as optic radiation.

INSIDE THE VISUAL CORTEX

Composed of specialized cells, this region of the brain is designed to receive, register, and refine signals produced in the retina and sent via the optic nerve.

- Cell columns react to one specific visual stimulus, such as lines at different angles, shown above.

Millions of cells fit on a pinhead.



VISUAL STIMULUS

The image of an object is sent to the eye as light reflects off the object.

INSIDE THE EYE

As you read these words light travels through the pupil and strikes the retina. This light passes through layers of nerve cells before reaching rods and cones that trigger electrochemical impulses.

Sources: *The Brain: A User's Manual,* CIBA, news reports.

Chicago Tribune/Stephen Ravenscraft

ments of many memories, ready to be called up when a particular network of connections is activated.

How many connections are kept depends on the learning experiences the brain is exposed to. The evidence indicates that the more connections you have, the smarter you are. "We do waste a lot of brain power because we're not quite sure how to exploit our brains to the maximum," said Lawrence Garey of the University of London. "We're just learning how to do that."

Wiesel and Hubel's discovery—that unused brain cells will seek out other jobs to perform—ultimately led to the solution of a problem that had long puzzled neuroscientists, phantom pain. Some amputees feel pain in their missing limbs, a sensation dismissed in the past as psychosomatic or emanating from messages sent from severed nerve endings in the stump.

Those notions began to crumble with the results from experiments on monkeys. When one finger was immobilized, brain cells controlling the useless finger switched their allegiance to brain cells that control other parts of the hand. The process of reallocating duties from one part of the brain to another is possible because of the brain's great plasticity. It is now understood to be the reason why stroke patients can regain speech and other functions through rehabilitation.

Intrigued by these findings, Vilayanur Ramachandran of the University of California at San Diego wanted to see if the brain of a young man named Derrick had been rewired after his left arm had been amputated above the elbow because of a motorcycle accident.

Doctors had tried to save his arm immediately after the accident by reattaching muscles and nerves. It didn't work. He couldn't move it, and it hurt. After the useless limb was finally removed, the man's phantom feelings of pain and paralysis began, sensations his brain apparently learned from the months his reattached limb had been in a sling.

Eight years later, and still feeling severe pain in his phantom limb, Derrick participated in a brilliant series of experiments. With Derrick's eyes closed, Ramachandran touched his cheek and asked him where he felt sensation. Derrick said it felt like his phantom hand had been touched. Then Ramachandran brushed a cotton swab across Derrick's jaw. This time he said he felt movement across his missing arm.

Since the areas in the brain that regulate the arms and face are adjacent, brain cells that had controlled the missing limb crossed over to the area controlling the face. Brain-wave studies confirmed that the rewiring had taken place.

But, despite this crossover, that part of the brain could not totally give up its former control of the paralyzed missing limb. Those brain cells insisted that the missing limb was still there. They kept sending messages around a useless closed loop, a painful reminder of their past duties.

Derrick eventually broke the painful spell by learning how to disconnect the faulty wiring in his brain. He did it with the help of a long, narrow box built by Ramachandran. The box was equipped with a mirror running its length so that when Derrick put his good right arm in the box he could see two arms. Pretending the mirror image was his missing limb, Derrick told himself that he was exercising both arms together, lifting a bucket, for instance. After a number of trials, he succeeded in feeling sensations in his missing limb that he had not felt for eight years. Tricking his brain into freeing his paralyzed phantom limb, Derrick also got rid of the pain. He had purposely corrected the errant wiring in his brain.

What happens when the brain is prevented from making connections between brain cells in response to experiences from the outside world can be devastating. University of Illinois scientists recently found that a defect in an important protein that appears to play a key role in building infant brains may cause the most common mental disorder inherited by males.

The disorder, known as the fragile X syndrome, affects one in 2,000 males, causing mental retardation ranging from mild to severe. Other features of the disorder may include a long narrow face and prominent ears, jaw, and forehead.

The normal version of the fragile X protein is crucial in forming the latticework of synaptic connections between brain cells, which enables a new brain to wire itself into a mature, thinking organ.

Discovering how the protein installs synaptic connections may also help scientists better understand how the brain learns and remembers, not only in childhood, but adulthood as well. The new findings suggest that when the fragile X protein is defective, brain development is arrested at an early, immature stage that results in retardation.

"The healthy type of the fragile X protein that is produced at synapses appears to be essential to normal synapse maturation and development of the wiring diagram of the brain," said the University of Illinois's Greenough. Although the research does not immediately lend itself to new treatments for the fragile X syndrome, it opens new pathways to understanding a common mental disorder and to the possibility of developing effective therapies.

Synaptic connections, the telephone lines that allow brain cells to communicate and to learn new things, are normally overproduced in newborn brains. Mental stimulation during early childhood activates brain cells to organize synaptic connections into networks for processing new information and setting down memories. These networks are essential for such skills as language and thinking. How the synapses get wired appears to be the job of the normal version of the fragile X protein.

Synapses that are welded into connections with brain cells become part of the maturing brain. Synapses that do not form connections are pruned away. In this way the oversupply of connections is reduced to form a functioning brain.

When the normal protein is defective, however, new connections are not made and the brain remains in an immature state, encumbered by too many nonfunctioning synapses. It is like giving a sculptor a block of marble but not giving him the tools with which to create a work of art by chipping away unwanted material.

"This protein seems to be necessary for that sculpting in the brain to take place," Greenough says. "This is the first molecular handle on the likely basis for the mental retardation we see in the fragile X syndrome. We really had nothing prior to this."

Autopsy studies of humans with the fragile X syndrome show that their brains are overcrowded with useless, immature synapses. The disorder is only passed on to males because the genetic defect responsible for the fragile X protein is located on the female X chromosome. Males inherit an X sex chromosome from their mothers and a Y male sex chromosome from their fathers. It is estimated that one out of 1,000 women carry a chromosome with the defective gene for the fragile X protein. Since girls inherit two X chromosomes, if one is defective, chances are the other one is normal and it will override the defect.

Scientists then developed a mouse model of the fragile X syndrome by deleting the gene that makes the good copy of the fragile X protein. The mice never go through the normal synapse-maturation and synapse-elimination process. Their brains stay locked in the phase of overproduced, unworking synapses.

Another important lesson scientists have learned is that words can be just as powerful as drugs in correcting errant brain pathways that are causing some mental diseases.

Using high-tech imaging devices that can "see" the living brain processing thoughts, scientists at the University of California at Los Angeles showed for the first time that behavior therapy produced the same kinds of physical changes in the brain as psychoactive drugs.

Experts hope that the findings will shed new light on the process by which psychotherapy, including the so-called "talking cure," can physically change the brain and that they will lead to better techniques for treating mental diseases. "Anytime you have a change in behavior you have a change in the brain," said UCLA psychiatrist Dr. Lewis Baxter. "Behavior therapy and drugs appear to rearrange brain circuitry in the same way."

Baxter and his colleagues studied the brains of obsessive-compulsive patients with PET (positron emission tomography) scans, a technique that measures the activity of cells in different areas of the brain. They found that an area called the caudate nucleus was overactive in these patients.

The caudate nucleus acts as a gatekeeper that prevents unwanted thoughts from establishing self-reinforcing circuits in the brain. Like a record stuck in the same groove, unwanted thoughts keep repeating themselves and drive compulsive behavior.

In some cases patients are afraid of dirty objects and repeatedly wash their hands. Others may be fearful of violence and check their door locks hundreds of times a day. Obsessive-compulsive disorder affects 2 percent of the population.

Fluoxetine (Prozac) is highly effective in curbing unwanted thoughts through a mechanism that is little understood, but which involves raising the level of an important brain chemical messenger called serotonin. Serotonin plays a key role in controlling impulses. So when serotonin is low, impulses such as repeated hand washing or constantly checking to make sure the stove is off can keep popping out.

Behavior therapy, which is also effective in breaking unwanted habits, involves gradual exposure to a fear-triggering agent, such as dirt, and teaching a patient not to respond to compulsive urges.

Although the two treatments appear to be highly dissimilar, PET scans showed that they produced identical changes in calming down caudate nucleus activity in both groups. Both therapies appear to correct the abnormal circuits causing unwanted thoughts by changing connections between brain cells in the caudate nucleus, Baxter said.

His experiment is one of the most dramatic demonstrations of the power that words have to physically change the brain.