SPECIAL SECTION FREUD AT 150: WHAT HIS INSIGHTS MEAN FOR US TODAY

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April/May 2006 www.sciammind.com

The Dawn of a New Science of Mind
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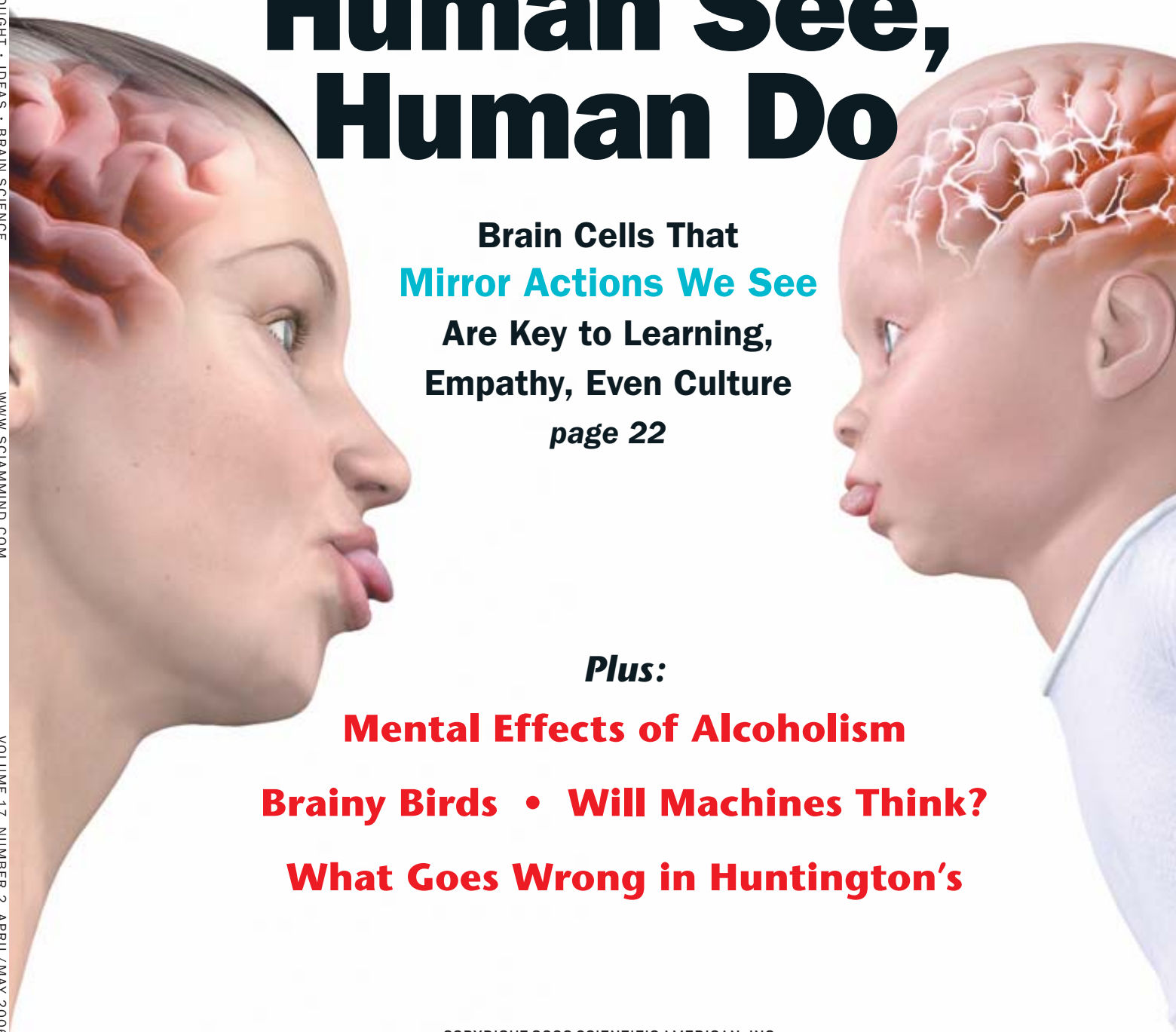
Human See, Human Do

Brain Cells That Mirror Actions We See Are Key to Learning, Empathy, Even Culture

page 22



Plus:

Mental Effects of Alcoholism

Brainy Birds • Will Machines Think?

What Goes Wrong in Huntington's

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COVER IMAGE BY PHIL SAUNDERS *Space Channel Ltd.*

Self-Reflections

It was one of those seemingly mundane moments, but I was thunderstruck when I realized the implications. Tossing on a cardigan, I happened to notice my toddler intently staring at me to figure out how to push a button through a hole in her sweater. Suddenly, I realized how much we learn how to do things and how to behave around others just by watching and copying.

At the time, nearly a decade ago, I had little idea about how extensively my child was mentally rehearsing my actions as she studied me. Since then, science has learned much more. When we see someone engaged in any activity—yawning, dancing, smiling—cells called mirror neurons that are scattered throughout the brain create an instant replay in our heads. Investigators believe that these cells may be the keys to cultural development and may even be responsible for humanity's collective "great leap forward" 50,000 years ago, as David Dobbs explains in his article, "A Revealing Reflection." Turn to page 22 to learn more.

Sigmund Freud, the iconic founder of psychoanalysis who was born 150 years ago on May 6, would have had a different take on my mother-daughter relationship (he held that girls were rivals with their moms for their fathers' attentions).

In this issue we mark the anniversary of his birth and his impressive influence on all things psychological in a special section, "Freud at 150." As neuropsychologist Mark Solms describes in "Freud Returns," starting on page 28, neuroscientists are finding that biological descriptions of the brain may fit together best with theories Freud developed. A second feature, "Neurotic about Neurons," by Steve Ayan, further details Freud's notions and his eventful life; go to page 36. The last installment provides a modern take. In recent years, scientists have been testing what works—and what does not—in talk therapy, thereby bringing the power of research to the couch with "empirically supported therapies." Surprisingly, these techniques are not without controversy, as psychologists Hal Arkowitz and Scott O. Lilienfeld explain in "Psychotherapy on Trial," beginning on page 42. We hope the section tickles your id, ego and superego.

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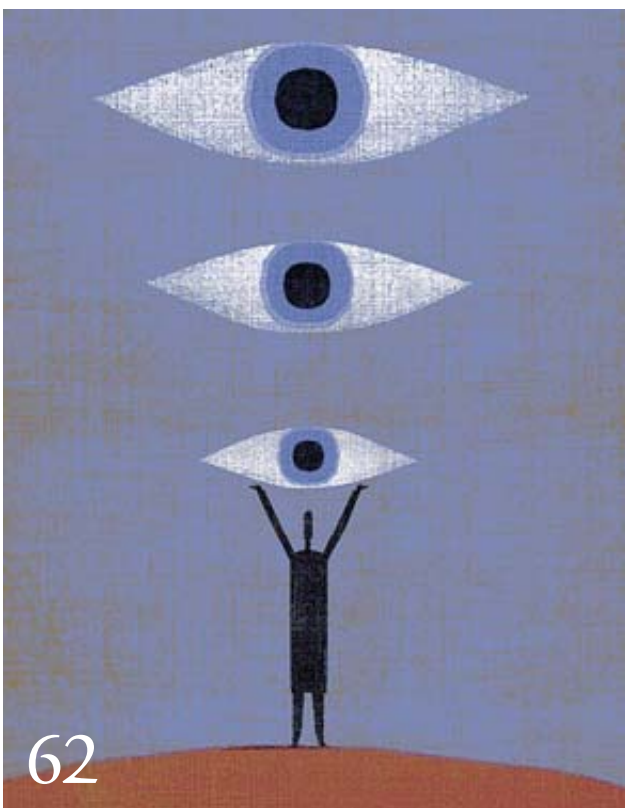
FEATURES



DEPARTMENTS

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(letters)

WHAT MAKES US who we are? *Scientific American Mind* explores that question at many levels in each issue, and Vol. 16, No. 4, was no exception. Many people would intuitively say that we are all products of our genetics (nature) and environment (nurture)—and that the complex and subtle roles of each in shaping our inner selves provide endless fascination. The magazine's features also probed what we can do about who we are. In "Erasing Memories," for instance, neuroscientist R. Douglas Fields described how we might remove horrific events from our recollection. Is that a good idea? Your viewpoint may depend on who you are—and who you want to be. Other readers share their reactions on the following pages.

TOTAL RECALL

I bought *Scientific American Mind* for the first time the other day at the PX (I am currently serving in Iraq as a civilian contractor), specifically because of the lines on the cover: "Memory Upgrade: Erasing bad memories could ease anxieties," in reference to the article by R. Douglas Fields.

I have had my share of bad memories—as a result of abuse, two divorces, deceased parents and so on. Sometimes I think it would be just great if I could wake up one day with amnesia and never remember all the pain and suffering I have endured myself and witnessed in others.

Would it really be beneficial to lose those memories? I mean, as much as I hate my ex-husbands, the experiences from those relationships have shaped who I am today. How would I remember my kids if I forgot everything dealing with their father? They did not just appear one day.

It has taken me a long time to pick up the pieces, but I am pretty comfortable where I am now. I do not think I would be the caring and supportive person I am if I had not suffered the bad things. Just a thought …

Hannah D. Bartley II
Baghdad, Iraq

FIELDS REPLIES: *As you put it so eloquently, we are our memories. Every experience shapes who we are, and our memory guides us as we change through our life experiences. Good memories stick with us, and bad ones, like all wounds, usually heal with time. Sometimes, however, such wounds do not heal. People suffering from post-traumatic stress disorder (PTSD) are overwhelmed because they relive horrific memories that will not recede into the past; these people need all the help medicine and science can offer.*

It is true that our memories are reconstructed from fragments and the connections among them are endless. For that reason, one could never completely expunge one memory selectively without affecting related memories.

Fields made an analogy of names and repetition and how it helps the mind remember names more easily if the person repeats the name in time intervals of 10 minutes rather than using immediate repetition. Does that rule apply to general reading also? Should I read a chapter once and wait a day before reading it again for optimal memory retention? Or can I read it again immediately for the same results?

David Chatham
via e-mail

FIELDS REPLIES: *I do not know specifically how this property of memory formation would relate to reading, but I expect that it would help commit text to memory. The necessity for a rest period between repetitions to move information from short- to long-term memory is deeply embedded in the molecular machinery of memory.*

Tim Tully and his colleagues at Cold Spring Harbor Laboratory used mild electric shocks to train fruit flies to avoid a particular odor. "Massed training," giving the flies the same number of training experiences in rapid succession, did not produce an enduring memory, but "spaced training"—that is, giving the same number of training sessions with a 15-minute rest period between each session—did.

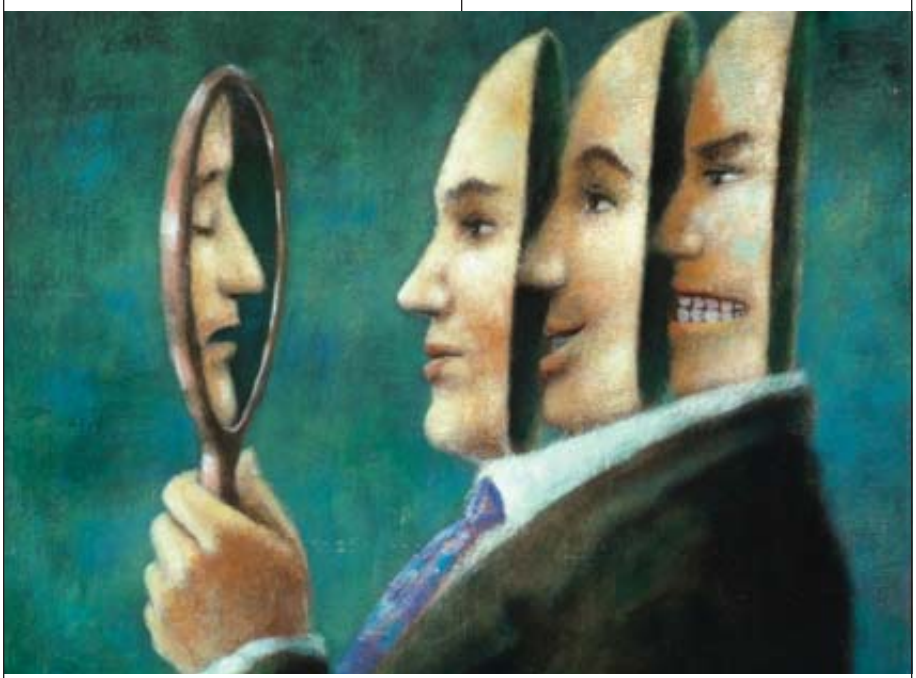
But who was it who told us that cramming for exams does not work and that repetition and a good night's rest are the way to learn? Now we know the molecular basis for Mom's advice. Memory consolidation takes place while we sleep, and it takes time for the molecular reactions controlling gene and protein synthesis to record long-term memories. On the other hand, do not rest too long. If the interval between sessions is excessive, the short-term memory will have weakened too much to benefit from repetition.

HARD TO READ

I missed mention of "backhand" writing in "Left Out," by Detlef B. Linke and Sabine Kersebaum. Right-handed students learning to write slant their paper to the left, making it an exten-

sion of their writing arm. If the teacher does not instruct left-handed students to rotate their paper the other way, they are forced to turn their hand backward and draw letters from the topside to see what they are writing. This awkward position degrades penmanship, leading to the myth that left-handed writing is poor writing. When I was a child, unfortunately, most teachers did not instruct left-handers appropriately and so inadvertently condemned them to a lifetime of being hard to read.

Chuck Kollars
Ipswich, Mass.



LUDVIK GLAZER-NAUDE *Images.com/Corbis*

Is a calm exterior the answer to controlling emotion?

INSPIRED BY ANGER

"Control Your Anger!" by Iris Mauss, was most interesting! A more holistic approach might further improve the discussion, however. For example, whereas the author notes that a calm exterior is a sign of inner mental and physical health, she omits mention of the fact that Japan has an extremely high suicide rate. Likewise, when Mauss discusses the Berkeley study on the consequences of controlling one's feelings in everyday life, it would be interesting to know whether data had been disaggregated according to common stereotypes—for example, the belief that women express their feelings more often than men.

Bob Louisell
St. Cloud State University

CONSPIRACY QUESTIONS

I need to voice concern regarding "Birth-Control Conspiracy?" by Kaspar Mossman, in Head Lines. The author states that "government programs to encourage the sterilization of black women persisted in back offices until the 1970s." What are Mossman's sources for such an incredible statement? He goes on to say that "even though decades have passed … there is no credible evidence for a current conspiracy."

What is the reader to glean? That there were conspiracies before the 1970s, but not any longer? Or that there is no credible evidence to support a conspiracy theory, period?

Thor Hougen
San Diego

MOSSMAN REPLIES: *I regret there was not space to specify that the statement, based on Sheryl Thorburn's published survey of African-American attitudes toward birth control ("Conspiracy Beliefs about Birth Control: Barriers to Pregnancy Prevention among African Americans of Reproductive Age," in* Health Education and Behavior, *Vol. 32, No. 4, pages 474–487; 2005), is supported by the chapter "The Dark Side of Birth Control," in* Killing the Black Body, *by Dorothy Roberts (Vintage, 1999), which itself cites several references.*

Policy leaders portrayed such programs as part of measures to alleviate the burgeoning population of poor people. Roberts recounts the 1973 class-action lawsuit initiated by Minnie Lee Relf, which revealed that at the time 100,000 to 150,000 poor women, half of them African-American, were sterilized every year under federally funded programs. Roberts also notes that during the 1950s and 1960s, state legislatures in Mississippi, Illinois, Iowa, Ohio, Virginia and Tennessee debated measures for the sterilization of single and welfare mothers.

TAILORED TREATMENTS

In Head Lines, "Schizophrenia Drugs Questioned," by Jamie Talan, will be welcomed by budgeters as the reason to deny newer drugs to schizophrenia patients. Yet there is, in fact, good reason to have the newer drugs available.

For each of the drugs, there is a group of patients who do very well, others whom the drug helps, others who are not helped, and some who are made worse. All drugs carry side effects that are undesirable.

What your story did not mention is that the group that does well is different for each drug. Not clinically different in the presentation of symptoms but a different subgroup of the total test population. Although this fact does not show up in this study, it has long been recognized by professionals. If suitable drugs are to be available for the most individuals possible, all the drugs need to be available to be used as needed. This is just a reflection of the fact that "schizophrenia" may not be a single illness but a label for a collection of mental ailments with similar symptoms and different root causes.

Gordon Thompson
Edmonton, Alberta

Head Lines

STAR zefa/Corbis

Weak Nerves May Cause Depression

In a painstaking experiment that may help revise our view of depression, a team at the Johns Hopkins University School of Medicine found that rats given Prozac did not merely experience a change in their brain chemistry but also grew new nerve fibers in mood-critical areas. This finding, which suggests that depression reflects problems of fine neural structure and not just chemistry (the prevailing model), should bolster the emerging "network hypothesis" of mood.

Over the past quarter of a century, it has become doctrine that depression is primarily a chemical issue. The prevailing model holds that depression occurs largely because shortages of the neurotransmitter serotonin in key synapses dampen mood-regulating neural signaling, opening the door to depression. But the recent results indicate that mood disorders stem at least partly from frail synaptic structures such as weak nerve endings and dead fibers, which cause signaling breakdowns.

Through intricate staining techniques, the Hopkins team found that rats treated with Prozac grew more axons—the neural branches that send messages—on serotonin-sensitive neurons in cortical and forebrain areas crucial to mood. Lijun Zhou, a researcher in neurosurgery, proposes that this local change is "the key structural effect of serotonin antidepressants" and may help explain some successful antidepressant therapy. The findings mesh with other recent human studies showing that both drug and talk therapy, when successful, raise levels of pervasive brain-growth chemicals called neurotrophins. Shortages of neurotrophins may contribute to the original structural weakening of neural-network circuits.

"This is one of the first [studies] to report anatomical changes in response to drugs," says University of Helsinki neuroscientist Eero Castrén, a specialist in neurotrophins and network theory. "It should help tell us where to look in humans for markers of similar change." That, in turn, could produce a richer understanding of depression, as well as more possibilities for treatment. *—David Dobbs*

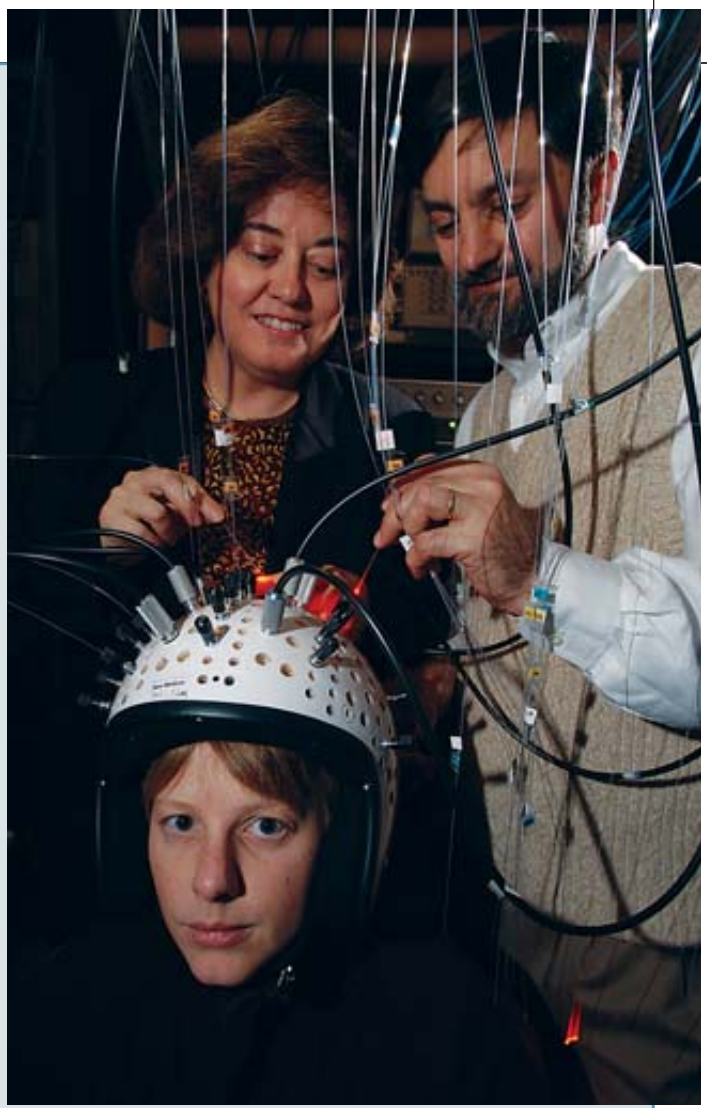
See What I Mean?

Scientists do not have a window into your thoughts yet, but they can now shine beams of light into your head and watch information flow around your brain. Gabriele Gratton and Monica Fabiani, neuroscientists at the University of Illinois, are pioneering the new technique based on the way brain tissue transmits light.

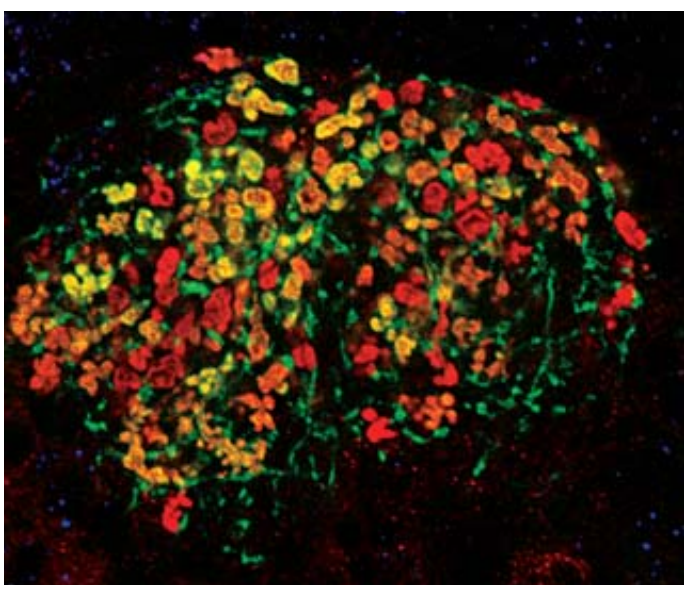
A test subject wears a helmet that allows Gratton and Fabiani to apply intense near-infrared illumination to the skull using fiber-optic cables. Sensitive detectors pick up faint reflections as the light bounces off countless microscopic surfaces on the brain's outer layer, the cortex. (This "scattering" is the reason a laser pointer, pressed into a fingertip, makes the finger glow red.) Heightened activity among neurons increases the scattering, producing a so-called event-related optical signal. One explanation is that when neurons fire they absorb water, which deforms cell membranes, forcing the light rays to travel along longer paths with measurable delay.

Gratton and Fabiani can produce a three-dimensional map of neuronal events in the cortex, including the regions that process input from the eyes, ears and other sensory organs. Light penetrates the cortex to a depth of three centimeters, and activity can be pinpointed to regions 0.5 centimeter across. "There may be areas we can't observe," Gratton says. "Nevertheless, we see most." The technique is blazingly fast—it can resolve events separated by milliseconds, whereas each slice of a functional MRI scan spans about one second and PET scans average data over 40-second intervals or longer. This fine temporal resolution means that Gratton and Fabiani can watch the order in which rapid neural events originate and then migrate to other regions of the cortex. For instance, they hope to understand how skilled operators such as air traffic controllers and military commanders interpret complex visual displays and prepare to take action. With their novel technique, thought processes may one day be made truly transparent.

—Kaspar Mossman



Fabiani (*left*) and Gratton prepare to beam a brain.



Proteins (*red*) forming in synapses may bolster memory.

THOMPSON McCLELLAN (*top*); SHOVON ASHRAF *Harvard University* (*bottom*)

Memory Watched as It Forms

Creating long-term memories means chemically altering the brain. Neuroscientists at Harvard University were recently able to observe, for the first time, new protein being synthesized at the synapses between neurons (*red regions in image*). The synthesis was observed in fruit flies and occurred as the flies learned to associate an odor with an electric shock. Molecular biologist Sam Kunes said his team "found a new biochemical pathway that determines if and where this protein synthesis happens."

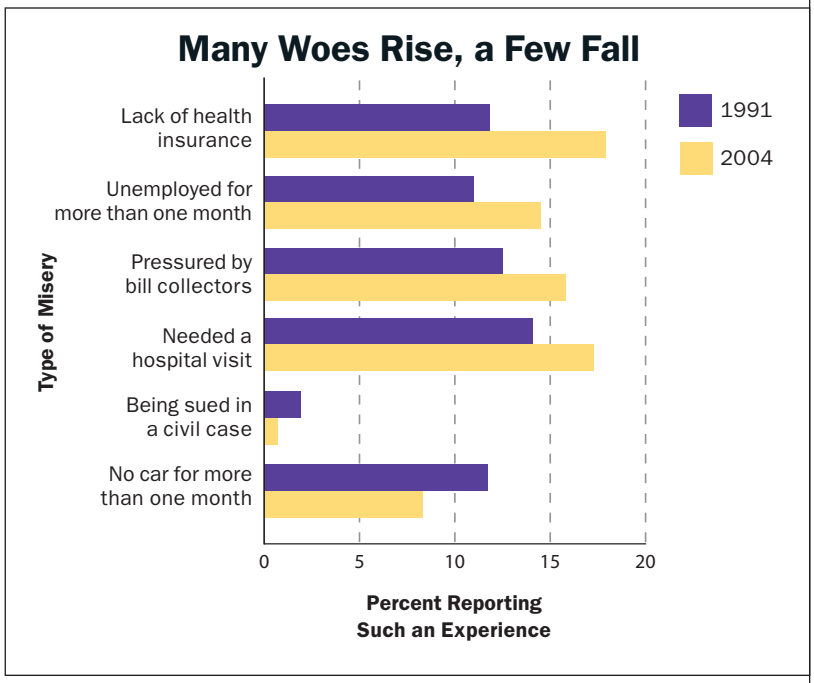
Using fluorescent markers, Kunes could see synapses modified after exposure to the odor. The altered synapse (*represented in green*) meant the difference between remembering something for an hour—a short-term memory—and a day, which is long-term for a fruit fly. Because the basic structure of this biochemical pathway is the same in mice and humans, Kunes believes these findings will lead to a better understanding of how memory works in higher animals—and could eventually result in therapies to bolster fading recall.

—Jonathan Beard

Misery Index Up

Americans are becoming more miserable, and lack of health insurance is one reason why, according to a survey by the University of Chicago's National Opinion Research Center. The center interviewed 1,340 Americans for a report entitled "Troubles in America: A Study of Negative Life Events across Time and Sub-Groups," as part of its semiannual General Social Survey. Subjects were asked whether they had experienced trouble in any of 58 categories within eight domains such as health, work and finances. Participants could also volunteer woes that did not fit into the questionnaire.

Overall, difficulty has increased since 1991, when the last misery index was calculated: 92 percent of respondents reported at least one major problem, up from 88 percent. Significantly, 17.9 percent lacked health insurance, up from 11.8 percent. "There's a ripple effect," says Tom W. Smith, director of the survey. Without health insurance, he explains, getting sick can lead to other discouraging consequences, including loss of a job. *—Kaspar Mossman*



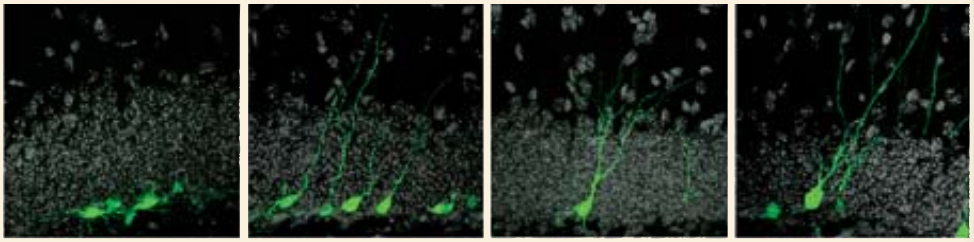
Lying Liars

Pathological lying may stem from an unusual imbalance of brain matter, say scientists at the University of Southern California. Working with senior investigators, doctoral student Yaling Yang scanned the brains of 12 self-described pathological liars as well as other volunteers who had no history of deception. Yang was surprised to find that the liars' brains had 22 percent more white matter in the prefrontal regions that govern decision making and judgment. So-called white matter makes up the wiring among neurons, which are sometimes collectively called gray matter.

Pathological lying can be very complicated. People who do so must present information that appears correct and yet harbors falsehoods. "It may just be easier for them to tell lies," Yang says, because the excessive white matter creates an abundance of connections among otherwise contradictory, compartmentalized data. Further studies are needed to determine if the fabricators are born with more white matter or develop it as a result of their frequent fibbing.

Other scientists who have done functional MRI scans of people lying in real time also point to excessive activation in the prefrontal lobes and say the patterns of activity can serve as reliable detectors of deception. If so, scanners could one day move from the lab bench to the court bench. *—Jamie Talan*

SCIENTIFIC AMERICAN MIND (*top*); MICHAEL FORBES *Getty Images* (*bottom*)



New neurons do not integrate (*far left*) until stimulated by GABA (*remaining images*).

Integrating Newbies

A common neurotransmitter that conveys signals among brain cells reverses its normal function to accommodate new neurons in the brain.

Since the remarkable 1998 discovery that people can grow new neurons well into old age, researchers have wanted to know how the newbies integrate themselves gracefully into existing neural networks without causing interference. Studies in embryonic rodents and monkeys suggested that the neurotransmitter GABA, which normally inhibits neurons from firing, may instead be stimulating young neurons to fire.

Sparked by this clue, a group at Johns Hopkins University turned to a part of the hippocampus called the dentate gyrus. In a common strategy for visualizing new neurons, they introduced a retrovirus into mice that makes dividing neurons fluoresce green. They then measured the responsiveness of these cells to different neurotransmitters.

Initially the new neurons were sensitive to GABA that had diffused into the space between cells. After a week the new cells connected to established neurons, which transmitted GABA in pulses. In another week the cells formed connections to receive glutamate, the major stimulatory neurotransmitter in adult neurons. The results indicate that despite differences between embryos and adults, "newly formed neurons must follow this sequence," says Yehezkel Ben-Ari, director of the Mediterranean Institute of Neurobiology in France, who is not connected to the Johns Hopkins work.

Apparently, an excess of chloride ions inside the young cells is responsible for their excitation by GABA. Chloride-deficient neurons that the scientists engineered showed a two-week delay in developing connections and eventually died. Johns Hopkins neuroscientist Hongjun Song says the team hopes to test whether applying GABA to stem cells at the right time and dose could help repair central nervous system injuries. *—JR Minkel*

Discipline Pays

Any teacher can tell you that smarts alone do not a good student make. But psychologists had never rigorously studied the connection between self-discipline and academic success, says former teacher Angela L. Duckworth, now a psychology graduate student at the University of Pennsylvania. Duckworth and her adviser, Martin E. P. Seligman, gave 300 eighth graders, their teachers and their parents a questionnaire about the students' ability to control impulses and follow rules. They also gave the children another questionnaire and behavioral test to assess their willingness to delay gratification. The reported self-discipline predicted final grades, school attendance and work habits better than IQ did. Moreover, the stronger the discipline, the better the outcomes.

The results could encourage young students to toe the line. Still, the research method may not be practical for routinely evaluating children, Duckworth says. "The effort that's involved in a study like this is kind of humongous." *—JR Minkel*

BASI

- **Fish is brain food.** Although many dietary wives' tales have no basis in science, this one apparently holds up. Recent studies show that six-month-old babies whose mothers ate more fish during their second trimester of pregnancy score higher on cognitive tests, and senior citizens who eat fish at least once a week do better on memory and mental acuity exams than peers who do not.

- **The widower effect** is strikingly real, according to a massive study released in February by Harvard Medical School and the University of Pennsylvania. For nine years, researchers followed more than 518,000 couples older than 65. The death of a wife in the previous 30 days increased a husband's risk of death by 53 percent, and the death of a husband increased a wife's risk of death by 61 percent. Additionally, the hospitalization of one partner elevated health risks for the other partner for nearly two years.

- **Bartenders,** as well as drinkers at home, unintentionally pour 20 to 30 percent more liquor into short, wide glasses than tall, slender ones when making a mixed drink. Economics professor Brian Wansink of Cornell University explains that people perceive tall glasses as holding more than short ones of the same volume—an optical illusion. They also focus on the level of the liquid, insufficiently compensating for its diameter and thus the total volume.

FROM "GABA REGULATES SYNAPTIC INTEGRATION OF NEWLY GENERATED NEURONS IN THE ADULT BRAIN," BY SHAOYU GE ET AL., IN *NATURE*, VOL. 439; FEBRUARY 2, 2006. REPRINTED BY PERMISSION FROM MACMILLAN PUBLISHERS LTD. (*top*); DAVID WOOLLEY *Getty Images* (*bottom*)

Loneliness Predisposed

If you feel lonely persistently, blame it partly on your genes. In a survey of 8,387 siblings, 48 percent of identical twins and 24 percent of fraternal twins reported similar levels of moderate to extreme loneliness, with much higher agreement than siblings who were not twins. The results come from a 12-year study done in the Netherlands by psychologists at Free University and the University of Amsterdam and at the University of Chicago.

The findings, along with ongoing investigation of a satellite of proximal genes on chromosome 12, suggest that some individuals have a genetic vulnerability to feelings of loneliness. Such a propensity should not, however, be thought of as an immutable trait, such as eye color, says psychology professor John T. Cacioppo of the University of Chicago. Rather the genetic bent should be viewed as a risk factor that makes certain individuals more sensitive to environmental factors that can cause loneliness.

Cacioppo believes that genetically based loneliness could have played an evolutionary role, giving humans an incentive to socialize and share resources. "Loneliness is a signal, just like pain, that something is wrong," he says. "It motivates you to do something. And the reward associated with that … motivates the maintenance of those relationships, which is critical to our survival."

Because loneliness is associated with medical conditions such as elevated blood pressure, knowing your inherited predisposition to it could allow you to make better health decisions. For instance, "you might not take that promotion that requires you to move across the country and leave friends and family behind," Cacioppo notes. *—Michael J. Battaglia*

Individuals prone to loneliness might decide to not move far away from family and friends.

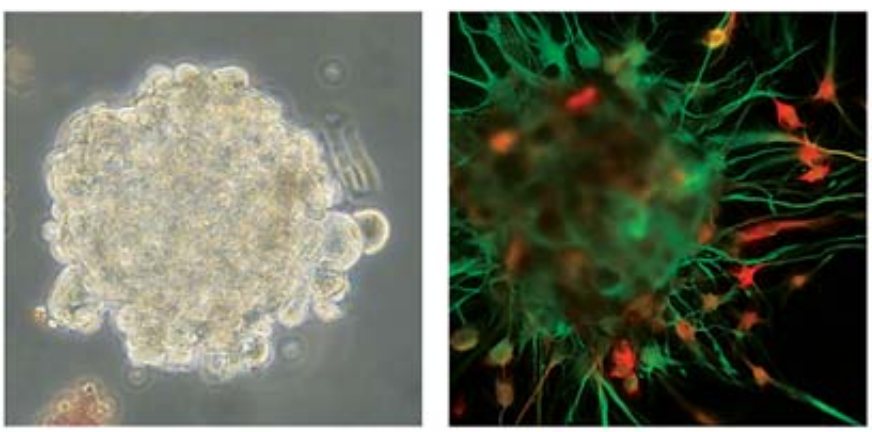
Stem Cells Cause Cancer

Stem cells are vital throughout life because they can develop into specialized tissue. Recently, however, scientists have discovered that damaged or altered stem cells may be the driving force behind some kinds of cancer when their specialization takes a malignant turn for the worse.

Stem cells were first identified in leukemia in 1997. Since then, they have been found in breast cancer and certain brain tumors, including glioblastoma multiforme, the most aggressive brain malignancy in adults. Although it was widely thought that most cells in a tumor could cause it to grow, researchers now believe that in some cancers, a small population of stem cells gives rise to all the other cells. When tumor cells are transplanted into experimental mice, only the stem cell variety spurs new cancer growth.

Neural stem cells normally develop into neurons, glia and other cell types. Stem cells found in brain tumors are similar but have genetic mutations that lead to uncontrolled growth. Harley Kornblum, director of the Neural Stem Cell Research Center at the University of California, Los Angeles, is searching for drugs that might inhibit or kill tumor stem cells. Because there are many kinds of brain cancer, Kornblum cautions that they must be approached individually. "We don't think there's a one-size-fits-all" mechanism, he says, pointing out that one type of brain tumor called medulloblastoma is caused by "external granule" cells.

Nevertheless, because stem cells activate their genes differently than other cells do, doctors may be able to use genetic analysis to assign more effective treatment to certain patients. Scientists are now focusing on methods to block the unique pathways by which cancer stem cells regenerate, because it seems clear that the stem cells must be eradicated to stop tumor growth. If they succeed, less destructive chemotherapy or radiation, or other treatments, may be possible. *—Kaspar Mossman*



Brain cancer stem cells (*left*) differentiate into adult tumor cells (*right*).

ROBERT WARREN *Getty Images (top)*; FROM "CANCEROUS STEM CELLS CAN ARISE FROM PEDIATRIC BRAIN TUMORS," BY H. D. HEMMATI ET AL., IN *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES USA*, VOL. 100, NO. 25; DECEMBER 9, 2003 (*bottom*)

Neurons firing in reverse sequence help to cement new learning.

Learn by Reverse Replay

Rats learn to navigate new spaces by replaying memories in reverse order, a study released in February suggests. After exploring an environment such as a maze, rats typically pause to eat, groom or rub their whiskers. Researchers had ignored such behavior because it seemed unimportant—rats being rats. But a pair of investigators from the Massachusetts Institute of Technology decided to see what the rat brain is doing during these interludes.

The team placed electrodes into a rat's hippocampus to monitor so-called place neurons, which fire in a specific sequence as a rat navigates a path. Surprisingly, when various rats paused on completion of a run, the place neurons fired in reverse order from the firing that had occurred during navigation. This reverse replay occurred more frequently after walking through new mazes than familiar ones, implying that the technique plays a role in learning.

The phenomenon is likely to prove important in people, too, says M.I.T.'s David J. Foster. "There is a wealth of data from experiments in many species, including humans, showing that if learning trials are spaced out in time, they are more effective." Reverse replay may explain why.

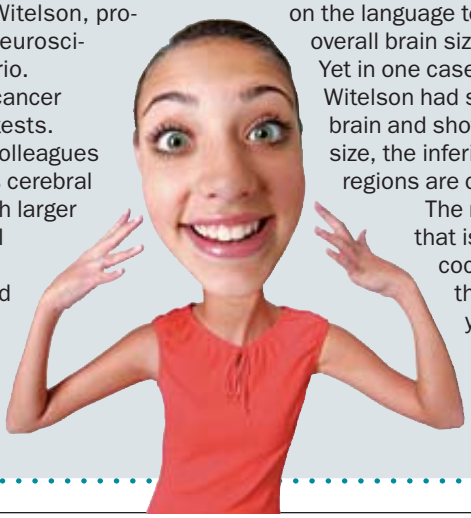
—JR Minkel

Bigger Is Brainier?

Size seems to matter—for certain kinds of intelligence—according to a new study by Sandra Witelson, professor of psychiatry and behavioral neuroscience at McMaster University in Ontario.

Witelson asked 100 terminally ill cancer patients to take a series of cognitive tests. After each person died, she and her colleagues measured the volume of the subject's cerebral hemispheres. On average, women with larger brains had performed better on verbal tests than women with smaller brains had. There was also a less pronounced association between brain size and visual-spatial ability. The results were equivalent for right-handed and nonright-handed women.

Right-handed men showed similar results for verbal skills, but no correlation registered among nonright-handed men; for lefties and ambidextrous males, brain volume did not predict how well they had done on the language tests. Witelson also found that for all men, overall brain size had no relation to visual-spatial abilities. Yet in one case, she found an exception. In earlier work, Witelson had studied the anatomy of Albert Einstein's brain and showed that although it was of average overall size, the inferior parietal lobes were expanded. These regions are crucial to processing visual imagery.



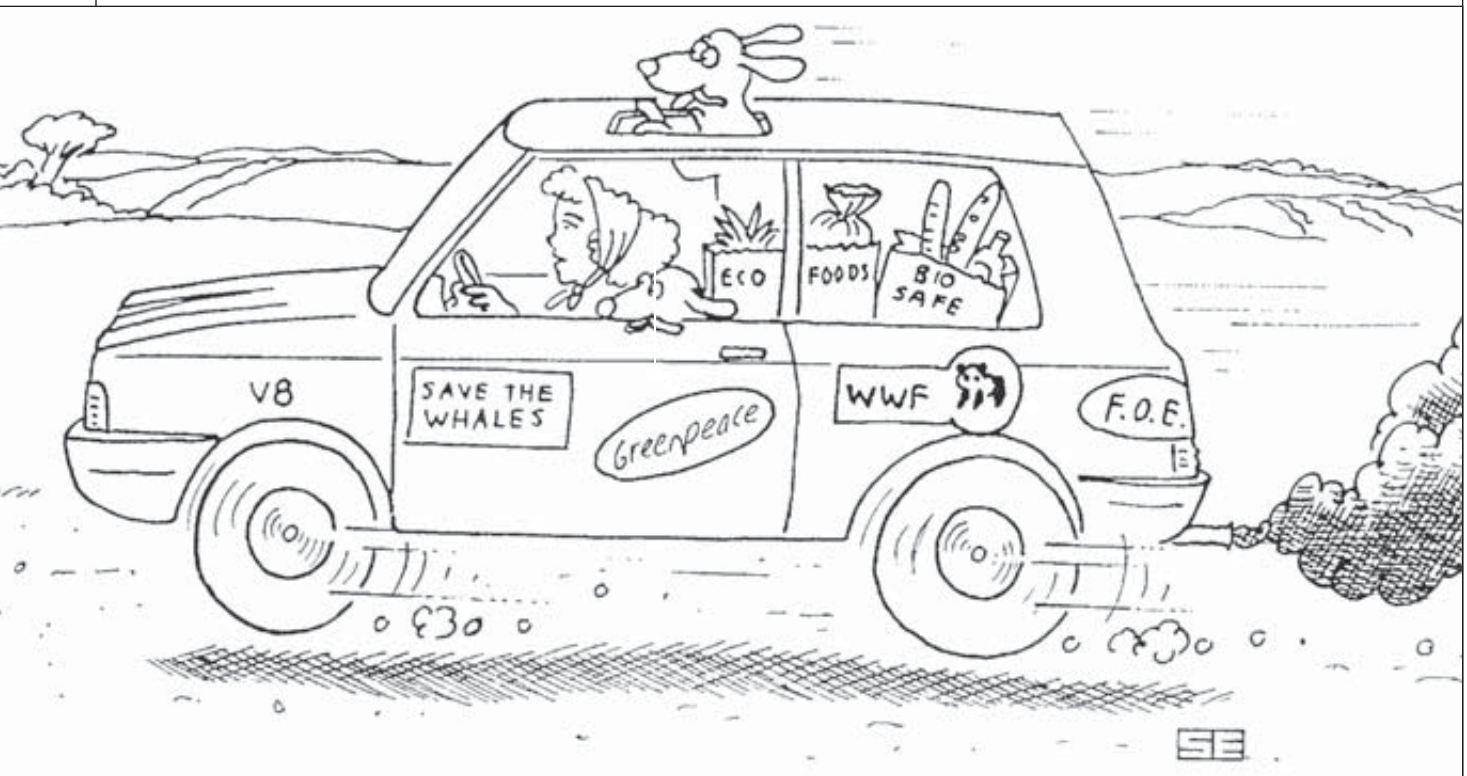
The new work also unveiled one correlation that is sure to make for a few sharp quips at cocktail parties. As men age from 25 to 80, the size of their brain generally decreases, yet age barely alters brain size in women. Experts do not yet know whether genes, hormones or environmental factors underlie different aging patterns.

—Jamie Talan

WILLIAM LOMBARDO *Getty Images (top)*; GETTY IMAGES *(bottom)*

Thinking Green

Most people claim to be pro-environment, but psychological and practical factors must be addressed before they will actually hop on a bus BY JOACHIM MARSCHALL



STAN EALES *CartoonStock*

SAFEGUARDING the environment ranks high on political and social surveys. Yet a yawning gap exists between good intentions and reality. Although Americans express strong support for reducing air and ground pollution, few give up their cars or recycle their AA batteries instead of throwing them in the trash.

Why are people's words and actions so contradictory? Economists who study such behavior say the only variables that really matter to most individuals are time and money: How much would a gallon of gasoline have to cost before the masses switch to mass transit? How frequently would buses have to run to attract crowds of riders? Fortunately, experts in the young discipline of environmental psychology point out that other influences can strongly affect our choices. Understanding these dynamics, and how to exploit them, may prod citizens to embrace greener ways.

Changing Attitudes

One feature to plumb is personality. P. Wesley Schultz, professor of psychology at California State University, San Marcos, is studying one trait that, surprisingly, has been largely ignored: the extent to which people feel they are part of the natural world. Schultz measures attachment to nature with a variation of the widely used Implicit Association Test. The computerized exercise determines how strongly a person associates his or her self-image with a particular concept, such as "trees" or "factory."

In a 2005 study Schultz found that individuals who demonstrated either a close or distant connection with nature could be moved by a long visit to a certain place. Subjects who spent a day at the zoo or on a hiking trail felt, at the end, somewhat more closely connected to nature than when they spent a day in a library or at a health club. Schultz concluded that attachment to nature is not a personality characteristic that is carved in stone. His results suggest that it would be

(It is much easier to **convince people** to protect nature if they have had direct experience with it.)

much easier to convince people to protect nature if they had direct experience with it—which is the force behind the rise of ecotourism.

Other characteristics, such as age, also influence how ecologically minded a person may behave. Although young people express concern for the environment, they are somewhat less likely to behave in an environmentally sustainable way than are older people. Political orientation holds sway as well: conservatives care significantly less about protecting the earth than do people who describe themselves as liberals.

Conscious awareness comes from forming **good habits**, such as checking a container's recycling symbol.

More important, according to some environmental psychologists, are basic attitudes. According to one accepted model called the theory of planned behavior, created by psychology professor Icek Ajzen of the University of Massachusetts Amherst, three factors determine whether we choose to carry out any particular action: attitude toward the behavior (Are the probable consequences of my deed compatible with my convictions?); social norms (Do others, whose opinions matter to me, expect me to behave like this?); and perceived behavioral control (Can I see anything that might help or hinder my carrying out this action?).

Only when all three questions can be answered positively do we conclude that we will actually carry out a proposed action. Christoph Weber, now at the University of Duisberg-Essen in Germany, tested this assessment on 240 people who planned to relocate to Stuttgart. Before they moved, half the group received a packet about the Stuttgart transit system that explained which bus stop would be nearest to their new address and provided a schedule for that line. Some envelopes included a one-day bus pass as an incentive. Weber surveyed the participants several weeks after they moved and found that those who had received the mailing did leave their cars at home more often. He concluded that because they knew more about departure times and connections, they were far more convinced that they could make sensible choices about how to get to work. The most avid transit users also indicated that the opinions of their friends and families had pushed them in the direction of taking buses.

Changing Habits

The theory of planned behavior assumes that we carefully consider pros and cons, which may be true in novel situations such as moving to a new city. But the theory neglects an important point: in everyday life we tend to be creatures of habit. We may have to overcome many habitual, or automated, acts to exhibit greener behavior. The decision to leave the lights on as we walk out of a room or to check the recycling symbol on a plastic container instead of just throwing it away may rarely involve conscious consideration.

Some environmental researchers also overlook very real constraints that can limit a person's choices. Florian G. Kaiser, who teaches social and environmental psychology at the Eindhoven University of Technology in the Netherlands, notes that positive attitudes toward nature are of little value without opportunities to take action. For example, whether or not the only supermarket near an individual's home carries eggs from free-range chickens will most likely be the only factor determining whether that person buys free-range eggs.

Kaiser examined the power of objective constraints by analyzing how students with different academic majors in Andalusia (in southern Spain) and in Switzerland engaged with green issues. He found that Spanish environmental science students behaved almost exactly like their local friends in business school but completely differently from Swiss environmental science students, even though the Swiss students shared a similar awareness of environmental issues.

Why the irony? Kaiser points out that students in balmy Andalusia were less concerned with the use of heating fuel than the Swiss were, but that is simply because the climate is warmer. And the Swiss donated more to green organizations and bought more organic products simply because they had more disposable income.

Such findings cast doubt on the sway of ephemeral factors such as a country's pride in environmental consciousness and raise the profile of pedestrian issues such as knowledge about bus schedules and money for organic fruit. As enthusiasts try to encourage others to act greener, they must consider basic practical factors and not just attractive philosophies.

JOACHIM MARSCHALL is a psychology student and freelance science writer in Mainz, Germany.

ALAN TOWSE *Ecoscene/Corbis*

Good Friends

Want to live longer? Diet and exercise will get you only so far BY KLAUS MANHART

RONNIE KAUFMAN *Corbis*

HERE IS ANOTHER REASON to call your old buddy to catch up: new findings show that it is not just fun or socially enriching to maintain solid relationships with close friends—it also helps you stay healthier and may extend your life span.

Psychologists have long known that having a set of cherished companions is crucial to mental well-being. In addition, a recent study by Australian investigators Lynne Giles, Gary Andrews and Mary Luszcz of Flinders University and Gary Glonek of the University of Adelaide concluded that our chums even help to prolong our lives. The scientists analyzed data from a decade-long survey called the Australian Longitudinal Study of Aging, which was initiated in 1992. It concentrated on the social environment, general health, lifestyle and age of death of 1,477 persons older than 70 years. Study participants were asked how much personal and telephone contact they had with friends, children, relatives and acquaintances.

Researchers were surprised to learn that friendships increased life expectancy to a far greater extent than, say, frequent contact with children and other relatives. This benefit held true even after these friends had moved away to another city and was independent of factors such as socioeconomic status, health and way of life.

(Friendships increased **life expectancy** more than frequent contact with relatives.)

What exactly underlies this effect on longevity? Apparently, the scientists posit, it is not merely the mutual buoying of spirits that occurs among associates. What is more important is that the support given and received by friends is voluntary and pleasurable and not just the result of a sense of duty or convention. In contrast to our own families, we are able to choose our friends.

According to the Australian scientists, the ability to have relationships with people to whom one is important has a positive effect on physical and mental health. Stress and the tendency toward depression are reduced, and behaviors that are damaging to health, such as smoking and drinking, occur less frequently. The investigators speculate that in times of calamity in particular, our support networks can raise our moods and feelings of self-worth and offer helpful strategies for dealing with difficult personal challenges.

In fact, the physiological pluses of such social interaction have already been demonstrated and include alleviating cardiovascular disease, high blood pressure and gastrointestinal problems. For example, physiologist and pharmacologist Eric B. Loucks of the Harvard School of Public Health discovered that considerably smaller amounts of a molecule called interleukin-6 circulate in the blood of older men with an extended set of connections than in that of loners. The elevated presence of this inflammation mediator is a risk factor for cardiovascular disease; it appears to favor the development of arteriosclerosis, a condition in which fatty deposits build up on blood vessel walls.

In addition to the benefits of friendship for individuals, our species as a whole has gained from the experience. It seems that social interaction contributed greatly to the evolution of our brain, making it the high-performance organ that it is today. Anthropologist and evolutionary psychologist Robin Dunbar of the University of Liverpool in England came to this conclusion a few years ago. It occurred to him that brain size and group size seemed to be correlated in apes, our closest relatives in the animal world. The more members there are on average in the extended families of a particular primate type, the larger the cerebrum is likely to be in those animals. Humans, with the bulkiest brains, have the biggest social networks.

From this notion, Dunbar derived his hypothesis of the "social brain." According to him, the development of social structures accelerated the evolution of the brain. The reason, presumably, is that the greater the size of the group, the more information the brain must process about each of its members so that the social unit will be able to function. By the same token, the processing capacity of the brain also limits the size of our immediate social circles—to about 150 persons [*see box above*].

Reasons enough to ring your pal—and perhaps even to renew a few dormant acquaintances from childhood or college. M

KLAUS MANHART is a philosopher of science, social scientist and independent author in Munich.

Circle of Friends

Your social circles may seem chaotic. But they actually form regular hierarchical structures—in the shape of concentric rings—according to evolutionary psychologist Robin Dunbar of the University of Liverpool in England.

Our closest intimates form an innermost hoop of three or four, or at most five, people. We feel our greatest emotional connection to them, and we share with them common interests, values and opinions. In crises they help us, and they advise us on personal, emotional and financial matters. Generally, we will be in contact with members of our "support group" at least once a week.

The next circle holds between 12 and 20. Our relationship with these individuals is less strong, but we maintain a caring mutual interest. The subsequent level contains between 30 and 50; our attachment is considerably looser, although we still have regular, if only occasional, contact. Dunbar believes that this third set corresponds to a band in traditional hunter-gatherer societies. He postulates at least two other loops with even looser relationships.

At each step in our growing circle of acquaintances, the number of individuals increases by approximately a factor of three, Dunbar discovered. For example, in many countries the smallest battle unit consists of 10 to 15 soldiers, a platoon of 35 and a company of 120 to 150. This magical maximum has cropped up again and again for millennia. The Roman army's basic unit, the *maniple,* had 150 soldiers. Today the size of most companies fluctuates between 120 and 150. —*K.M.*

(Further Reading)

- **Discrete Hierarchical Organization of Social Group Sizes.** W. X. Zhou, D. Sornette, R. A. Hill and R. I. Dunbar in *Proceedings of the Royal Society B,* Vol. 272, No. 1561, pages 439–444; February 22, 2005.
- **Social Integration Is Associated with Fibrinogen Concentration in Elderly Men.** E. B. Loucks, L. F. Berkman, T. L. Gruenewald and T. E. Seeman in *Psychosomatic Medicine,* Vol. 67, No. 3, pages 353–358; May–June 2005.
- **Effects of Social Networks on 10 Year Survival in Very Old Australians: The Australian Longitudinal Study of Aging.** L. C. Giles, G. F. Glonek, M. A. Luszcz and G. R. Andrews in *Journal of Epidemiology and Community Health,* Vol. 59, No. 7, pages 574–579; July 2005.

Follow-Up

Sexuality and Choice

An exclusive national poll commissioned by *Scientific American Mind* reveals diverse and conflicting opinions about the nature of sexuality

ALAN SCHEIN zefa/Corbis

Do Gays Have a Choice?

Science offers a clear and surprising answer to a controversial question

By Robert Epstein

On a typical summer Saturday morning Matt Avery and his wife, Sheila (not their real names), cook breakfast with their two sons, ages five and eight. Then they get organized with towels, goggles and water wings and load the family into the car for an afternoon at the pool. "Weekends are all about family time," Matt says.

Matt and Sheila have been happily married for 11 years. "She's my soul mate," Matt says. "I wouldn't trade my life for the world."

But some people would claim that Matt's life is based on an illusion—that he could not possibly be a dedicated husband and father. Why? Because Matt used to be gay.

CAN WE CHOOSE our sexual orientation? Given the polarized nature of the discussion among national leaders, it would be logical to think that the public's opinions must be equally divided. On the one hand, religious conservatives argue that being homosexual is a choice. On the other, the National Gay and Lesbian Task Force and at least a few experts counter that sexual orientation is immutable, something that we are born with. After running an article by psychologist Robert Epstein in the February/March issue—"Do Gays Have a Choice?"—that explored the related research, the editors at *Scientific American Mind* wanted to know how the public felt about these issues. We recently commissioned a nationwide poll to find out—and received some surprising results.

Although the editors worried that people might not be comfortable answering questions about sexuality, the online poll conducted by Zogby International drew more than 4,200 responses. Half the respondents believed that sexual orientation is not a choice but rather is "innate, genetic or predetermined by other factors such as environment." Another 34 percent believed that "sexual orientation is determined by both choice and other factors." In contrast, only 11 percent agreed that "sexual orientation is a conscious choice." Six percent were not sure. The margin of error for the sample was plus or minus 1.5 percentage points.

"I think the results are surprising and spectacular," says Epstein, a visiting scholar at the University of California, San Diego. "There is clearly a myth about what people generally believe about sexuality."

Epstein's article made the point that sexuality exists on a continuum, with both genetics and environment playing a role in determining where people end up. The majority occupy the heterosexual end of the continuum, as a result of both genetics and a "push" provided by social pressures. For people who fall near one extreme or the

Men and women were **deeply divided** in their perceptions of sexual orientation in the poll.

other (exclusive attraction to either same-sex or opposite-sex partners), choice about sexual orientation is very limited, if it exists at all. As a result, "reparative" therapies and other techniques that seek to switch homosexuals to heterosexuality work only if an individual's makeup permits.

Likewise, responses to the poll indicated that people believe that sexual orientation occurs along something of a spectrum, with both straight and gay people having the potential to be attracted to individuals of either sex.

Some 47 percent of the poll respondents, a slight plurality, agreed with the following statement: "I believe that all people have the potential to be sexually attracted to members of both sexes." But a distinct majority (53 percent) said they believed that "a straight person may occasionally experience sexual attraction to individuals of the same sex." An even higher number (62 percent) believed that "a gay person may occasionally experience sexual attraction to individuals of the opposite sex."

Group Variations

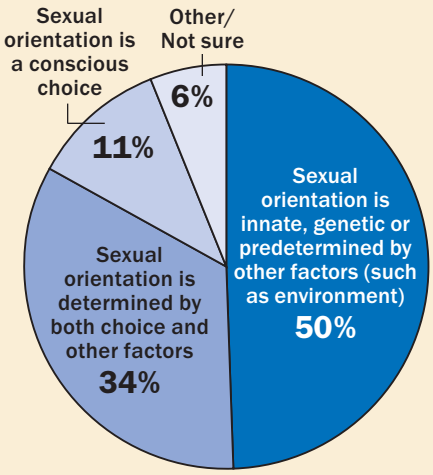
Although the belief that sexuality is not a choice is generally widely held, a closer look at some groups reveals differences of opinion as well. For instance, the idea that sexuality is innate was particularly prevalent among Americans aged 50 to 64 (53 percent) and aged 18 to 29 (51 percent), single people (58.5 percent), Hispanics (57 percent) and Democrats (72 percent).

People who identified themselves as conservatives were more likely to think that sexual orientation was either fully or partly a choice. This opinion was especially common among those who said they were "very conservative"; nearly 80 percent held that sexuality is a choice, with only 15 percent believing that it is determined by genetics or other factors.

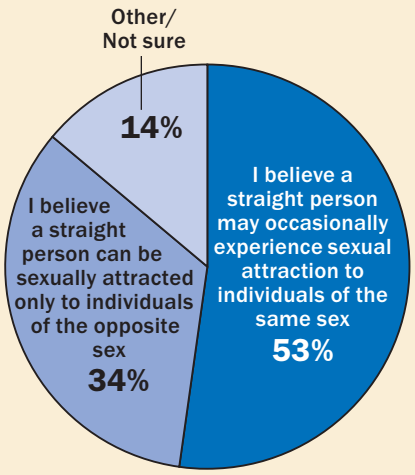
Men and women were deeply divided in their perceptions of sexual orientation: 60 percent of females believed it is "innate, genetic or predetermined by other factors such as environment." Only 39 percent of men agreed.

Sexuality Poll Results

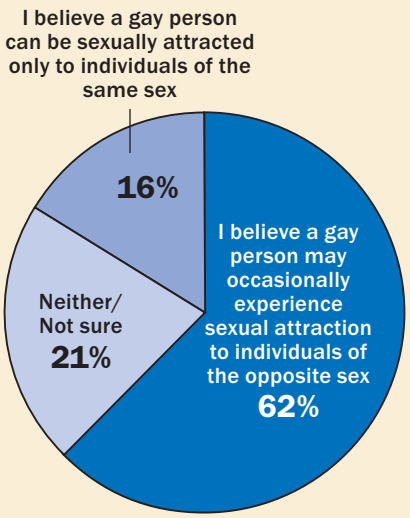
Which of the following best describes your perception of sexual orientation?



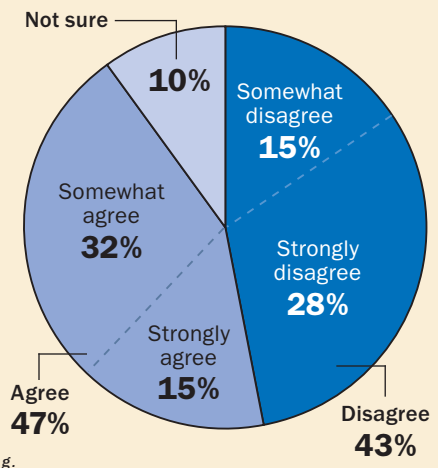
Which of the following two statements comes closer to your own opinion?



Which of the following two statements comes closer to your own opinion?



Do you strongly agree, somewhat agree, somewhat disagree or strongly disagree with the following statement: "I believe all people have the potential to be sexually attracted to members of both sexes"?



NOTE: Some totals are not 100% because of rounding.

The belief that "all people have the potential to be sexually attracted to members of both sexes" was especially prevalent among adults younger than 30 (66 percent). Groups that expressed high levels of disagreement included people aged 65 and older (53 percent), those who identified themselves as frequent Wal-Mart shoppers (58 percent), NASCAR fans (56 percent), and those who called themselves born-agains (59 percent). *—The Editors*

(Further Reading)

- To take the new Epstein Sexual Orientation Inventory, which tells you where you are on the Sexual Orientation Continuum and estimates how much choice you have in expressing your sexuality, visit **www.MySexualOrientation.com**

Touching Illusions

Startling deceptions demonstrate how tactile information is processed in the brain

BY VILAYANUR S. RAMACHANDRAN AND DIANE ROGERS-RAMACHANDRAN

HUMANS, LIKE ALL PRIMATES, are highly visual creatures. Most of the back of our brain is devoted to visual processing, and half of the cortex is involved with sight. In addition, when visual inputs conflict with clues from other senses, vision tends to dominate. This supremacy is why, for example, ventriloquists are so compelling. We see the dummy talking, and we are fooled into hearing the voice coming from it—a case of what scientists call "visual capture." (With eyes closed, however, we can correctly localize the dummy voice to the ventriloquist.)

If information from vision and touch are incompatible, visual dominance may cause us to actually feel things differently than if we relied only on touch (without looking).

Curved Touch

In a simple but striking demonstration by James Gibson in the 1930s, a subject is first presented with a short straight metal rod and asked to feel it with his eyes closed. Of course, he correctly feels it is straight. He then lets go of the rod and is asked to open his eyes and look down at it. Unbeknownst to him, it is the same rod but viewed through a wedge prism, which causes the rod to appear curved rather than straight. Not surprisingly, he now reports seeing a curved rod. But what happens when he reaches out and touches the rod while looking at it? Subjects reported nothing unusual: they noticed no rivalry, instability or averaging between the senses; the rod that they saw as curved they simply also felt as curved.

In short, vision redirects the tactile perception so that no conflict is experienced. Similarly, the late Irvin Rock of the University of California, Berkeley, showed that when shape or size perception for single simple objects was made to conflict between the senses (by the introduction of distorting lenses), perception conveyed by active touch was modified to conform to visual perception.

a

Yet another example of vision influencing touch occurs in patients with phantom limbs. After amputation of an arm, the vast majority of patients continue to feel vividly the presence of the missing arm, a phenomenon termed phantom limb in the late 1800s by physician and author Silas Wier Mitchell. Many people report that their phantom limb is frozen, paralyzed in a constant or fixed position, and that this is sometimes painful.

We wondered whether touch sensations in the phantom arm could be influenced by visual input. We positioned a mirror on the table in front of a pa-

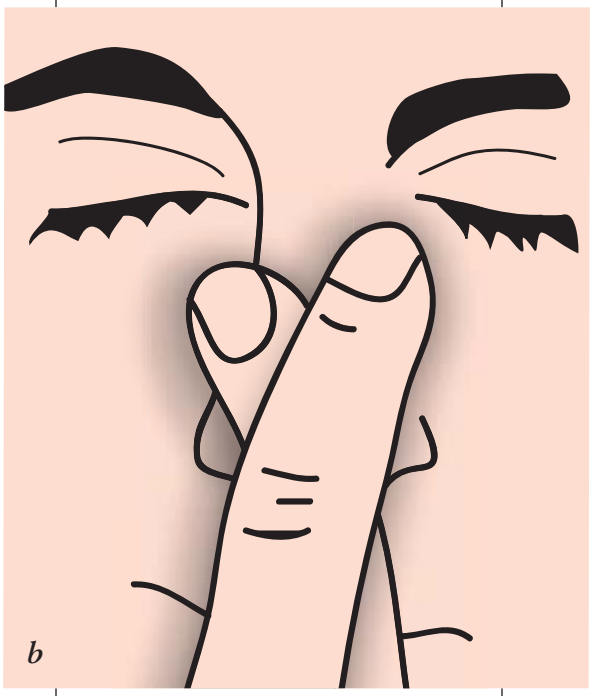
When he looked at the reflection of his normal hand in the mirror, he felt the phantom being **visually resurrected**.

JASON LEE

So the brain interprets the tactile experience as "I must have **two noses**."

tient, along his midline, and asked him to position his intact arm and stump/phantom hand symmetrically on either side of the mirror (*a*). When he looked at the reflection of his normal hand in the mirror, he experienced the phantom being visually resurrected. Remarkably, if the patient moved his normal hand while looking at its reflection in the mirror, the previously frozen phantom seemed to become animated; he not only saw the hand but also *felt* it move. In some cases, this sensation seemed to alleviate the pain associated with the phantom.

The visual-capture effect also indicates our need for a single, sensible narrative of the world. That is, we (our brains) tend to reinterpret or discard some information, even when doing so may produce errors or illusions (as with the ventriloquist). This influence of vision has resulted in a kind of vision chauvinism in research, leading scientists to pay less attention to the other senses.



Touched in the Head?

The neural basis of these intermodality illusions has not been studied in detail. Recent work by Krish Sathian of Emory University and Alvaro Pasqual-Leone of Harvard University suggests that somatosensory signals (those having to do with touch) may be seen in the primary visual cortex under certain circumstances—for example, in blind Braille readers. The tactile signals processed in the somatosensory centers of the brain may actually send feedback all the way to the very early stages of visual processing, instead of being merely combined at some higher level. Studies on visual capture suggest that the converse may also be true—namely, that visual input may project to what is traditionally considered primary somatosensory cortex. These interactions between the senses, in addition to informing us about brain mechanisms for information processing, may also provide a useful tool for rehabilitation for neurological disorders.

We would like to consider here some tactile illusions that bear a striking similarity to visual illusions. Try the following experiment. Place two coins in your freezer till they are chilled (maybe 20 minutes). Remove them and place them on a table flanking a similar coin that has been kept at room temperature, so that the three coins now form a row. Now place the tips of the index and ring finger of one hand on the two cold coins and the middle finger on the middle coin. Amazingly, the middle finger feels equally cold. Perhaps the temperature-sensing pathways of the brain simply do not have the resolving power to discern two discrete sources. Yet the middle finger does not feel cold unless it is in contact with a neutral coin; if there are no tactile sensations emerging from it, the brain is reluctant to "fill in," or ascribe cold to, this region.

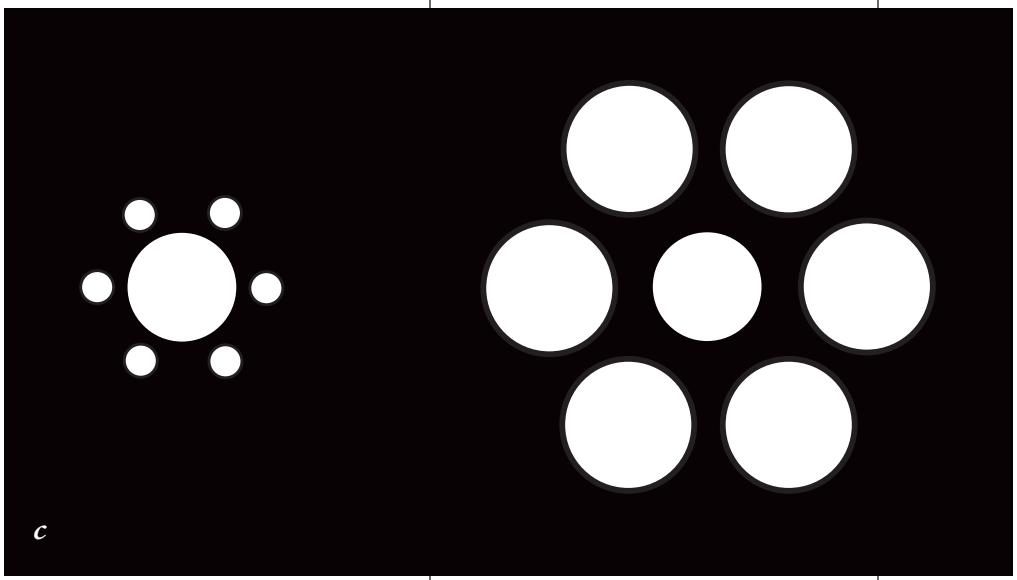
But how "clever" is this filling-in mechanism? What if the middle finger pressed against velvet or sandpaper rather than a coin? Does it have to be similar to what is being touched by the index and ring fingers? If so, how similar? And does this interpolation of cold occur early in sensory processing—for example, in the spinal cord or thalamus (the "gateway" for sensory inputs to the brain)? Or does it happen "higher up" in later processing stages in the brain?

One way to find out is to see what happens if you simply bend the middle finger upward and then put the middle finger *of the other hand* in its place. The illusion now disappears, suggesting that the filling in occurs at an early stage of tactile information processing, not at the higher level of space representation in the brain. (We know this occurs at an early stage because the sensory signals from two hands project to two separate hemispheres in the brain; information from them can be compared only at a relatively late stage of processing.)

What if the two outer coins were very hot and icy cold, respectively; would the middle coin take on the average temperature, or would it alternate between the two? What about an intermediate case? Say you crossed the index finger under the middle digit, so that you formed a row with the index between the ring and middle fingers, the middle and ring fingers resting on the cold coins. Would the index finger now feel cold because of its intermediate location in space?

The reader might wish to dream up

The middle disk at left is the **same size** as the one at right, but the left looks larger because it is surrounded by small disks.



c

his or her own experiments: that is what makes the study of perception so much fun. You do not need to be an expert to do experiments that have far-reaching implications. If you attempt such an experiment, we would love to hear from you.

Let us try something different. Cross your left middle finger over your left index finger, making a small V at the end. Now place the V formed by the fingers on your nose (*b, preceding page*). Astonishingly, many people who perform this "Aristotle Illusion" maneuver report a distinct feeling of having two noses! How is this effect possible?

One way to interpret the phenomenon is to realize that given the normal, habitual spatial arrangement of the fingers, the only way the *left* side of your left middle finger will be stimulated simultaneously with the *right* side of your left index finger is when they are touching two objects. So the brain interprets the tactile experience as "I must have two noses." According to psychologist Stuart Anstis of the University of California, San Diego, the nose is not the only appendage in which perceptual doubling can be produced.

Last, look at the visual illusion on this page (*c*). Believe it or not, the middle disk in the left panel of circles is the same size as the one on the right, but the left looks larger because it is surrounded by small disks. This optical trick is a powerful demonstration of the contextual nature of perception. (The skeptical reader may make a cardboard occluder with two holes to directly compare the two.) Is there an equivalent of this effect for touch?

Jelly or Velvet

The following demonstration may be a related effect. Get some coarse chicken-cage mesh, preferably mounted in a wooden frame. Then hold the mesh between the palms of your hands. Nothing peculiar so far. Now start rubbing your palms against each other with the wire between them. Remarkably, your palms will feel like jelly or velvet. The cause of this striking illusion has yet to be determined. One possibility is that it has something to do with sensing and signaling the contrast between the sharp wire and the "neutral" touch sensations on the skin—the opposite of sharp being velvety or jellylike. A version of this illusion can be found in many science museums.

You can even get your hands to "float"—a well-known trick, sometimes called the Kohnstamm effect, reintroduced to us by our 11-year-old son, Jayakrishnan Ramachandran. Stand in the middle of an open doorway and use your arms to apply outward pressure on the two sides as if you were pushing them away from your body. After about 40 seconds, suddenly let go and relax, stand normally and just let your arms hang by your sides. If you are like most of us, your arms will involuntarily rise up as if pulled by two invisible helium balloons. The reason? When you apply continuous outward force, your brain gets used to this as the "neutral state"—so that when the pressure suddenly disappears, your arms drift outward.

This simple demonstration shows that the sensory areas of your brain are not the passive recipients of signals from your sense organs. Instead we should think of them as being in a state of dynamic equilibrium with the outside world, an equilibrium point that is constantly shifting in response to a changing environment. M

VILAYANUR S. RAMACHANDRAN and DIANE ROGERS-RAMACHANDRAN are at the Center for Brain and Cognition at the University of California, San Diego.

(Further Reading)

◆ **The Sensory Hand: Neural Mechanisms of Somatic Sensation.** Vernon Mountcastle. Harvard University Press, 2005.

(calendar)

EXHIBITIONS

Neuroscapes 2006
Neuroscientists' images from cutting-edge technologies "capture landmark concepts of how the brain works." The exhibition marks the 100th anniversary of the Nobel Prize for Santiago Ramón y Cajal and Camillo Golgi, for their work on the structure of the nervous system.
Barcelona Science Museum, Spain
Spring 2006
+34 91 585 4735
www.neuroart2006.com/

1 Brain: The World inside Your Head
A lively show that uses modern exhibition technology to engage your brain while showing you its inner workings.
North Carolina Museum of Natural Sciences, Raleigh
January 28–May 7
919-733-7450 or 877-4NATSCI
www.naturalsciences.org/

2 Supporting Structure
An exhibition on the spine and spinal surgery highlights the treatment of spinal injury, from historical to state-of-the-art.
International Museum of Surgical Science, Chicago
Permanent exhibition
312-642-6502
www.imss.org/exhibits.htm

CONFERENCES

American Society of Addiction Medicine
The 37th Annual Medical-Scientific Conference is designed to "improve our understanding of the pathophysiology of addiction" with respect to alcohol, drugs, eating disorders and pathological behaviors and is geared toward professionals and students in the field.
San Diego
May 4–7
301-656-3920
www.asam.org/

Association for Psychological Science
The 18th Annual Convention of the association (formerly known as the American Psychological Society) features a keynote speech on behavioral genetics by Sir Michael Rutter of King's College London, a "Bring the Family Address" by *Blink* author Malcolm Gladwell and a symposium on "The Mind in the Media" organized by APS president Michael S. Gazzaniga.
New York City
May 25–28
202-783-2077
www.psychologicalscience.org/convention/

MOVIES/RADIO

Failure to Launch
Emotional immaturity and prolonged adolescence are comic fodder when the parents of Tripp (Matthew McConaughey) try to dupe him into leaving the comfort of the nest to follow the girl of his dreams (Sarah Jessica Parker).
Paramount Pictures
In wide release
www.failuretolaunchmovie.com/

3 Our Brand Is Crisis
James Carville and a team of consultants helped to elect the president of Bolivia in 2002 (who fled to Miami only 14 months later). The documentary picks apart the slick, sometimes sleazy, manipulation of public opinion.
Koch Lorber Films
In wide release
www.filmstransit.com/our_brand.html

Basic Instinct 2: Risk Addiction
Once again, writer Catherine Tramell (Sharon Stone) engages in a psychosexual duel with a police psychiatrist, this time from London's Scotland Yard, Dr. Michael Glass (David Morrissey).
Sony Pictures
In wide release
www.sonypictures.com/movies/basicinstinct2/index.html

The Da Vinci Code
Conspiracy theorists' dream or occult hooey? You be the judge as you watch an exceptional cast led by Tom Hanks and Audrey Tautou as a symbologist and a cryptographer who unravel ancient secrets in this film rendition of the popular book.
Sony Pictures
Opening May 19
www.sonypictures.com/movies/davincicode/site/home.html

The Infinite Mind
A weekly program broadcast on NPR "explores the art and science of the human mind." Upcoming episodes: "The Science of Winning" (airs starting April 5) and "Sex Talk" (airs starting April 12). Past programs available on CD or in MP3.
Stations and times at www.lcmedia.com/stations.htm

WEB SITES

www.neurosurgery.org/cybermuseum/index.html
The American Association of Neurological Surgeons has a continually expanding virtual museum of exhibits and archives.

www.bbc.co.uk/science/humanbody/mind/index.shtml
The BBC in London brings you psychology tests and surveys such as "Morals," "Lonely Hearts" and "Sniffing the Decades" and perception tests such as "Do You Hear What I Hear?" in a Web site chockablock with overview articles on psychology, memory, emotions and personality.

4 www.nimh.nih.gov/healthinformation/ptsdmenu.cfm and www.ncptsd.va.gov/
From the malevolent intent of 9/11 to the cataclysm of Hurricane Katrina, post-traumatic stress disorder, or PTSD, has become as familiar a concept among civilians as it has been for the military and its veterans. Here are two Web sites, from the National Institute of Mental Health and from the Department of Veterans Affairs, packed with information and help for survivors, their families and for students of the field.

Send items to editors@sciammind.com

CLEAR CHANNEL EXHIBITIONS (1); COURTESY OF THE ASSOCIATION FOR PSYCHOLOGICAL SCIENCE (2); BOYNTON FILMS, COURTESY OF KOCH LORBER ENTERTAINMENT (3); NATIONAL INSTITUTE OF MENTAL HEALTH (4)

A Revealing Reflection

MIRROR NEURONS ARE PROVIDING STUNNING INSIGHTS INTO EVERYTHING FROM HOW WE LEARN TO WALK TO HOW WE EMPATHIZE WITH OTHERS

BY DAVID DOBBS

RON MILLER *Getty Images*

Sometime just before my second child was born, I read that if you stick your tongue out at a newborn, he will do the same. So in young Nicholas's first hours, even as my wife was still in the recovery room after 40 hours of labor and a C-section, I tried it. Holding the gooing, alert lad before me in my hands, I stuck my tongue out at him. He immediately returned the gesture, opening his mouth and subtly but distinctly moving his tongue. I hadn't slept in two days. I laughed till I cried.

I did not know it then, but Nick was showing off what some consider one of the greatest drivers of human progress and one of the prime discoveries in recent neuroscience: mirror neurons. These neurons are scattered throughout key parts of our brain—the premotor cortex and centers for language, empathy and pain—and fire not only as we perform a certain action but also when we watch someone else perform that action.

These neurons have been studied in the past for their roles in movement and other functions. Now, however, researchers are examining them

MIMICRY
Mirror neurons enable infants and toddlers to learn facial expressions and physical maneuvers through imitation.

JAKOB HELBIG PHOTOGRAPHY *Getty Images*

We mentally imitate every action we witness, prompting us to dance, grieve and yawn with others.

intensely for what seems to be an additional function—the way they fire in response to something observed. The discovery of this mechanism, made about a decade ago, suggests that everything we watch someone else do, we do as well—in our minds. At its most basic, this finding means we mentally rehearse or imitate every action we witness, whether it is a somersault or a subtle smile. It explains much about how we learn to smile, talk, walk, dance or play tennis. At a deeper level, it suggests a biological dynamic for our understanding of others, the complex exchange of ideas we call culture, and psychosocial dysfunctions ranging from lack of empathy to autism. Comprehending mirror neurons helps us make sense of everything from why yawns are contagious to why, watching Lawrence Olivier fall to his knees, we share Hamlet's grief for Ophelia.

For some, this explanatory power makes mirror neurons the biggest neuroscientific discovery in recent times. "This completely changes the way we think about how the brain works," says Marco Iacoboni, a mirror-neuron researcher at the University of California, Los Angeles. Cognitive neuroscientist Vilayanur S. Ramachandran of the University of California, San Diego, even ventures that "mirror neurons will do for psychology what DNA did for biology: they will provide a unifying framework and help explain a host of mental abilities that have hitherto remained mysterious and inaccessible to experiments." In Ramachandran's view, mirror neurons may clarify not only how we come to learn and to understand others but how humans took a "great leap forward" about 50,000 years ago, acquiring new skills in social organization, tool use and language that made human culture possible.

The Raisin Incident

Big-picture speculation is not needed to see the wonder of mirror neurons, however. Even their basics astonish.

The neuroscientists who discovered the cells found them by happenstance. Giacomo Rizzolatti, Vittorio Gallese and Leonardo Fogassi of the University of Parma in Italy had run electrodes to individual neurons in a monkey's premotor cortex, to study neural activity as the mon-

S. LUKASH

CONTAGION When we see another person yawn, mirror neurons in primal brain regions tell us to do the same. Group laughter can be catching, too.

key reached for different objects. The eureka moment came when Fogassi walked into the room where the macaque was and casually reached out and picked up a raisin. As the monkey watched him, its premotor neurons fired just as they had earlier, when the monkey had picked up the raisin itself. The men could hardly believe what they had witnessed. But after replicating that experiment and similar ones many times, they realized they had discovered something new, and in a series of 1996 papers they gave the "mirror neurons" their name.

Since then, the Parma team, working often with Iacoboni, Michael A. Arbib of the University of Southern California and Christian Keysers of the University of Groningen in the Netherlands, has significantly expanded those findings. The researchers have learned, for instance, that mirror neurons do not just fire when an animal is watching someone else perform an action. Mirror neurons also fire if a monkey hears the sound of someone doing something it has experienced—say, tearing a piece of paper. And as the scientists began studying humans (using brain imaging rather than electrodes), they found groups of mirror neurons in higher numbers and in more places than occur in monkeys. Mirror neurons revealed themselves in the premotor cortex and the inferior parietal areas—associated with movement and perception—as well as in the posterior parietal lobe, the superior temporal sulcus and the insula, regions that correspond to our abilities to comprehend someone else's feelings, understand intention and use language.

From Action to Understanding

Unlike monkeys, humans also use mirror neurons to directly imitate actions and to understand their meanings. It appears we use mirror neurons to learn everything from our first smiles and steps to our most suave expressions and graceful dance moves. We also use them to appreciate these things, to feel the meaning behind a smile or to enjoy—in a sense by doing it at a premotor neural level—the thrill of hitting a tennis ball as we watch a Pete Sampras backhand.

These functions became evident in the first round of mirror-neuron studies in the late 1990s. Since then, imaging studies have shown that mirror neurons in humans encompass many more areas and functions. In 1998 Rizzolatti and Arbib discovered that one of the regions particularly rich in mirror neurons is the famous Broca's area, which Paul Broca found in the 1850s to be critical for language processing.

ERIK DREYER *Getty Images*

EMPATHY Theatergoers feel the pain of an actress spurned because their mirror neurons fire as if they were experiencing their own rejection firsthand.

Mirror-neuron theory began to mesh with existing language theory, which held that actions have a syntax similar to that of spoken or signed language. For mirror neurons, "hand grasps ball" is the same whether it is an action or expressed in sign language or a spoken sentence. Thus, language arises from the syntactic understanding generated by our mirror neurons. This idea gained credence in 2005: an international team that included Gallese and Rizzolatti found that when people listened to sentences describing actions, the same mirror neurons fired as would have had the subjects performed the actions themselves or witnessed them being performed. Remarkably, the cells responded to an abstract representation of a process that would seem to be quite visual and visceral.

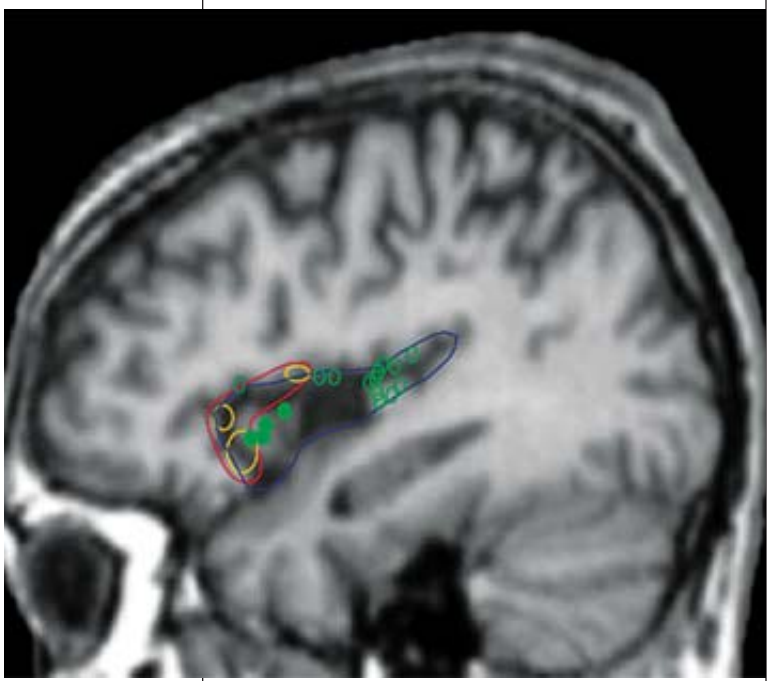
Another major insight relates to our understanding of other people's intentions and emotions. Several studies have demonstrated the dynamics of empathy, two with particular elegance.

One, described by Iacoboni in 2005, shows that our mirror neurons work in elaborate sets. We possess a basic set of mirror neurons corresponding to an action's most essential form—reaching, for instance—that is supplemented by other groups of mirror neurons that selectively

(The Author)

DAVID DOBBS (www.daviddobbs.net) profiled Joseph LeDoux and his work on fear in the February/March issue of *Scientific American Mind.*

More complex mirror-neuron systems may have sparked the advance of human cultures 50,000 years ago.



Neurons inside the red outline fired when one test individual experienced disgust because of a foul odor. Neurons inside the yellow outlines fired later when the same subject watched another person experience disgust. The areas overlap strongly, indicating mirror neurons. (Blue and green outlines represent the region and method of testing.)

fire according to the action's perceived purpose. Iacoboni had volunteers watch films of people reaching for various objects within a teatime setting—a teapot, a mug, a pitcher of cream, a plate of pastries, napkins—in different contexts. In every instance, a basic collection of "reaching" mirror neurons fired. But different additional mirror neurons would also fire depending on what expected action was suggested by various details in the scene. If the viewer saw a neatly set table and expected the hand to pick up a teacup to drink, one array fired; if the viewer saw a messy table and expected the hand to pick up a cup to clear it away, another group fired. Thus, mirror neurons seem to play a key role in perceiving intentions—the first step in understanding others and also in building social relations and feeling empathy.

A number of experiments, meanwhile, have shown that mirror neurons help us share other people's experiences as reflected in their expressions, providing a biological basis for empathy and for the well-known contagiousness of yawns, laughter, and good or bad moods. One of the most convincing (and certainly the most memorably titled) observations appeared in a 2003 paper, "Both of Us Disgusted in *My* Insula: The Common Neural Basis of Seeing and Feeling Disgust," published by Bruno Wicker of the University of the Mediterranean in Marseilles, France. Using functional magnetic resonance imaging (fMRI), Wicker's team found that feeling disgust and seeing a look of revulsion on someone's face caused the same set of mirror neurons to fire in the insula, a part of the cortex active in synthesizing convergent information.

When the Mirror Fogs

Given that mirror neurons are so fundamental to understanding, it makes sense that faults among them might create profound problems. Indeed, it appears that deficits may help account for difficulties ranging from excessive reserve to autism. The possible failure of mirror neurons in autism is particularly intriguing. The cause and even the nature of this strange condition have eluded researchers for decades, leaving sufferers and their families and caregivers with little knowledge about why the behaviors are happening, let alone how to treat them. But recent research suggests that an inactive mirror-neuron system may explain the deep troubles with language, learning and empathy that do so much to isolate the autistic person.

The findings indicate breakdowns in both basic and complex mirror-neuron activity. One study at Harvard Medical School, for instance, found that mirror neurons that fired in nonautistic people when they watched someone else make meaningless finger movements fired much less often in autistic children. This lack of response could reflect a failure of mirror neurons' most basic function, that of recognizing others' actions. In another study, researchers showed pictures of people with distinctive facial expressions to autistic and nonautistic adolescents. Both sets of subjects could imitate the expressions and say what emotions they expressed. But whereas the nonautistic teens showed robust activity in mirror neurons corresponding to the emotions expressed, the autistic teens showed no such activity. They understood the expressions cognitively but felt no empathy.

How these discoveries might lead to treatments is not clear. Yet identifying this apparent deficit, if the findings hold up, could be a major advance in pinning down the neural roots of autism.

FROM "A UNIFYING VIEW OF THE BASIS OF SOCIAL COGNITION" BY V. GALLESE, C. KEYSERS AND G. RIZZOLATTI IN *TRENDS IN COGNITIVE SCIENCES*, VOL. 8, NO. 9, SEPTEMBER 2004

JUTTA KLEE *Getty Images*

SOCIALIZATON Using mirror neurons, we develop elaborate forms of social interaction that constitute human culture.

Reflections Deep and Dark

Mirror neurons' role in understanding others lies at the heart of the deeper claims about them. Some, such as Ramachandran, believe that mirror neurons were crucial in the development of the elaborate social skills, social networks and knowledge infrastructure we call culture—from tool use to reveling in Shakespeare, from collaborative hunting to hip-hop. The archaeological record suggests that this "great leap forward"—the beginnings of human culture—began about 50,000 years ago. But human brains underwent no growth spurt then; indeed, they have been roughly their present size for about 200,000 years. So what changed? Ramachandran and others speculate that the change was a genetic adaptation that gave key neurons the mirroring capacity they now hold, paving the way for accelerating advances in understanding, communication and learning. For the first time, information could be spread, built on and modified to create the intellectual and social dynamic of culture.

Mirror neurons do not always reflect on us kindly, of course. For example, they may be implicated in the influence of violent video games. Initial studies by Iacoboni suggest that such games reinforce, at a basic neuronal level, an association of pleasure and accomplishment with inflicting harm—an impetus that society would not want to encourage. Iacoboni speculates that the strength of mirror neurons may be such that imitative violence, if reinforced, may be harder to resist than we would like to think. The power of mirror-neuron systems, Iacoboni says, "suggests that imitative violence may not always be a consciously mediated process"—that is, not so easily subject to our control.

Work on mirror neurons has greatly accelerated in the past five years and seems sure to upshift even more. Whether Rizzolatti, Fogassi and Gallese's breakthrough of 1996 will turn out to be as big as James D. Watson and Francis Crick's 1953 discovery of DNA remains to be seen. Yet mirror neurons already constitute one of the richest areas in neuroscience, both intellectually and experimentally. If their enormous explanatory power is backed by more robust results, they might indeed become regarded as the DNA of neuroscience. In the meantime, mirror neurons explain some intriguing wonders. My son Nicholas is now four years old, which is advanced enough to enable him to stick his tongue out at me of his own accord. I have no idea where he learned such a thing. But at least I know how. M

(Further Reading)

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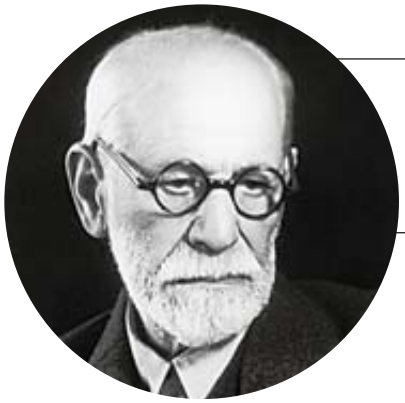
- **How Mimicry Begat Culture.** Beth Azar in *Monitor on Psychology,* Vol. 36, No. 9, pages 54–57; October, 2005. Available at **www.apa.org/monitor/oct05/mimicry.html**
- **From Monkey-Like Action Recognition to Human Language: An Evolutionary Framework for Neurolinguistics.** Michael Arbib in *Behavioral and Brain Sciences,* Vol. 28, pages 105–167; 2005.



Freud Returns

The founder of psychoanalysis

was born 150 years ago, and in 2006 his theories are enjoying a rebirth. New life indeed, because not too long ago his ideas were considered dead.

For the first half of the 1900s, Sigmund Freud's explanations dominated views of how the human mind works. His basic proposition was that our motivations remain largely hidden in our unconscious minds. Moreover, they are actively withheld from consciousness by a repressive force. The executive apparatus of the mind (the ego) rejects any unconscious drives (the id) that might prompt behavior that would be incompatible with our civilized

GETTY IMAGES

Neuroscientists are finding that their biological descriptions of the brain may fit together best when integrated by psychological theories that Freud sketched a century ago

By Mark Solms

conception of ourselves. This repression is necessary because the drives express themselves in unconstrained passions, childish fantasies, and sexual and aggressive urges.

Mental illness, Freud said until his death in 1939, results when repression fails. Phobias, panic attacks and obsessions are caused by intrusions of the hidden drives into voluntary behavior. The aim of psychotherapy, then, was to trace neurotic symptoms back to their unconscious roots and expose these roots to mature, rational judgment, thereby depriving them of their compulsive power.

As mind and brain research grew more sophisticated from the 1950s onward, however, it became apparent to specialists that the evidence Freud had provided for his theories was rather tenuous. His principal method of investigation was not controlled experimentation but simple observations of patients in clinical settings, interwoven with theoretical inferences. Drug treatments gained ground, and biological approaches to mental illness gradually overshadowed psychoanalysis. Had Freud been alive, he might even have welcomed this turn of events. A highly regarded neuroscientist in his day, he frequently made remarks such as "the deficiencies in our description would presumably vanish if we were already in a position to replace the psychological terms by physiological and chemical ones." But Freud did not have the science or technology to know how the brain of a normal or neurotic personality was organized.

By the 1980s the notions of ego and id were considered hopelessly antiquated, even in some psychoanalytic circles. Freud was history. In the new psychology, the updated thinking went, depressed people do not feel so wretched because

Patients may no longer lie on a couch, but many of today's psychological counseling practices stem from Freud's early techniques.

TOM STEWART *Corbis*

something has undermined their earliest attachments in infancy—rather their brain chemicals are unbalanced. Psychopharmacology, however, did not deliver an alternative grand theory of personality, emotion and motivation—a new conception of "what makes us tick." Without this model, neuroscientists focused their work narrowly and left the big picture alone.

Today that picture is coming back into focus, and the surprise is this: it is not unlike the one that Freud outlined a century ago. We are still far from a consensus, but an increasing number of diverse neuroscientists are reaching the same conclusion drawn by Eric R. Kandel of Columbia University, the 2000 Nobel laureate in physiology or medicine: that psychoanalysis is "still the most coherent and intellectually satisfying view of the mind."

Freud is back, and not just in theory. Interdisciplinary work groups uniting the previously divided and often antagonistic fields of neuroscience and psychoanalysis have been formed in almost every major city of the world. These networks, in turn, have come together as the International Neuro-Psychoanalysis Society, which organizes an annual congress and publishes the successful journal *Neuro-Psychoanalysis*. Testament to the renewed respect for Freud's ideas is the journal's editorial advisory board, populated by a who's who of experts in contemporary behavioral neuroscience, including Antonio R. Damasio, Kandel, Joseph E. LeDoux, Benjamin Libet, Jaak Panksepp, Vilayanur S. Ramachandran, Daniel L. Schacter and Wolf Singer.

Together these researchers are forging what Kandel calls a "new intellectual framework for psychiatry." Within this framework, it appears that Freud's broad brushstroke organization of the mind is destined to play a role similar to the one Darwin's theory of evolution served for molecular genetics—a template on which emerging details can be coherently arranged. At the same time, neuroscientists are uncovering proof for some of Freud's theories and are teasing out the mechanisms behind the mental processes he described.

Unconscious Motivation

When Freud introduced the central notion that most mental processes that determine our everyday thoughts, feelings and volitions occur unconsciously, his contemporaries rejected it as impossible. But today's findings are confirming the existence and pivotal role of unconscious mental processing. For example, the behavior of patients who are unable to consciously remember events that occurred after damage to certain memory-encoding structures of their brains is clearly influenced by the "forgotten" events. Cognitive neuroscientists make sense of such cases by delineating different memory systems that process information "explicitly" (consciously) and "implicitly" (unconsciously). Freud split memory along just these lines.

Neuroscientists have also identified unconscious memory systems that mediate emotional learning. In 1996 at New York University, LeDoux demonstrated the existence under the conscious cortex of a neuronal pathway that connects perceptual information with the primitive brain structures responsible for generating fear responses. Because this pathway bypasses the hippocampus—which generates conscious memories—current events routinely trigger unconscious remembrances of emotionally important past events, causing conscious feelings that seem irrational, such as "Men with beards make me uneasy."

Neuroscience has shown that the major brain structures essential for forming conscious (explicit) memories are not functional during the first two years of life, providing an elegant explanation of what Freud called infantile amnesia. As Freud surmised, it is not that we forget our earliest memories; we simply cannot recall them to consciousness. But this inability does not preclude them from affecting adult feelings and behavior. One would be hard-pressed to find a developmental

neurobiologist who does not agree that early experiences, especially between mother and infant, influence the pattern of brain connections in ways that fundamentally shape our future personality and mental health. Yet none of these experiences can be consciously remembered. It is becoming increasingly clear that a good deal of our mental activity is unconsciously motivated.

Repression Vindicated

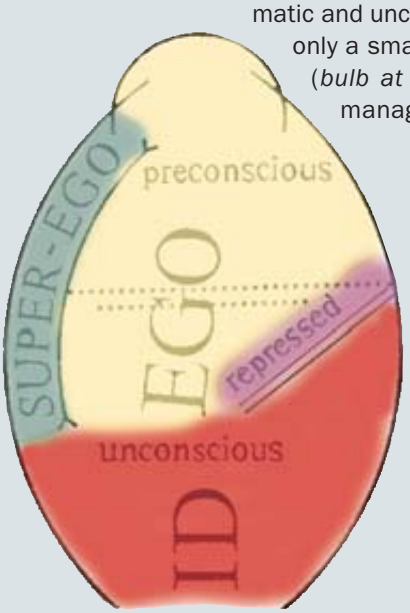
Even if we are mostly driven by unconscious thoughts, this does not prove anything about Freud's claim that we actively repress unpalatable information. But case studies supporting that notion are beginning to accumulate. The most famous one comes from a 1994 study of "anosognosic" patients by Ramachandran, a behavioral neurologist at the University of California, San Diego. Damage to the right parietal region of these people's brains makes them unaware of gross physical defects, such as paralysis of a limb. After artificially activating the right hemisphere of one such patient, Ramachandran observed that she suddenly became aware that her left arm was paralyzed—and that it had been paralyzed continuously since she had suffered a stroke eight days before. This showed that she was capable of recognizing her deficits and that she had unconsciously registered these deficits for the previous eight days, despite her conscious denials during that time that there was any problem.

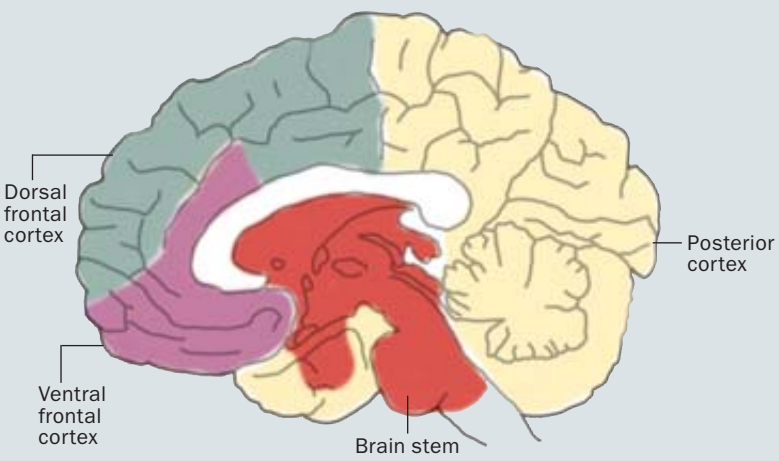
Significantly, after the effects of the stimulation wore off, the woman not only reverted to the belief that her arm was normal, she also forgot the part of the interview in which she had acknowledged that the arm was paralyzed, even though she remembered every other detail about the interview. Ramachandran concluded: "The remarkable theoretical implication of these observations is that memories can indeed be selectively repressed.... Seeing [this patient] convinced me, for the first time, of the reality of the repression phenomena that form the cornerstone of classical psychoanalytical theory."

Like "split-brain" patients, whose hemispheres become unlinked—a situation made famous in studies by Nobel laureate Roger W. Sperry of the California Institute of Technology

Mind and Matter

Freud drew his final model of the mind in 1933 (*below left; color has been added*). Dotted lines represented the threshold between unconscious and conscious processing. The superego repressed instinctual drives (the id), preventing them from disrupting rational thought. Most rational (ego) processes were automatic and unconscious, too, so only a small part of the ego (*bulb at top*) was left to manage conscious experience, which was closely tied to perception. The superego mediated the ongoing struggle between the ego and id for dominance. Recent neurological mapping (*right*) generally correlates to Freud's conception. The core brain stem and limbic system—responsible for instincts and drives—roughly correspond to Freud's id. The ventral frontal region, which controls selective inhibition, the dorsal frontal region, which controls self-conscious thought, and the posterior cortex, which represents the outside world, amount to the ego and the superego.





A. W. FREUD ET AL., BY ARRANGEMENT WITH PATERSON MARSH LTD., LONDON (*left*); OLIVER TURNBULL (*right; all coloring*)

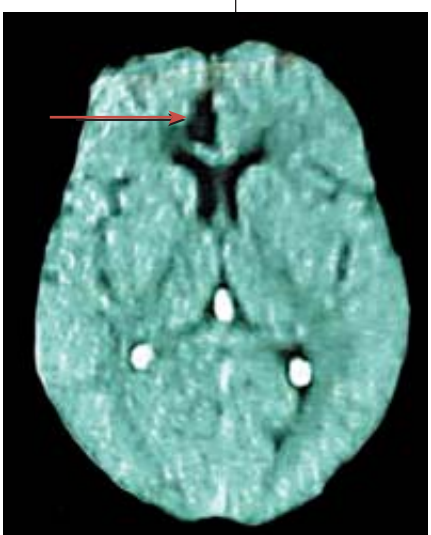
Freud himself anticipated the day when neurological data would round out his psychological ideas.

in the 1960s and 1970s—anosognosic patients typically rationalize away unwelcome facts, giving plausible but invented explanations of their unconsciously motivated actions. In this way, Ramachandran says, the left hemisphere manifestly employs Freudian "mechanisms of defense."

Analogous phenomena have now been demonstrated in people with intact brains, too. As neuropsychologist Martin A. Conway of Durham University in England pointed out in a 2001 commentary in *Nature,* if significant repression effects can be generated in average people in an innocuous laboratory setting, then far greater effects are likely in real-life traumatic situations.

The Pleasure Principle

Freud went even further, though. He said that not only is much of our mental life unconscious and withheld but that the repressed part of the unconscious mind operates according to a different principle than the "reality principle" that governs the conscious ego. This type of unconscious thinking is "wishful"—and it blithely disregards the rules of logic and the arrow of time.



Brain scans show the damage that causes disorders of psychological function, which Freud could study only clinically. A recent MRI image of a patient who confabulates grandiose stories of his life reveals a lesion (*arrow*) in the cingulate gyrus—part of the medial frontal lobe that serves functions Freud posited would normally prevent unconscious wishes from altering a person's rational self-image.

If Freud was right, then damage to the inhibitory structures of the brain (the seat of the "repressing" ego) should release wishful, irrational modes of mental functioning. This is precisely what has been observed in patients with damage to the frontal limbic region, which controls critical aspects of self-awareness. Subjects display a striking syndrome known as Korsakoff's psychosis: they are unaware that they are amnesic and therefore fill the gaps in their memory with fabricated stories known as confabulations.

Durham neuropsychologist Aikaterini Fotopoulou studied a patient of this type in my laboratory. The man failed to recall, in each 50-minute session held in my office on 12 consecutive days, that he had ever met me before or that he had undergone an operation to remove a tumor in his frontal lobe that caused his amnesia. As far as he was concerned, there was nothing wrong with him. When asked about the scar on his head, he confabulated wholly implausible explanations: he had undergone dental surgery or a coronary bypass operation. In reality, he had indeed experienced these procedures—years before—and unlike his brain operation, they had successful outcomes.

Similarly, when asked who I was and what he was doing in my lab, he variously said that I was a colleague, a drinking partner, a client consulting him about his area of professional expertise, a teammate in a sport that he had not participated in since he was in college decades earlier, or a mechanic repairing one of his numerous sports cars (which he did not possess). His behavior was consistent with these false beliefs, too: he would look around the room for his beer or out the window for his car.

What strikes the casual observer is the wishful quality of these false notions, an impression that Fotopoulou confirmed objectively through quantitative analysis of a consecutive series of 155 of his confabulations. The patient's false beliefs were not random noise—they were generated by the "pleasure principle" that Freud maintained was central to unconscious thought. The man simply recast reality as he wanted it to be. Similar observations have been reported by others, such as Conway and Oliver Turnbull of the University of Wales. These investigators are cognitive neuroscientists, not psychoanalysts, yet they interpret their findings in Freudian terms. They claim in essence that damage to the frontal limbic region that produces confabulations impairs cognitive-control mechanisms that underpin normal reality monitoring and releases from inhibition the implicit wishful influences on perception, memory and judgment.

Animal Within

Freud argued that the pleasure principle gave expression to primitive, animal drives. To his Victorian contemporaries, the implication that human behavior was at bottom governed by urges that served no higher purpose than carnal self-fulfillment was downright scandalous. The moral outrage waned during subsequent decades,

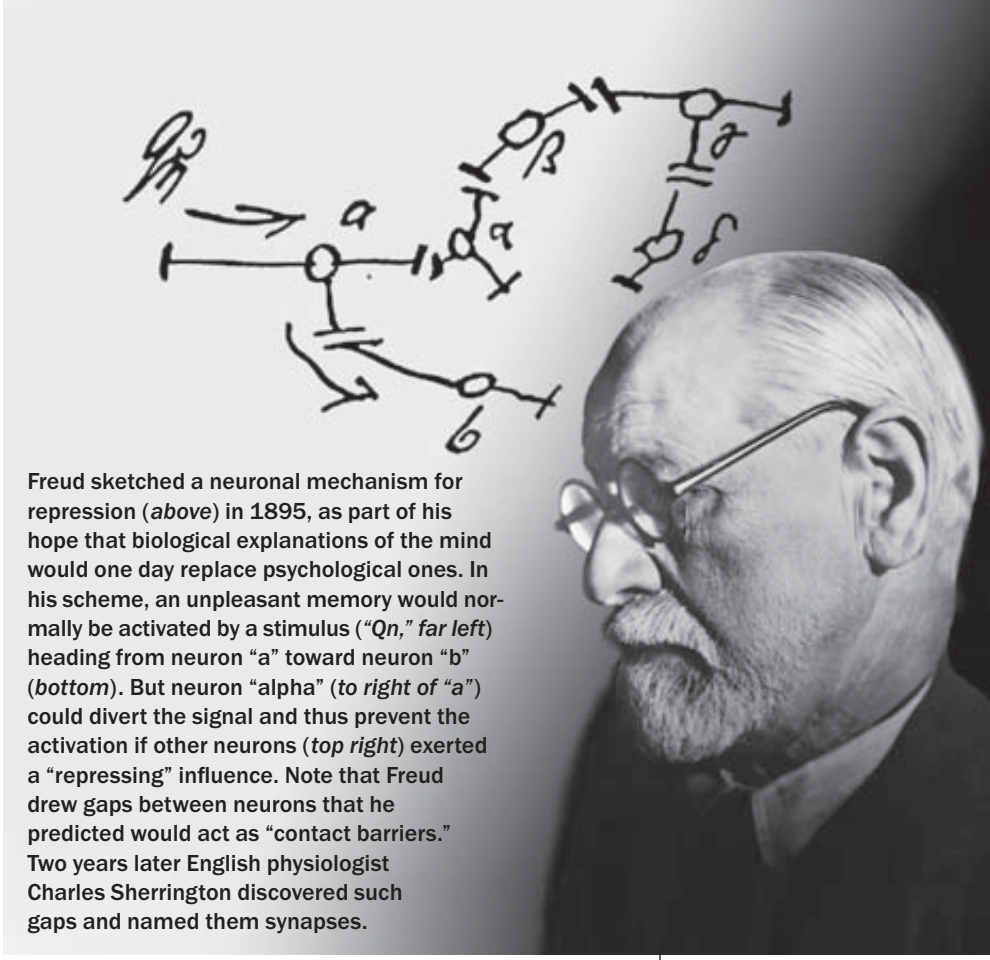
COURTESY OF OLIVER TURNBULL

but Freud's concept of man-as-animal was pretty much sidelined by cognitive scientists.

Now it has returned. Neuroscientists such as Donald W. Pfaff of the Rockefeller University and Panksepp of Bowling Green State University believe that the instinctual mechanisms that govern human motivation are even more primitive than Freud imagined. We share basic emotional-control systems with our primate relatives and with all mammals. At the deep level of mental organization that Freud called the id, the functional anatomy and chemistry of our brains is not much different from that of our favorite barnyard animals and household pets.

Modern neuroscientists do not accept Freud's classification of human instinctual life as a simple dichotomy between sexuality and aggression, however. Instead, through studies of lesions and the effects of drugs and artificial stimulation on the brain, they have identified at least four basic mammalian instinctual circuits, some of which overlap. They are the "seeking" or "reward" system (which motivates the pursuit of pleasure); the "anger-rage" system (which governs angry aggression but not predatory aggression); the "fear-anxiety" system; and the "panic" system (which includes complex instincts such as those that govern social bonding). Whether other instinctual forces exist, such as a rough-and-tumble "play" system, is also being investigated. All these systems are modulated by specific neurotransmitters, chemicals that carry messages between neurons.

The seeking system, regulated by dopamine, bears a remarkable resemblance to the Freudian "libido." According to Freud, the libidinal or sexual drive is a pleasure-seeking system that energizes most of our goal-directed behavior. Modern research shows that its neural equivalent is heavily implicated in almost all forms of craving and addiction. It is interesting to note that Freud's early experiments with cocaine—mainly on himself—convinced him that the libido must have a specific neurochemical foundation. Unlike his successors, Freud saw no reason for antagonism between psychoanalysis and psychopharmacology. He enthusiastically anticipated the day when "id energies" would be controlled directly by "particular chemical substances." Today treatments that integrate psychotherapy with psychoactive medications are widely recognized as the best approach for many disorders. And brain imaging shows that some talk therapy affects the brain in similar ways to such drugs.



Freud sketched a neuronal mechanism for repression (*above*) in 1895, as part of his hope that biological explanations of the mind would one day replace psychological ones. In his scheme, an unpleasant memory would normally be activated by a stimulus (*"Qn," far left*) heading from neuron "a" toward neuron "b" (*bottom*). But neuron "alpha" (*to right of "a"*) could divert the signal and thus prevent the activation if other neurons (*top right*) exerted a "repressing" influence. Note that Freud drew gaps between neurons that he predicted would act as "contact barriers." Two years later English physiologist Charles Sherrington discovered such gaps and named them synapses.

BETTMANN/CORBIS (*photograph*); A. W. FREUD ET AL., BY ARRANGEMENT WITH PATERSON MARSH LTD., LONDON (*drawing*)

Dreams Have Meaning

Freud's ideas are also reawakening in sleep and dream science. His dream theory—that nighttime visions are partial glimpses of unconscious wishes—was discredited when rapid eye movement (REM) sleep and its strong correlation with dreaming were discovered in the 1950s. Freud's view appeared to lose all credibility when investigators in the 1970s showed that the dream cycle was regulated by the pervasive brain chemical acetylcholine. REM sleep occurred automatically, every 90 minutes or so, and was driven by brain chemicals and structures that had nothing to do with emo-

(The Author)

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tion or motivation. This discovery implied that dreams had no meaning; they were simply stories concocted by the higher brain to try to reflect the random cortical activity caused by REM.

But more recent work has revealed that dreaming and REM sleep are dissociable states, controlled by distinct, though interactive, mechanisms. Dreaming turns out to be generated by the forebrain's instinctual-motivational circuitry. This discovery has given rise to a host of theories about the dreaming brain, many strongly reminiscent of Freud's. Most intriguing is the observation that others and I have made that dreaming stops completely when certain fibers deep in the frontal lobe have been severed—a symptom that coincides with a general reduction in motivated behavior. The lesion is the same as the damage that was deliberately produced in prefrontal leukotomy, an outmoded surgical procedure once used to control hallucinations and delusions. This operation was replaced in the 1960s by drugs that dampen dopamine's activity in the same brain systems. The seeking system, then, might be the primary generator of dreams. This possibility has become a major focus of current research.

If the hypothesis is confirmed, then the wish-fulfillment theory of dreams could once again set the agenda for sleep research. But even if other interpretations of the new neurological data prevail, all of them demonstrate that "psychological" conceptualizations of dreaming are scientifically respectable again. Few neuroscientists still claim—as they once did with impunity—that dream content has no primary emotional mechanism.

Finishing the Job

Not everyone is enthusiastic about the reappearance of Freudian concepts in mental science. It is not easy for the older generation of psychoanalysts, for example, to accept that their junior colleagues now can and must subject conventional wisdom to an entirely new level of biological scrutiny. But an encouraging number of elders on both sides of the Atlantic are at least committed to keeping an open mind.

For older neuroscientists, resistance to the return of psychoanalytical ideas comes from the specter of the seemingly indestructible edifice of Freudian theory in the early years of their careers. They cannot acknowledge even partial confirmation of Freud's fundamental insights; they demand a complete purge [*see box on opposite page*]. In the words of J. Allan Hobson, a renowned sleep researcher and Harvard Medical School psychiatrist, the renewed interest in Freud is little more than unhelpful "retrofitting" of modern data into an antiquated theoretical framework. But as Fred Guterl wrote in a 2002 interview with Panksepp in *Newsweek* magazine, for neuroscientists who are enthusiastic about the reconciliation of neurology and psychiatry, "it is not a matter of proving Freud wrong or right, but of finishing the job."

If that job can be finished—if Kandel's "new intellectual framework for psychiatry" can be established—then the time will pass when people with emotional difficulties have to choose between the talk therapy of psychoanalysis, which may be out of touch with modern evidence-based medicine, and the drugs prescribed by psychopharmacology, which may lack regard for the relation between the brain chemistries it manipulates and the complex real-life trajectories that culminate in emotional distress. The psychiatry of tomorrow promises to provide patients with help that is grounded in a deeply integrated understanding of how the human mind operates.

Whatever undreamed-of therapies the future might bring, patients can only benefit from better knowledge of how the brain really works. As modern neuroscientists tackle once more the profound questions of human psychology that so preoccupied Freud, it is gratifying to find that we can build on the foundations he laid, instead of having to start all over again. Even as we identify the weak points in Freud's far-reaching theories, and thereby correct, revise and supplement his work, we are excited to have the privilege of finishing the job. M

> If scientists can reconcile neurology and psychology, patients could receive more integrated treatment.

(Further Reading)

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Freud Returns? Like a Bad Dream

BY J. ALLAN HOBSON

Sigmund Freud's views on the meaning of dreams formed the core of his theory of mental functioning. Mark Solms and others assert that modern science is now validating Freud's conception of the mind. But similar scientific investigations show that major aspects of Freud's thinking are probably erroneous.

For Freud, the bizarre nature of dreams resulted from an elaborate effort of the mind to conceal, by symbolic disguise and censorship, the unacceptable instinctual wishes welling up from the unconscious when the ego relaxes its prohibition of the id in sleep. But most neurobiological evidence supports the alternative view that dream bizarreness stems from normal changes in brain state. Chemical mechanisms in the brain stem, which shift the activation of various regions of the cortex, generate these changes. Many studies have indicated that the chemical changes determine the quality and quantity of dream visions, emotions and thoughts. Freud's disguise-and-censorship notion must be discarded; no one believes that the ego-id struggle, if it exists, controls brain chemistry. Most psychoanalysts no longer hold that the disguise-censorship theory is valid.

Without disguise and censorship, what is left of Freud's dream theory? Not much—only that instinctual drives could impel dream formation. Evidence does indicate that activating the parts of the limbic system that produce anxiety, anger and elation shapes dreams. But these influences are not "wishes." Dream analyses show that the emotions in dreams are as often negative as they are positive, which would mean that half our "wishes" for ourselves are negative. And as all dreamers know, the emotions in dreams are hardly disguised. They enter into dream plots clearly, frequently bringing unpleasant effects such as nightmares. Freud was never able to account for why so many dream emotions are negative.

Another pillar of Freud's model is that because the true meaning of dreams is hidden, the emotions they reflect can be revealed only through his wild-goose-chase method of free association, in which the subject relates anything and everything that comes to mind in hopes of stumbling across a crucial connection. But this effort is unnecessary, because no such concealment occurs. In dreams, what you see is what you get. Dream content is emotionally salient on its face, and the close attention of dreamers and their therapists is all that is needed to see the feelings they represent.

DUSAN PETRICIC

Solms and other Freudians intimate that ascribing dreams to brain chemistry is the same as saying that dreams have no emotional messages. But the statements are not equivalent. The chemical activation-synthesis theory of dreaming, put forth by Robert W. McCarley of Harvard Medical School and me in 1977, maintained only that the psychoanalytic explanation of dream bizarreness as concealed meaning was wrong. We have always argued that dreams are emotionally salient and meaningful. And what about REM sleep? New studies reveal that dreams can occur during non-REM sleep, but nothing in the chemical activation model precludes this case; the frequency of dreams is simply exponentially higher during REM sleep.

Psychoanalysis is in big trouble, and no amount of neurobiological tinkering can fix it. So radical an overhaul is necessary that many neuroscientists would prefer to start over and create a neurocognitive model of the mind. Psychoanalytic theory is indeed comprehensive, but if it is terribly in error, then its comprehensiveness is hardly a virtue. The scientists who share this view stump for more biologically based models of dreams, of mental illness, and of normal conscious experience than those offered by psychoanalysis.

J. Allan Hobson, professor of psychiatry at Harvard Medical School, has written extensively on the brain basis of the mind and its implications for psychiatry. For more, see Hobson's book Dreaming: An Introduction to the Science of Sleep *(Oxford University Press, 2003).*

(FREUD at 150)
Original Ideas

Neurotic about Neurons

Scientists today are using the latest imaging technologies to investigate Sigmund Freud's most fundamental tenets: that dreams represent unfulfilled wishes, that the three parts of the psyche—the ego, id and superego—have neuronal bases, and that "talk therapy" changes the physical networks of neurons in the brain. The fact that such work is happening at all represents an apparent comeback for psychoanalysis [see "Freud Returns," by Mark Solms, on page 28]. No one would be happier than Freud himself. Although his followers like to think of his work as pure psychology, the young Freud built his theories on his own detailed investigation of animal and human brains. To him, every mental illness stemmed from a physical defect in the brain.

GETTY IMAGES

Freud's theories sprang directly from neuroscience, until he began interrogating sexually frustrated women

By Steve Ayan

His point of view changed, however, when he began treating women who were diagnosed as being "hysterical." They suffered from what appeared to be suppressed sexual desires. These cases and others prompted him to discard his own model of the brain as a kind of neuronal machine and replace it with a model of the mind as an entity driven by secret desires. Freud constructed his fantastic theories of dreaming, repression, and ego and id based on years of listening to troubled patients tell of their woes while lying on his office couch—a career move from the brain lab motivated primarily by Freud's need to make enough money to support his rapidly expanding family. And yet in his final writings, he acknowledged his own repressed hope that one day science would recast his maxims in neurology.

Rooted in Biology

Sigismund Schlomo Freud came into the world on May 6, 1856, as the first of eight children. He was born in Freiberg in the Austro-Hungarian Empire—today the town of Pribor in the Czech Republic. Four years later his mother and father, a wool dealer, moved the family to Vienna for good. The wool business never went well, and like most Eastern European Jewish immigrants the family struggled against anti-Semitism and poverty. Yet the Freuds set great hopes on their firstborn and nurtured his ambitions.

Young Freud, called Sigmund for short, enrolled as a medical student at the University of Vienna in 1873. The place had some of the finest minds in medical education. Among Freud's teachers was Ernst Brücke, a prominent physiologist, and at age 20 Freud entered his lab as an assistant, dedicated to studying the nervous systems of lower animals. His early publications included titles such as "On the Origin of the Posterior Nerve Roots in the Spinal Cord of Ammocoetes."

Neurophysiological research was a new but rising discipline. Brücke was a member of the Berlin Physical Society, whose motto was, "We have pledged ourselves to make this truth known: that within the organism no other forces are at work beyond normal physical-chemical ones." Freud, armed with a dissection knife and a microscope, strived to inform this strictly biological model.

In the summer of 1882—a year after receiving his degree—Freud was engaged to Martha Bernays, who came from a prominent family. The gifted but penniless physician now urgently needed money and status before he could marry Bernays, five years his junior. He wanted to continue in research but saw no prospects for rapid promotion in the university. So that same year he took a position at Vienna General Hospital, where over the next three years he would make rounds in all the important departments, including surgery, internal medicine and psychiatry.

Freud's Journey from Neurology to Psychology

1856
On May 6 Sigismund Schlomo Freud is born in Freiberg, Moravia (today Pribor). In 1860 the family moves to Vienna

Freud's birth house

The 16-year-old with his mother

1867
Karl Marx's *Das Kapital* is published

1873
In the fall the young Freud begins his medical studies at the University of Vienna in Austria. After an unusually long time—eight years as a student—he receives his medical degree, at the age of 25

1875
Wilhelm Wundt begins teaching at the University of Leipzig in Germany, where four years later he will establish the first psychological institute in the world

1856 1867 1873 1875

The psychiatry department was headed by Theodor Meynert, a world-renowned brain researcher and a proponent of the idea of cerebral localization. This school of thought, much in vogue at the time, held that every psychopathological symptom—whether a speech defect, hallucination or mental illness—originated from a physical defect in the brain. An investigator's most important task was to locate such defects during autopsies. Meynert was convinced that psychiatric illness could be traced back to neuronal sources. He was suspicious of any patient's complaint that lacked a recognizable, organic cause; without such evidence, a patient's claim must simply spring from imagination or even be deliberately feigned.

Talk Therapy Begins

During his years with Meynert, Freud became an expert in cerebral localization. But soon his career would take a completely different path. Thanks to a traveling fellowship from his department, he left Vienna in 1885 to spend six months at the Salpêtrière hospital in Paris, where psychiatrist Jean-Martin Charcot was searching for a therapy for a disorder common among women: so-called hysteria.

The victims of hysteria suffered from sudden attacks of paralysis and aphasia (inability to comprehend speech). Some of them babbled as if delirious or became highly aroused sexually. The cause of this odd disorder was obscure, and the usual treatments—hydrotherapy or massage—seldom helped. So the charismatic Charcot hypnotized his patients and suggested to them that they were, right then and there, experiencing the symptoms. Often the patients acted "hysterical," but once they were awakened from hypnosis they reported feeling improved. Freud was so caught up in Charcot's enthusiasm that he would later name his first son after the French doctor.

As soon as Freud returned to Vienna, he married Bernays, and the couple had six children in rapid succession. To earn enough to feed his growing family, Freud gave up research to become a neurologist in private practice. In 1891 the clan moved to larger quarters in Vienna—a house big enough to accommodate a room to treat patients. They stayed there for almost 50 years, until they had to flee the Nazis in 1938.

Soon after the move Freud furthered his relationship with Joseph Breuer, a physician who was experimenting with hypnosis as treatment for various mental ills. In 1895 the two jointly published *Studies on Hysteria*. This classic book of case studies marked the birth of psychoanalysis. The two doctors explained that hysterical women suffered, above all, from "reminiscences"—fragmentary memories of traumatic events such as sexual abuse—that broke into their conscious minds in the form of anxiety fantasies. This experiential, unconscious process contradicted the then dominant localization theory that every mental illness was traceable to a physical origin.

Freud developed the technique of "free association" as a means to gain access to the repressed memories of hysterical people and of those who exhibited compulsive behavior. Because the content of these memories was generally "hidden" in the unconscious and repressed from breaking

A contemporary painting shows Jean-Martin Charcot hypnotizing a young woman

The famous couch, now a museum exhibit

1885
At the Salpêtrière hospital in Paris, Freud gets to know Jean-Martin Charcot, the French psychiatrist. Charcot's hypnosis of frantic female patients awakens Freud's interest in hysteria and ways to treat it

The bride, Martha

1886
Freud marries Martha Bernays. Over the next 10 years she will bear six children

1879
Albert Einstein is born in Ulm, Germany

1891
Freud moves his family to a larger home in Vienna, at street address Berggasse 19. Freud lives and works there for 47 years, until he and his family flee the Nazis

1895
Together with Joseph Breuer, Freud publishes *Studies on Hysteria*. The case studies in this collection form the cornerstone of psychoanalysis as a treatment method for mental ills

1899
In November, Freud's now famous *The Interpretation of Dreams* appears. The title page shows the date as 1900 to emphasize its historical significance

1879 1885 1886 1891 1895 1899

through to the patients' conscious awareness, Freud told his patients to relax on his couch and challenged them to tell him whatever came into their heads. The analyst noted everyday experiences, dreams and feelings. Even his patients' jokes and casual remarks were sources that could unveil the dramas of the unconscious mind. Freud's postulate was that bringing a neurotic disturbance into conscious discussion through therapy would cause the troubling notion to dissolve, by way of a mechanism he called the "cathartic" effect of psychoanalysis.

Freud's heart was not in treating patients, however. The tedious therapy sessions served above all as a laboratory for the refinement of his theories. Freud readily took the knowledge he obtained and applied it to people in general. As he wrote: "What analytic research originally had in mind was no more than finding the causes of a few pathological mental conditions, but in achieving this we were able to discover relationships of fundamental significance, and thus create a new psychology."

In 1899 Freud laid the foundations of psychoanalytic theory in his book *The Interpretation of Dreams*. The script presented a set of ideas that has influenced modern thought just as strongly as has Darwin's theory of evolution or Einstein's theory of relativity. In later decades Freud would revise, expand and even discard individual ideas within the theory; after World War I he postulated a second source of psychic energy—in addition to the libido—that he called Thanatos, or the "death instinct." The division of the psyche into three interactive parts—the driven id, the moralistic superego and the ego that negotiated between the two—was chiefly delineated in the 1920s. But psychoanalysis persevered.

Dreams marked a complete turn away from neurology, treading purely in psychology. In it, Freud wrote, "We shall wholly ignore the fact that the psychic apparatus concerned is known to us also as an anatomical preparation, and we shall carefully avoid the temptation to determine the psychic locality in any anatomical sense. We shall remain on psychological ground." This position affected not just therapy but research methodology. The interpretation of reported dreams, for instance, had nothing in common with the search for brain injuries or arousal of the central nervous system.

Nevertheless, when it came to the "psychic apparatus," Freud continued, as before, to see both psychological and biological principles at work. This conundrum led him to the heart of the ancient mind-body problem—whether the mind is purely the outcome of neurons firing throughout the nervous system or whether it arises as a higher state. Freud had already imagined resolving it in 1895, when he drafted a report called *Project for a Scientific Psychology*. "The intention," he wrote, "is to furnish a psychology that shall be a natural science: that is, to represent psychic processes as quantitatively determinate states of specifiable material particles, thus making

(The Author)

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The secret "Committee," which set itself the goal of maintaining a pure doctrine of psychology unencumbered by physical brain considerations. From left: Otto Rank, Freud, Karl Abraham, Max Eitington, Sándor Ferenczi, Ernest Jones and Hanns Sachs

C. G. Jung, circa 1904

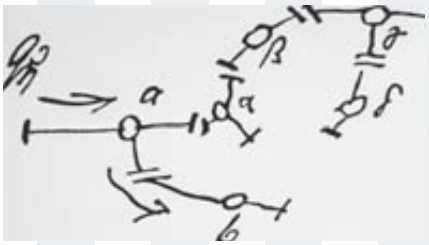

Diagram penned by Freud shows how he thought neurons repressed the flow of memories

1902
The first regular meetings of the Wednesday Psychoanalytic Society begin in Freud's home on Berggasse. From this circle of students, the Vienna Psychoanalytic Society arose in 1908. The first president of the International Psychoanalytic Association, founded in 1910, was C. G. Jung, a doctor from Zurich

1909
Together with Jung and Ferenczi, Freud travels to the U.S., where his talks about psychoanalysis arouse great interest

1913
Freud breaks ranks with Jung, his one-time "crown prince"

1914
World War I begins after the assassination of Archduke Franz Ferdinand, heir to the Austro-Hungarian throne, in Sarajevo

1923
Freud publishes *The Ego and the Id.* The ego mediates between the primal, driven id and the moralistic superego

those processes perspicuous and free from contradiction." The "material particles" were most likely neurons, which were in contact with one another via synapses. What Freud meant by "quantities" was the level of psychic energy flowing through the neurons. The energy arose from arousal either by a sensory organ or—far more important—by the body's own drives. Discharging this energy—in the sex act, for instance—creates pleasure for the individual, whereas blocking its discharge creates displeasure.

Even this terse description makes it clear that Freud's metaphor for the organ of the mind was an electric motor. His psychodynamic model resembles an internal relay station that directs constantly flowing "current" into a complex, highly branched system. Occasionally, in some unknown way, this current quantity was transformed into quality—conscious experience. "Every psychic act begins as an unconscious one," Freud declared in his draft report.

Conflicted

Despite seemingly certain statements, Freud struggled mightily with whether to place his faith in biology or psychology. While working on *Project for a Scientific Psychology* in October 1895, he wrote to his friend Wilhelm Fliess in Berlin: "Everything fell into place, the cogs meshed, and the thing really seemed to be a machine which in a moment would run of itself." Yet just five weeks later he admitted his disappointment: "I no longer understand the state of mind in which I concocted this psychology." At the end, Freud discarded his plan for a neuronal machine, and the unfinished *Project* manuscript disappeared into a drawer.

Freud failed to reconcile the brain and mind because he saw no possibility of finding a neurological basis for distinguishing between conscious and unconscious processes—the magical hub around which his entire psychology revolved. The dead end is not surprising, given that research into brain function was still primitive. No one knew how the brain worked. Wilhelm Waldeyer had just introduced the concept of the neuron in 1891. The big question was whether the dense tissue of the brain was a single, spongelike mass, as Italian physician Camillo Golgi believed, or whether it was made of many tiny units, the concept favored by Spanish histologist Santiago Ramón y Cajal. Golgi developed a staining method that allowed scientists to study thin sections of brain under a microscope. Using it, Ramón y Cajal was able to identify narrow gaps between neuron cell bodies, leading him to the image of a myriad of intercommunicating units in the brain. This advancement brought Golgi and Ramón y Cajal the Nobel Prize in Physiology or Medicine in 1906.

Scientists were also largely in the dark about anatomical brain function. It had been 20 years since losses in certain regions of the mysterious gray organ had been linked to specific pathological symptoms. Paul Broca, a French neuroanatomist, investigated an aphasic who had unusual speech problems. The patient understood most of what was said to him yet could not produce a single intelligible sentence. After the patient died, Broca autopsied his brain and discovered lesions in a part of the left frontal lobe, known today as Broca's area; the ability to produce speech is lo-

Many Austrians hail the union with Nazi Germany in 1938

1930
Freud receives the Goethe Prize, the highest literary award of the Weimar Republic, for his life's work. His mother, Amalia, dies the same year

1933
The National Socialists take power in Germany

1938
In March the Wehrmacht marches into Vienna. In June the Freuds flee the city to London via Paris

On the train to Paris, with daughter Anna, in 1938

1939
Assisted suicide: Freud dies on September 23 of an overdose of morphine, injected by his physician Max Schur at Freud's request. Freud had suffered for many years from exceptionally painful cancer of the jaw

Freud's burial urn in London

1930 1933 1938 1939

KEYSTONE/GETTY IMAGES (*Nazi march*); MARY EVANS PICTURE LIBRARY/SIGMUND FREUD COPYRIGHTS (*Freud and Anna*); GOLDERS GREEN CREMATORIUM, LONDON, U.K./BRIDGEMAN ART LIBRARY (*urn*)

cated there. Broca's German colleague, Carl Wernicke, discovered the neurological seat of speech understanding—a part of the frontal lobe far above Broca's area; a patient with damage there cannot understand even the simplest speech but can still produce grammatically correct, though often meaningless, sentences.

Few other anatomical associations had been found by 1895, however. Physicians hoped every one of the gyri and sulci—the characteristic hills and valleys of the cerebral cortex—might be charted according to its function, but Freud was skeptical. What would that say about the psychic events taking place within them? His answer: Nothing. "We know two things concerning what we call our psyche or mental life: firstly, its bodily organ and scene of action, the brain (or nervous system) and secondly, our acts of consciousness, which are immediate data and cannot be more fully explained by any kind of description. Everything that lies between these terminal points is unknown to us, and, so far as we are aware, there is no direct relation between them. If it existed, it would at the most afford an exact localization of the processes of consciousness and would give us no help toward understanding them."

These words are found in the opening of *An Outline of Psychoanalysis,* Freud's last work, which he began shortly before his death in 1939. Here again Freud collected the most important points of his psychology. "The phenomena with which we have had to deal do not belong to psychology alone; they have an organic and biological side as well.... We have adopted the hypothesis of a psychic apparatus extended in space, appropriately constructed, developed by the exigencies of life, which gives rise to the phenomena of consciousness only at one particular point and under certain conditions. This hypothesis has put us in a position to establish psychology on foundations similar to those of any other science."

Was Freud's flirtation with biology no more than a "self-misunderstanding," as philosopher Jürgen Habermas wrote? Or did it merely serve as a pretext he used to endow his teachings with the prestige of science? There is a great deal of evidence that Freud did believe that psychoanalysis would, one day, have empirical foundations.

Some experts today are indeed attempting to lay the groundwork of "neuropsychoanalysis." Modern neuroscience, they claim, possesses the necessary methods and findings to support Freud's assumptions. Yet Freud himself realized that the converse might be true: "Biology is truly a land of unlimited possibilities. We may expect it to give us the most surprising information, and we cannot guess what answers it will return in a few dozen years to the questions we have put to it. They may be of a kind that will blow away the whole of our artificial structure of hypothesis." M

(Further Reading)

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Psychotherapy on Trial

In the past half a century psychotherapy research has blossomed, with thousands of studies confirming its positive effects for a wide array of clinical problems, including depression, anxiety, eating disorders and sexual dysfunction. Yet in recent years, intense controversy over whether and how to put these findings into practice has erupted, further widening the "scientist-practitioner gap," the deep gulf that has separated many researchers and psychotherapists for decades.

The current debate centers on the growing use of empirically supported therapies, or ESTs, which are specific therapies for specific problems—for example, depression

Empirically supported therapies seek to bring the power of research-proven techniques to the therapist's office. So why are they controversial?

By Hal Arkowitz and Scott O. Lilienfeld

and bulimia—that meet certain criteria (such as a given number of well-designed studies showing positive effects) for treatment efficacy. Proponents have welcomed ESTs for their clear guidelines on what works for patients and their explicit manuals prescribing administration of treatment. Critics have sharply questioned ESTs on a number of grounds, namely, whether their research base is adequate, whether their one-size-fits-all approach can address the needs of individual patients, and whether their focus should be primarily alleviation of symptomatic distress or changes in underlying dispositions and vulnerabilities.

The debate's resolution bears important implications for treatments that psychotherapy patients seek and receive. A survey of nearly 10,000 adults published in 2005 showed that one out of four Americans meets the criteria for a diagnosis of a psychological disorder in any given year and that slightly less than half of all people in the U.S. will suffer from a psychological disorder over the course of their lifetimes [see "Half Are Mentally Ill," by Jamie Talan, Head Lines; *Scientific American Mind,* Vol. 16, No. 3; 2005].

Before we wrote this article, one of us (Arkowitz) had been highly critical of ESTs (though not of placing psychotherapy on a more scientific basis). The other one of us (Lilienfeld) had been a strong advocate of ESTs. Ultimately we found considerable common ground on many points regarding the proper role of research in informing clinical practice. In this feature, we hope to offer a modest step toward reconciling opposing views on ESTs.

Laying the Groundwork

Fifty years ago the foundations of modern psychotherapy research were just being laid. One

How We Can Be Fooled

A variety of factors can lead unwary clinicians and researchers to conclude that a useless psychotherapy is in fact effective. These factors help to explain why psychotherapy research is necessary.

Spontaneous remission	Some psychotherapy clients may become better on their own
Placebo effects	Improvement results from the mere expectation of improvement
Regression to the mean	Extreme scores tend to become less extreme over time
Initial misdiagnosis	Some clients diagnosed with a mental disorder may either have no disorder at all or have a milder disorder
Multiple-treatment interference	Clients often obtain other types of treatment at the same time
Demand characteristics	Some clients may report what they believe their therapists want to hear, resulting in overly positive reports of improvement
Selective attrition	Clients who do not benefit from treatment may tend to drop out of psychotherapy, leaving only those clients who do benefit
Effort justification	Clients may feel a need to rationalize the time, energy and money they have expended in psychotherapy

participant at a 1950 conference was being only partially facetious when he commented: "Psychotherapy is an undefined technique applied to unspecified problems with unpredictable outcomes. For this technique we recommend rigorous training."

Just two years later an eminent British psychologist named Hans Eysenck questioned the scientific basis of talk therapy in a landmark paper—asserting that it was no more effective than the absence of treatment. Researchers soon rose to Eysenck's challenge, and thousands of studies over the ensuing decades demonstrated conclusively that psychotherapy does help many patients. But which are the most effective therapies and for which problems? Further studies sought answers.

In 1995 a task force of a division of the American Psychological Association (APA), chaired by Boston University psychologist David H. Barlow, issued the first of several reports that set forth initial criteria for ESTs, along with lists of therapies that met those criteria. The current task force list is widely used today, especially in university settings in which future clinical psychologists are educated [*see box on page 47*].

We should note that the list tells only whether a treatment has been found to work in controlled studies but not necessarily in clinical practice outside the laboratory. Most experiments have examined cognitive-behavioral therapy; psychoanalytic, humanistic and integrative methods have received less research attention [*see box on page 48*]. If a treatment is absent from the list, it means one of two things: either studies have shown that the treatment does not work, or it has not been tested and, therefore, we do not know whether or not it works. Most of the more than 500 "brands" of

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psychotherapy are not on the EST list, because they fall in the second category.

The Case for ESTs

Advocates have advanced three major arguments in favor of a list of efficacious therapies for specific disorders: it protects patients against fringe psychotherapies, it empowers mental health consumers to make appropriate choices for their care, and it aids in training future therapists.

First, in recent years consumers have been beset by a seemingly endless parade of fad therapies of various stripes [*see box on page 49*]. Despite scant scientific support—or sometimes outright debunking—some fringe treatments continue to be used widely. For example, surveys of doctoral-level therapists in the 1990s indicated that about one quarter regularly employed two or more recovered-memory techniques. Facilitated communication, discredited by scientific research in the 1990s, is still popular in some communities. Counselors who administer crisis debriefing number in the thousands; in the aftermath of the September 11 terrorist attacks, one crisis-debriefing outfit in Atlanta alone dispatched therapists to 200 companies. All these treatments have been found to be ineffective or even harmful. Some studies have discovered that crisis debriefing, for example, increased the risk of post-traumatic stress disorder in trauma-exposed individuals. The EST list makes it harder for practitioners who administer these and other questionable techniques to claim that they are operating scientifically.

Second, the EST list benefits patients because by providing them with information regarding which treatments have been proven to work, it puts them in a better position to make good choices for their care. Like the Food and Drug Administration's list of approved medications, the EST list performs a quality-control function. It serves a similar purpose for managed care organizations and health care agencies, which want to make scientifically informed decisions about which treatments should—and should not—be reimbursed. By placing the burden of proof on a treatment's proponents to show that it is efficacious, the EST list helps to ensure that therapies promoted to the general public have met basic standards.

Third, the EST list can improve the education and training of graduate students in clinical psychology, social work and other mental health fields. The sprawling psychotherapy research literature is often confusing and contradictory; without such a list, novice clinicians have no clear research guidance concerning which treatments to administer and which to avoid.

The Case against ESTs

Critics have responded with four concerns: EST research findings may not apply to psychotherapy as practiced in the "real world"; the list may be biased toward cognitive-behavioral therapies; the EST view of psychotherapy is narrow; and techniques emphasized by such lists may not be the key ingredients of therapeutic change.

First, critics have attacked ESTs for both the science underlying their "empirical support" and their applicability to clinical practice. "The move to worship at the altar of these scientific treatments has been destructive to clients in practice, because the methods tell you very little about how to read the real and complex people who actually come in for therapy," said psychiatrist Glen O. Gabbard of the Baylor College of Medicine in a 2004 *New York Times* article.

To satisfy requirements for good research, which seeks to eliminate any variables that could confound the results, investigators must sacrifice a great deal of what practicing psychotherapists believe is important. EST manuals often sharply constrain therapists' flexibility to tailor the treatments to clients' needs, resulting in a one-size-fits-all approach. Researchers reject up to 90 percent of subjects who are initially recruited, in the name of ensuring a "pure" group with the diagnosis of interest. As a result, participants in these studies typically represent only a small percentage of those who might be seen in actual practice.

The all-or-none nature of the EST list also has been criticized. By categorizing treatments as either empirically supported or not, the list omits potentially useful information, such as the degree of efficacy of different EST therapies. Further, many of the ESTs have modest or even rela-

Many therapies leave clients slightly better or not helped at all. Can we call them "empirically supported"?

tively weak effects. That is, they leave many clients slightly improved or not helped at all, with a high likelihood of relapse. Is it reasonable to call such therapies "empirically supported"?

In 2001 psychotherapy researchers Drew Westen, now at Emory University, and Catherine M. Novotny, now at the Department of Veterans Affairs Medical Center in San Francisco, published an analysis of a large number of efficacy studies for depression and some anxiety disorders. Most of the therapies they examined were variants of cognitive-behavioral therapy. Their findings revealed a glass that is both half-full and half-empty.

Third, ESTs focus almost exclusively on symptoms and distress to the exclusion of other important factors that lead people to seek therapy. These considerations include predispositions, vulnerabilities and personality characteristics that often persist after the symptoms are gone. Many psychotherapists believe that it is important to focus on these types of problems in therapy, in order to enhance the quality of the client's life and help reduce the chances of a relapse. The emphasis of ESTs on standardized techniques similarly ignores not only the uniqueness of individuals but also the salutary power of the therapist-client relationship.

The EST movement has placed evidence-based practice squarely on the agenda of clinical psychology.

On the positive side, they learned that 51 percent of depressed clients and 63 percent of those with panic disorder were significantly better or no longer had symptoms. But the glass seems emptier if we recognize that many patients who had improved still exhibited symptoms at the end of treatment and that others were not helped at all. If we include people who dropped out of therapy, the success percentages plunge considerably. In addition, follow-up studies reveal high rates of relapse. For example, only 37 percent of those depressed clients who completed treatment remained improved one to two years later.

Second, some critics have argued that EST therapies are biased in favor of cognitive-behavioral techniques. Reviews of research on psychoanalytic and humanistic therapies suggest positive effects broadly comparable to those of cognitive-behavioral therapies. Although less research has been conducted on these therapies than on cognitive-behavioral therapy, their underrepresentation on EST lists raises questions of bias.

Fourth, the techniques emphasized by the EST list may not be what produces change in many cases. Most studies comparing the efficacy of two or more therapies find that they all do about equally well. This surprising result is termed the "Dodo Bird verdict," after the Dodo Bird in *Alice's Adventures in Wonderland,* who declares (following a race) that "everybody has won and all must have prizes." Psychotherapy researchers intensely debate the meaning of the Dodo Bird verdict. Some argue that actual important differences exist among therapies but that problems with study design have masked them. Such problems include small samples and the limited range of therapies that have been compared. It is also possible that although average outcomes of various therapies may not differ, some clients may do better with one therapy, whereas other clients may do better with another.

Still other researchers have accepted the Dodo Bird verdict and attempted to account for it. One explanation suggests that therapeutic change is caused more by "common factors" that therapies share rather than by specific techniques. Such factors include instilling hope and providing a believable theoretical rationale with associated therapeutic "rituals," which can make clients feel that they are taking positive action to solve their problems. This perspective also emphasizes the healing power of the therapist-patient relationship.

Future Directions

The EST movement has succeeded in placing the importance of evidence-based practice

(The Authors)

HAL ARKOWITZ and SCOTT O. LILIENFELD hope to bring some insights to the contentious discussion surrounding empirically supported therapies. Arkowitz, associate professor of psychology at the University of Arizona, has served as editor of the *Journal of Psychotherapy Integration.* He has received two awards from the Arizona State Psychological Association for distinguished contributions to the practice of psychology and distinguished contributions to the science of psychology. Lilienfeld, associate professor in the department of psychology at Emory University, is former president of the Society for a Science of Clinical Psychology and editor of *Scientific Review of Mental Health Practice.*

Research-Supported Therapies

Below are selected therapies deemed "empirically supported" by the American Psychological Association Division 12 Committee.

THERAPY AND PROBLEM	DESCRIPTION OF THERAPY
Behavior therapy for depression	■ Monitor and increase positive daily activities ■ Improve communication skills ■ Increase assertive behaviors ■ Increase positive reinforcement for nondepressed behaviors ■ Decrease negative life stresses
Cognitive-behavior therapy for depression	■ Teach clients to identify, reevaluate and change overly negative thinking associated with depressed feelings ■ Conduct between-session experiments to test thoughts for accuracy ■ Monitor and increase daily activities
Interpersonal therapy for depression	■ Help clients identify and resolve interpersonal difficulties associated with depression
Cognitive-behavior therapy for bulimia	■ Teach ways to prevent binge eating and create alternative behaviors ■ Develop a plan for a regular pattern of eating ■ Support skills to deal with high-risk situations for binge eating and purging ■ Modify attitudes toward eating and one's physical appearance
Cognitive-behavior therapy for panic disorder	■ Induce panic attacks during sessions to help clients perceive them as less "dangerous" (to reassure them that they will not, for example, "go crazy" or die) ■ Introduce breathing retraining to prevent hyperventilation ■ Control exposure to situations that trigger panic attacks

squarely on the agenda of clinical psychology. Because EST lists have many inherent problems, however, they may prove more useful as a catalyst for helping the field move toward scientifically informed practice than they will be as the final word.

Several promising proposals recently have attempted to refine or replace ESTs in ways that retain their emphasis on science-based practice. One comes from the work of University of New Mexico psychologist William R. Miller. Miller constructed a list of all researched therapies for alcoholism, ranking them by the quality of the research and magnitude of the effects. His method provides access to all relevant information about all therapies studied, not just those that meet the all-or-none criteria for inclusion on the EST list.

Others have suggested that we seek empirically based "principles of change" rather than empirically supported therapies. For example, repeated exposure to feared objects and events is a central principle underlying most effective

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Major Approaches to Psychotherapy

More than 500 "brands" of psychotherapy exist. Below is a sampler.

TYPE OF THERAPY	SUBTYPES	VIEW OF CLINICAL PROBLEMS	THERAPY STRATEGIES
Cognitive-behavior	Behavior Cognitive	Result from dysfunctional learning and thinking	Encourage and teach new behaviors; teach people to challenge and correct dysfunctional thinking
Psychoanalytic	Classic Freudian Object relations Self-psychological Relational	Conscious or unconscious psychological conflicts; problems in self-regulation of emotions and impulses; problematic ways of thinking and feeling about the self and others	Help make unconscious processes and conflicts conscious; encourage examination of problematic interpersonal patterns in and out of therapy; teach understanding of how these patterns developed but are no longer adaptive in the present; work to correct these patterns as they are manifested in the therapy relationship
Humanistic-experiential	Client-centered Gestalt Process-experiential Existential	Result from obstacles to the innate growth (self-actualization) processes of being human	Support the client's experience of understanding, caring and empathy, leading to changed views of the self; introduce exercises to provide opportunities that increase awareness of feelings and that facilitate change
Integrative	*Theoretical integration:* Integrating two or more therapies *Systematic eclecticism:* Selecting and matching treatment to the person and problem *Common factors:* Combining the factors that different therapies share	Incorporate all major psychotherapies and ways of understanding clinical problems	Draw from any existing therapy approaches

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We begin to see the outlines of positions that may assuage the concerns of researchers and practitioners.

treatments for anxiety disorders. Therapists can derive many ways of flexibly implementing a principle of change to fit clients without being constrained by a specific technique or manual. In a similar vein, others have recently suggested that we focus on "empirically supported relationship factors," such as therapist empathy and warmth. But there is not yet sufficient agreement concerning which change or relationship principles should qualify as empirically supported.

Another alternative to ESTs was proposed by a committee appointed by past APA president Ronald F. Levant. The concept, which is called evidence-based practice, has been widely embraced in many areas of medicine. In its 2005 policy statement, the APA committee defined evidence-based practice as "the integration of the best available research with clinical expertise in the context of patient characteristics, culture, and preferences."

The term "best available research" is much broader than evidence based on psychotherapy studies alone. It encompasses research across the entire field of psychology, including personality, psychopathology and social psychology. "Clinical expertise" relates to therapist competencies that are not tied directly to research but that are believed to promote positive therapeutic outcomes. These capabilities inform the ability to form therapeutic relationships with clients and to devise and implement treatment plans. Finally, inclusion of client characteristics, culture and preferences points to the importance of tailoring treatments to individuals.

Although this APA report is a noble effort to grapple with some of the controversies, its long-term impact remains unclear. Many EST proponents have been dissatisfied with the recommendation to employ "the best available research" as being so vague, at least compared with the specificity of ESTs, as to be of little value. Many EST advocates have also objected to the inclusion of clinical expertise in a definition of evidence-based practice.

Given the shortcomings of ESTs and the existing alternatives to them, it is clear that the field is just beginning to incorporate science-based practice. Nevertheless, we can begin to see the broad outlines of promising positions that are less dogmatic than earlier ones. Such trends may help assuage the legitimate concerns of both researchers and practitioners. Ultimately we believe that the field must move beyond a narrow definition of ESTs toward views that bridge the gap between researchers and practitioners. After all, whatever their differences may be, aren't all clinical psychologists seeking better ways to help troubled people feel happier and live enriching lives? M

Therapies to Avoid?

A selective sampling of treatments for which there is scant scientific support.

- **Energy therapies**
  Purport to treat clients' anxiety disorders by manipulating their invisible energy fields
- **Recovered-memory techniques**
  Suggestive methods (such as hypnosis, guided imagery, keeping journals) designed to unearth "memories" of early child abuse
- **Rebirthing therapies**
  Claimed to treat adolescents' and younger children's anger by forcing them to reenact the trauma of birth
- **Facilitated communication**
  Said to allow mute autistic children to type sentences on a computer keyboard with the aid of an assistant who guides their hand movements
- **Crisis debriefing**
  Intended to ward off post-traumatic stress disorder in trauma victims by strongly encouraging them to "process" the emotions and memories associated with the anxiety-provoking event, even if they do not feel ready to do so

(Further Reading)

- **The Great Psychotherapy Debate: Models, Methods, and Findings.** Bruce E. Wampold. Lawrence Erlbaum Associates, 2001.
- **Evidence-Based Practices in Mental Health: Debate and Dialogue on the Fundamental Questions.** Edited by John C. Norcross, L. E. Beutler and R. F. Levant. American Psychological Association Press, 2005.

Psychologist Irene Pepperberg with Alex, a parrot that can manipulate many nouns, verbs and numbers.

RICK FRIEDMAN *Corbis*

Bird Brains? Hardly

Parrots demonstrate impressive cognitive feats that rival the talents of chimps and dolphins

By Christine Scholtyssek

The telephone rings. A man hurries through his apartment, picks up the handset and says hello. Yet the ringing continues—because the sound came from the man's pet parrot. The owner shoots the bird a nasty glare as he hangs up, mutters about being fooled again and stalks out of the room.

Scenes like this, used in cartoons and comedies, are based on the fascinating ability of parrots to closely mimic common sounds and human voices. But some cognitive scientists who have spent years working with parrots are convinced that these birds, and others, are capable of much more. According to the experts, the animals can not only understand what we say and respond sensibly, but they can also grasp higher concepts such as "same or different" and the continued existence—or permanence—of objects that are shown and then hidden from view. The implication is that parrots and other avian groups, despite their simple-looking brains, may in some ways be as intelligent as primates and aquatic standouts such as dolphins.

More Than Imitation

For decades, biologists thought instinct alone controlled the behavior of parrots. This view was supported by characteristics of the birds' brains, which, outwardly, appear much simpler than those of mammals [*see illustration on opposite page*]. The animals' talent for producing speech was explained as pure imitation, devoid of any understanding of meaning. In the late 1970s Irene Pepperberg of Purdue University began a long series of experiments that she has continued to this day, now at Brandeis University. Her goal has been to determine, concretely, just how intelligent these birds are. The results are surprising.

Pepperberg first had to solve a fundamental problem: How could she evaluate her feathered subjects? Their ability to mimic the human voice seemed to provide a solution. Human sounds are indeed foreign to the interparrot repertoire, yet it might be possible for the birds to use the sounds to communicate with humans deliberately.

Language acquisition by humans and song learning by birds have much in common. Both are based on the child or chick imitating the behavior of elders, and in both cases the learning requires many repetitions. Pepperberg adapted a training method developed by Dietmar Todt—the Model/Rival Technique—that mirrors the learning behavior of people and birds. A typical session might work in the following way: Two trainers sit on opposite sides of a small table in front of a parrot. Various objects are on the table. The first trainer picks up an item, shows it to the other person and asks her, "What is this?" The partner answers, "Ball. That is a ball." Trainer one then praises trainer two and hands her the ball as a reward. Sometimes, however, trainer two purposely answers incorrectly by saying, for example, "That is a clothespin." Trainer one scolds her and removes the object from view for a few minutes.

The parrot is also queried and is praised or chided according to its answers. If it voices the correct label, it gets to play with the object for a while. In this scheme, trainer two is both a model for the parrot and its rival for attention from trainer one. Once the parrot learns a few words, it can sometimes take over the role of trainer two to teach other birds.

After three decades of lessons, Pepperberg's first subject, a grey parrot named Alex, has acquired a respectable vocabulary and is still going strong (some parrot species can live 60 years). Alex knows labels for about 50 objects, seven colors, five shapes, seven materials, six numbers and even a few verbs.

> Alex and his pals **know the meaning** of "same or different" as well as the notion of "and."

Knowing What "Different" Means

A comprehensive vocabulary, however, is by itself no evidence for higher cognitive functions—just for a good memory. The bigger question is whether parrots understand what they are saying. To find out, Pepperberg has been subjecting Alex, and three other grey parrots that have learned speech in the lab, to numerous experiments. The results collected thus far are clear: the birds understand the meaning of individual words and show higher cognitive abilities.

Pepperberg's parrots, without exception, respond accurately to standard questions such as "What is this?" as well as to questions about an object's shape or color. Alex and his pals, however, have also garnered an understanding of conceptual categories such as color, shape and material. Such an insight is achieved only if the animal realizes that red, green and blue are possible variants of one category of object. Pepperberg's parrots do. Furthermore, they have learned the meaning of "same or different." Show a red triangle and a red circle and ask, "What is same?" and the parrot will respond, "Color." Ask, "What is different?" and the reply will be "Shape." These are remarkable achievements, because the bird must first interpret the question correctly, then identify the right category, and reply with an acoustic signal not used by other parrots. Alex also replies "none" if nothing is the same or different, demonstrating understanding of the concept of absence.

In addition, Alex seems to understand the notion of "and" as well as how to employ it. Given the question "What is rectangular and red?" he can pick the one object with both characteristics

(The Author)

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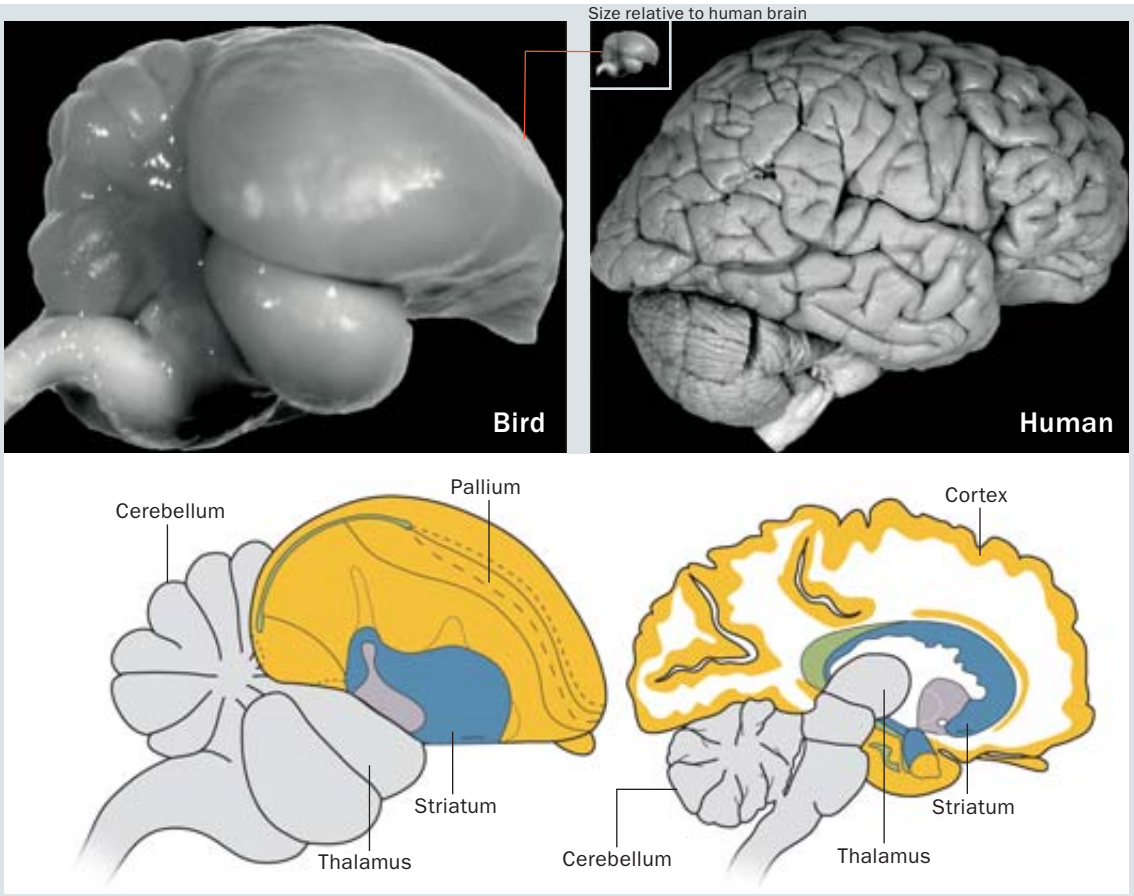
Deceptively Smooth



Anyone who sees an avian brain next to a mammalian brain is struck by two observations: it looks similarly shaped, yet it is much less furrowed. Given the well-known dictum that more convolution means higher cognitive function, most scientists have long assumed that birds have limited mental powers. This opinion was strengthened by the mistaken assumption that the avian cerebrum corresponds to regions in mammalian brains that control "lower" reflexive behaviors.

Recent research is making it clear, however, that the largest part of the avian brain, the pallium, works along with structures below it to control complex behaviors. The larger the pallium, the more intelligent the animal. Among mammals, the cerebral cortex originates in the pallium, and proportionally larger means greater cognitive ability.

Although the nervous systems of the two classes of animals are constructed very differently, they have functional similarities. Many parts of the brain are comparably connected by nerve pathways that have similar functions. For example, when parrots learn to produce new sounds, the structures activated are analogous to those that are activated in humans.

An international research team led by Erich D. Jarvis, a neurologist at Duke University Medical Center, considered this new work when it rewrote the traditional nomenclature describing the regions of the avian brain. The scientists abandoned many of the century-old names and replaced them with new terms (*shown*) that are homologous with corresponding regions in mammals. —*C.S.*

FROM "AVIAN BRAINS AND A NEW UNDERSTANDING OF VERTEBRATE BRAIN EVOLUTION," BY ERICH D. JARVIS ET AL. IN *NATURE REVIEWS NEUROSCIENCE*, VOL. 6; FEBRUARY 2005 (*photographs*); SIGANIM *Gehirn & Geist* (*illustrations*)

from a selection of items. His performance in comparing items is impressive. He can solve questions such as "What color bigger?" (which means "What color is the bigger object?"). The correct reaction makes it obvious that Alex understands the idea of relativity—among a group, which item is bigger.

Quantities are manageable, too. If Alex sees a display with four red balls and three green balls plus five red blocks and six green blocks arranged randomly, he can answer "How many red blocks?" correctly with "Five." Recent data suggest that Alex is counting the larger sets of objects one by one and recognizing the smaller numbers intuitively, at a glance, the way people can.

The grey parrots can even use verbs and com-

Intelligence in the Wild

Alex and his friends exhibit impressive mental feats, but these birds have been living for decades in captivity. What happens among parrots in the wild? The order Psittaciformes, or "parrot," includes a number of long-lived species: macaws can reach an age of 50 or more in the wild, and even little Australian cockatiels live for 10 to 15 years, twice as long as European songbirds of similar sizes. A good memory is virtually essential for such long life spans, because the birds must remember the locations of many different sources of water and food as well as nesting places and mates. Longevity also means there is a high chance that they will experience major environmental changes such as floods or droughts—several times. To survive, they need a certain measure of mental flexibility; the birds must set aside routinized behaviors and recall previous experiences to adapt to new situations.

Almost all parrots live in flocks that, in structure, resemble groups of primates and, accordingly, require high levels of social intelligence. The birds must be able to distinguish among many individuals and interact with each one appropriately, based on previous encounters. Like human couples, mated parrots spend quite a bit of time together even when they are not rearing their young. In some species, the pair may even learn to sing a special song together, a duet in which each bird fills in notes for the other.

The use of tools has also been observed among several parrot species. Male palm cockatoos gnaw off sticks and use them to drum loudly on hollow tree trunks, as a way of marking their territories. Other cockatoo species throw twigs and small stones down at raptors to drive them off.

Parrots play, too. Young mammals learn the behaviors and social talents that they will need for adult survival by cavorting among themselves and exploring their environment, and parrots have a distinctive repertoire of play as well. Australian cockatoos take rides on the whirling blades of windmills, and young keas play together with sticks. These birds are probably capable of learning throughout their lives, constantly expanding their archive of experiences. —*C.S.*

FRANS LANTING *Minden Pictures*

Parrots such as these macaws in Peru have high levels of social intelligence that allow them to live successfully in large flocks.

bine them with different objects. For example, one will say, "Want apple" or "Want go chair." The trainers grant these wishes so that the birds experience the consequences of their utterances. Here, too, the parrots evidently understand what they say. If Pepperberg hands over the wrong object, the parrot will reject it by saying, "No," and then repeat the original request. If brought to the wrong place, the bird will refuse to hop off the trainer's arm and will reiterate the demand.

Another example of abstract thinking is the so-called object permanence problem—the realization that an object continues to exist even when it changes position or can no longer be seen. This basic concept in understanding one's environment is not as straightforward as it may seem. Among humans, this ability develops only gradually during the first year of a baby's life.

Adult dogs, cats and pigeons possess a rudimentary idea of object permanence, but it is much less powerful than for parrots, apes or humans. They fail, for example, in a shell game. After watching a trainer hide a ball under one of three cups and then move the cups around, the animals are no more successful than chance at indicating which cup still contains the ball. Some adult primates and parrots, however, do about as well as mature humans. Studies of young parrots reveal that object permanence develops in stages tied to the development of specific brain regions.

Give Me a Banerry

Over the years the researchers have been continually surprised by their subjects' abilities. Alex, who has lived the longest in Pepperberg's lab, is the master. Several times he has invented useful new terms to describe objects—such as when he was supposed to learn "apple." At that time Alex had already learned the names of several edible fruits, including banana, cherry and grape. He had tasted apples, too, but had never been taught anything about them. One day the trainer picked up an apple and asked, "What is this?" Alex answered, "Banerry," and bit into the fruit. The trainer sought to correct him and repeated "apple" several times, but Alex insisted on "banerry," using the same careful diction the trainer always used when introducing a new word.

From then on, Alex stubbornly applied this term to every apple he saw. Pepperberg will never know for certain what happened inside Alex's brain when he coined the term, but she thinks he combined two words he knew—for banana and cherry. Perhaps apples taste something like bananas to him, and any fruit with red skin would look like a large cherry.

When Alex saw his reflection for the first time, he suddenly asked a trainer, "What color?" while pointing with his head toward the mirror. Alex had been asked this question, though only in reference to colored objects in the lab. The query was not just evidence for his understanding of the concept of color; Alex was transferring the question from a familiar setting to a new one. After the trainer overcame her initial surprise, she told him, "Grey. You are a grey parrot." Alex asked the same question five more times and got the same answer each time. From that day on, "grey" was part of his vocabulary.

Dogs and cats fail at the shell game, but parrots can identify which shell contains the ball.

These examples are clear evidence that parrots—and probably several other types of bird—are not merely bound by instinct. They possess splendid memories and understand complex relations. They can learn an intricate communication system, enjoy robust social lives and be impressively curious. Their intelligence may at least match that of primates and dolphins—which have heretofore been considered the smartest animals—and in some situations may surpass them. Pepperberg's parrots have already passed tests that are considerably more demanding than those completed by mammals.

The study of Alex and his friends is far from concluded. Right now the birds are learning to sound out letters and even to use a specially designed computer. Perhaps someday they will get their own home page or blog, and we will be able to chat with them online. M

(Further Reading)

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- **Avian Brains and a New Understanding of Vertebrate Brain Evolution.** E. D. Jarvis et al. in *Nature Reviews Neuroscience*, Vol. 6, No. 2, pages 151–159; February 2005.
- More details about parrot research are at **www.alexfoundation.org**

Better understanding of how alcohol alters brain chemistry reveals mechanisms for beating dependency

Staying SOBER

By Andreas Heinz

Former alcoholics have a tough time resisting the urge to drink in two particularly trying situations. Analysis of what is happening in their heads under these circumstances is greatly improving neurobiologists' understanding of how chronic alcohol use changes the brain. And their findings suggest measures that could help people abstain.

The following case illustrates one of the most tempting situations. Hank had been dry for several weeks thanks to a radical withdrawal program, but a simple walk past Pete's Tavern on any given night almost erased his will to abstain. During the daytime he did not feel a craving for alcohol, but when he passed the bar in the evening—when he saw the warm light through the windows and heard the glasses clinking—he would be sorely tempted to run inside for a beer. Addiction researchers call this phenomenon "conditioned desire." If a person had always consumed alcohol in the same situation, an encounter with the familiar stimuli will make the feeling of need for the substance almost irresistible. Then, even after years of abstinence, consuming a single drink can set off a powerful longing to imbibe more and more.

Ken's story illustrates the other common temptation. Ken had given up alcohol and was doing fine, even after he had lost his job and had begun collecting unemployment. But on one visit to the unemployment office downtown, a bureaucrat refused to approve his benefits. After a fruitless argument, Ken left. While standing on the subway platform for a train home, he suddenly began to sweat, twitch and feel sick. What he really wanted was a bottle. Before he had given up drinking, he would have automatically taken a swig whenever he faced a tense situation. After the argument, his brain—shaped by experience—expected the calming effect of alcohol. When the drug did not come, he began to suffer what experts call "conditioned withdrawal" symptoms.

PAUL THOMAS *Getty Images (opposite)*; AGE FOTOSTOCK *(above)*

MICHAEL NEMETH *Getty Images*

The very people who can drink others under the table are the ones who are especially at risk.

Conditioned desire and conditioned withdrawal are produced in the brain by different mechanisms. In recent years, neuroscientists have investigated both phenomena thoroughly. They now feel comfortable explaining how routine alcohol consumption changes circuitry in the brain in ways that lead to addiction, and they are beginning to develop new medications that could dramatically reduce the chances of falling off the wagon.

High Tolerance Is Bad

For centuries, societies have labeled alcoholics as self-indulgent people who lack willpower. Although the decision to drink in the first place does rest with each individual, traits inherent in a person's brain cells can strongly influence the slippery slope into addiction. Furthermore, once a person is addicted, simple willpower may be insufficient to break the grip; drugs that can reverse the brain's alcohol-altered chemistry may be necessary.

An individual's sensitivity to alcohol's effects on neurons significantly influences the chance that he or she can become addicted. According to Marc A. Schuckit, a psychiatry professor at the University of California, San Diego, and director of the VA San Diego Healthcare System's Alcohol and Drug Treatment Program, one of the best protections against addiction is nausea; people who readily get sick as they drink are less likely to consume enough, consistently, to the point that they

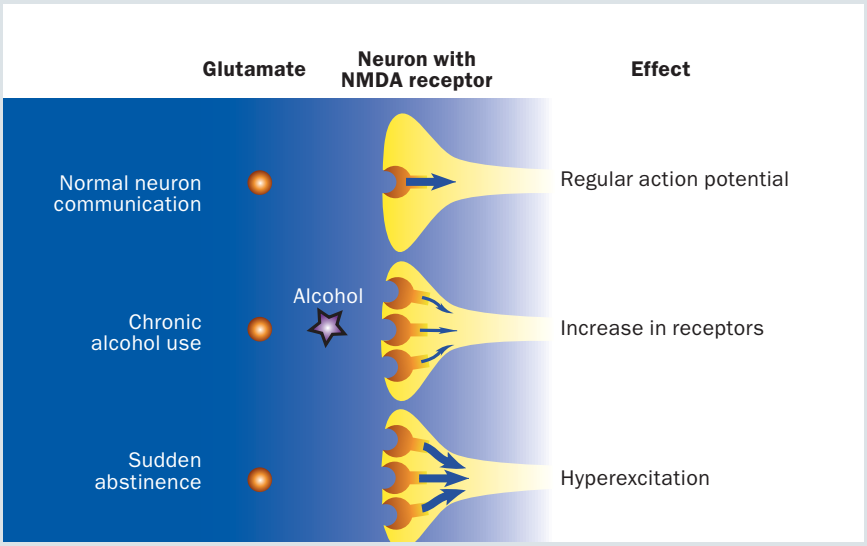
Why Withdrawal Occurs

Glutamate, an amino acid, is one of the most important messenger substances used by the nervous system. Signals in the brain advance along networks of neurons largely because glutamate exits one neuron, crosses a synapse (gap) and enters an adjacent neuron, exciting it so that the signal is forwarded on. The cell membrane of the receiving neuron has NMDA receptors (*brown dot, top*) that bind the incoming glutamate. Binding leads to a flood of sodium and calcium ions inside the neuron (*blue arrow*), setting off an action potential that arouses the cell.

Alcohol blocks the binding of glutamate to NMDA receptors—slowing or stopping the forwarding of messages. To compensate—and raise the chance of capturing glutamate—the number of receptors and their sensitivity are increased (*middle*) in the brains of people who chronically consume alcohol.

Yet if the alcohol supply is interrupted—during a period of abstinence or even during a single night's sleep for the most dependent alcoholics—the receptors continue to be more sensitive, because the brain cannot adjust quickly enough to the new chemical situation. As a result, neurons overreact to glutamate (*bottom*). This hyperexcitatory condition is a major factor leading to withdrawal symptoms such as cramps, unstable blood circulation and anxiety. The excessive activity can also kill off large numbers of neurons—essentially by poisoning them with too many chemicals—causing dementia or lasting damage to the nervous system.

—*A.H.*



become addicted. The very people who can drink others under the table are the ones who are especially at risk. Inhibitory and excitatory messenger substances in the brain become unbalanced in response to excessive alcohol doses. The people who can handle more drinking send more alcohol to the brain, thereby increasing over time the chance that a permanent imbalance will develop.

This brain chemistry was partially worked out in rhesus monkeys that had to grow up without their mothers, some in the laboratory and some in the wild. James Dee Higley, a research psychologist at the National Institute on Alcohol Abuse and Alcoholism, learned that these monkeys reacted less to drinks of high-proof alcohol than normal monkeys did. The motherless monkeys were similarly insensitive to other substances that, like alcohol, increase the impact of the neurotransmitter GABA (gamma aminobutyric acid), which inhibits signals between neurons so the cells do not get overexcited.

As a result of this reduced sensitivity, the rhesus monkeys raised in isolation could drink an unusually large quantity of alcohol—and they sought to do so when researchers provided free access to the drug. Human studies have revealed similar changes in people's brains.

Altered brain chemistry resulting from experience is just one factor that contributes to individual differences in susceptibility. Genes play a role, too. Schuckit maintains that up to half the causal factors for reduced sensitivity to alcohol are inherited. In a small-scale study that tracked people for 15 years, Schuckit's research group found that a variation in the gene that codes for a part of the GABA receptor may be related to low sensitivity to alcohol.

Although high tolerance to alcohol from adjusted brain chemistry or genetics may seem like a protective trait, it is ultimately damning. If such an individual consumes quantities of alcohol reg-

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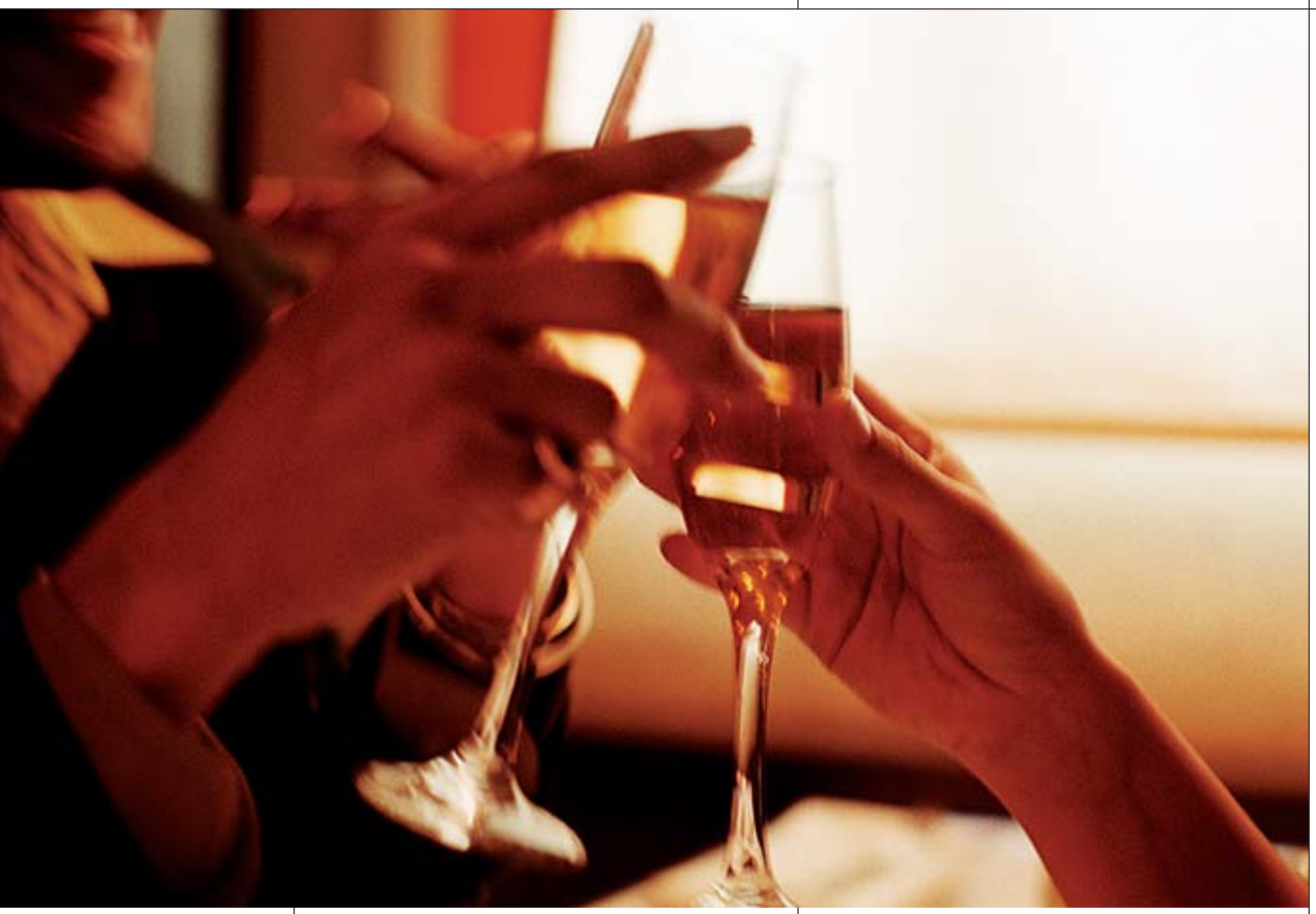
SIGANIM *Gehirn & Geist*



FIRSTLIGHT Getty Images

ularly, his or her brain and body will gradually become accustomed to the poison, almost assuring the person will become addicted.

Dangerous Accommodation

Tinkering with the GABA system could perhaps offer a fix, but alcohol's effects on brain chemistry depend on more than just GABA uptake. The drug does not merely boost the inhibitory function of GABA on neurons; it also blocks the excitatory effects of their NMDA (*N*-methyl-D-aspartate) receptors. These receptors bind glutamate, which comes from neighboring neurons and enables the receiving neuron to forward signals on to others in the network. Guochuan Tsai, now at the University of California, Los Angeles, and Joseph T. Coyle of Harvard Medical School have discovered that the brain, when exposed to chronic alcohol consumption, creates additional NMDA receptors to compensate for the blocking effect [*see box on preceding page*]. The brain is trying to find a new balance between the underexcitatory action of glutamate and the overinhibitory action of GABA.

The repercussions come, however, when alcohol is withdrawn for a few days or, for hard-core drinkers, even overnight. The NMDA receptors maintain their increased sensitivity, and the GABA receptors maintain their reduced sensitivity. Yet without the alcohol that this new balance is attempting to counter, the brain's networks fire erratically, causing withdrawal symptoms. Anyone who wakes up with tremors, sweating or nausea and immediately needs alcohol is already critically dependent. The victim's brain is so utterly adapted to the drug that even the few nighttime hours without it are enough to throw the new chemistry into a tailspin.

Such withdrawal symptoms can be combated with agents such as chlormethiazol or a benzodiazepine, which restore the sensitivity of GABA receptors and calm the patient. Acamprosate suppresses NMDA receptors and seems especially helpful for persons suffering from conditioned withdrawal. Clinical studies show that 30 to 40 percent of patients remain dry for the first year after detoxification while taking acamprosate. The drug is particularly effective during the first

few hard months of abstinence, when relapse rates are the highest. The results still leave a high failure rate, however, necessitating additional therapeutic measures such as self-help groups and individual counseling.

One reason medication can be insufficient is that alcohol also works on dopamine, the neurotransmitter that runs the motivation and reward system. Normally, stimuli that are important to survival—related, for example, to feeding and sex—trigger the release of dopamine. The neurotransmitter increases our anticipation of happiness and makes us want these things. The pleasant reward feelings, in turn, make us seek the sensations again and again, and we engage more strongly in the behaviors that cause dopamine to be released. Addictive drugs such as heroin unleash the same mechanisms.

As it does for GABA and NMDA, brain chemistry related to the reward system also adapts to fit the constant presence of alcohol. The brain reduces the number of dopamine binding sites on neurons, called D2 receptors, to protect itself from a persistent oversupply of the neurotransmitter. Alcohol affects other aspects of the motivation system as well. When alcoholics look at photographs of beer or wine, the regions of their brain that control attention are aroused more than they are for nonalcoholics, according to MRI imaging studies done in my lab. The fewer the D2 receptors they have, the more activity is elicited in their attention centers by the sight of alcohol.

This predilection explains why it is so difficult for alcoholics to find other stimuli pleasant and rewarding. It seems almost impossible for them to become interested in anything new that might bring satisfaction—be it a relationship, a hobby or even good food. The more serious the damage to the dopamine system, the more fixated attention becomes on the familiar images of alcohol—even when the person is lying inside the narrow, noisy tube of an MRI machine, when the brain knows it is not about to receive beer or whiskey.

The extent to which the attention centers can be activated in this lab situation highlights the severe problems recovering alcoholics have ignoring the advertising all around them. About a third of the subjects in our studies complain about the powerful effects of television commercials, especially when they are broadcast in situations in which patients would previously have been drinking, such as while watching a football game.

Tainted Pleasure

Although dopamine directs desire, the actual feeling of pleasure comes from endorphins—the body's own opiatelike substances. Once again, regular drug use changes the system. Alcoholics develop a higher number of binding sites for endorphins. When they drink, their neurons bind more endorphins, producing a greater feeling of pleasure.

Certain medications have been designed to alter this interchange. Naltrexone, for example, blocks the receptors and can reduce the risk of relapse considerably. Recovering alcoholics say that if they are taking naltrexone and have a drink, the taste is foreign, to the point of being terrible. Yet the drug alone, without psychosocial care, is not enough, because for some patients the second or third drink will start to taste good again. A patient must want to live abstinently; then, naltrexone will help him or her avoid that first sip.

With the expanding understanding of how alcohol alters the action of neurotransmitters, it is becoming clear that people addicted to alcohol are suffering from dramatic changes in brain activity. No particular personality type is prone to becoming dependent. The culprit is excessive alcohol consumption itself, which changes the brain so that victims can no longer free themselves from the bottle. It is time to destigmatize alcoholism and to develop better methods of breaking dependency and preventing relapse. The knowledge gained from research certainly opens avenues for creating new drugs. Still, alcoholics need one aid above all: people who will listen to and stand by them as they strive to recover. M

Drugs can reduce the alcoholic brain's oversensitivity to glutamate and oversupply of dopamine.

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ESSAY

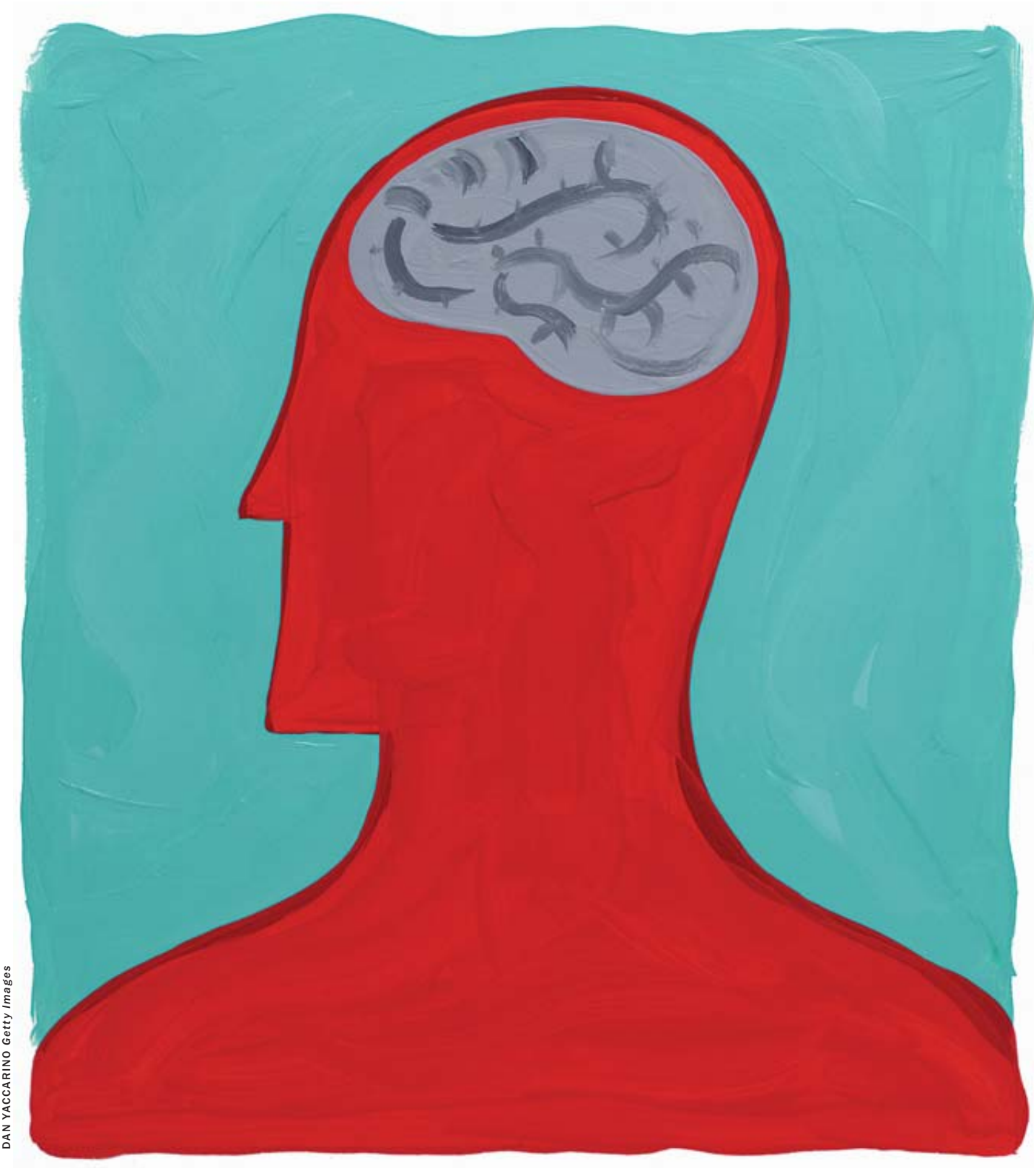
THE NEW SCIENCE OF MIND

A FORECAST OF THE MAJOR PROBLEMS SCIENTISTS NEED TO SOLVE

BY ERIC R. KANDEL

Understanding the human mind in biological terms has emerged as the central challenge for science in the 21st century. We want to understand the biological nature of perception, learning, memory, thought, consciousness and the limits of free will. That biologists would be in a position to explore these mental processes was unthinkable even a few decades ago. Until the middle of the 20th century, when I began my career as a neuroscientist, the idea that mind, the most complex set of processes in the universe, might yield its deepest secrets to biological analysis and perhaps do this on the molecular level could not be entertained seriously.

The dramatic achievements of biology during the past 50 years have now made this possible. The discovery of the structure of DNA by James Watson and Francis Crick in 1953 revolutionized biology, giving it an intellectual framework for understanding how information from the genes controls the functioning of the cell. That discovery led to a basic understanding of how genes are regulated, how they give rise to the proteins that determine the functioning of cells, and how development turns genes and proteins on and off to establish the body plan of an organism. With these extraordinary accomplishments behind it, biology



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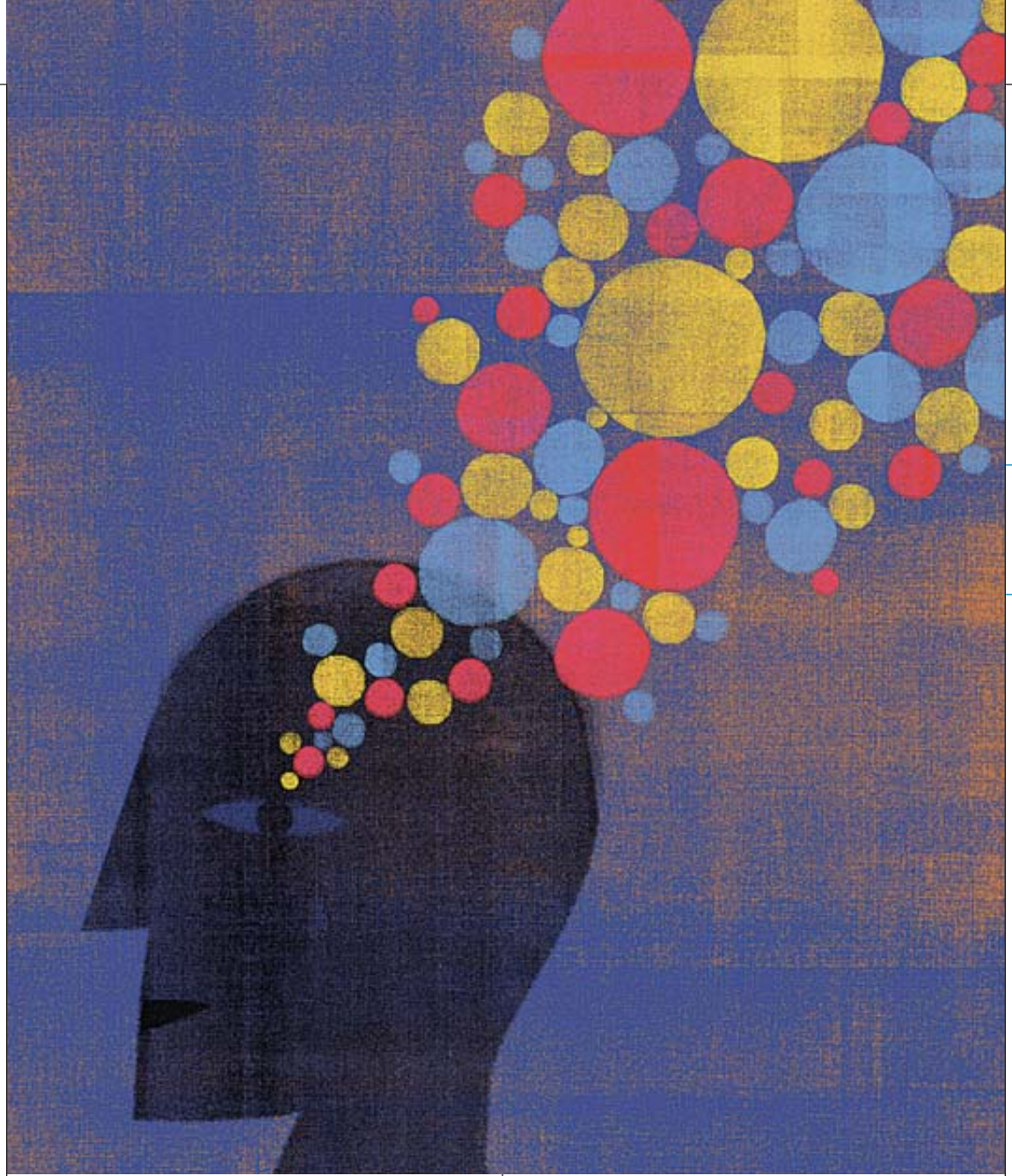


JIM FRAZIER *Images.com/Corbis*

assumed a central position in the constellation of sciences, in parallel with physics and chemistry.

Imbued with new knowledge and confidence, biology turned its attention to its loftiest goal: understanding the biological nature of the human mind. This effort, long considered to be prescientific, is already in full swing. Indeed, when intellectual historians look back on the last two decades of the 20th century, they are likely to comment on the surprising fact that the most valuable insights into the human mind to emerge during this period did not come from the disciplines traditionally concerned with mind—philosophy, psychology or psychoanalysis. Instead they came from a merger of these disciplines with the biology of the brain, a new synthesis energized recently by dramatic achievements in molecular biology.

Mind Is Brain

The result has been a new science of mind, a science that uses the power of molecular biology to examine the great remaining mysteries of life. This new science is based on five principles. First, mind and brain are inseparable. The brain is a complex biological organ of great computational capability that constructs our sensory experiences, regulates our thoughts and emotions, and controls our actions. The brain is responsible not only for relatively simple motor behaviors, such as running and eating, but also for the complex acts that we consider quintessentially human, such as thinking, speaking and creating works of art. Looked at from this perspective, mind is a set of operations carried out by the brain, much as walking is a set of operations car-

ried out by the legs, except dramatically more complex.

Second, each mental function in the brain—from the simplest reflex to the most creative acts in language, music and art—is carried out by specialized neural circuits in different regions of the brain. This is why it is preferable to use the term "biology of mind" to refer to the set of mental operations carried out by these specialized neural circuits rather than "biology of *the* mind," which connotes a place and implies a single brain location that carries out all mental operations.

Third, all of these circuits are made up of the same elementary signaling units, the nerve cells. Fourth, the neural circuits use specific molecules to generate signals within and between nerve cells. Finally, these specific signaling molecules have been conserved—retained, as it were—through millions of years of evolution. Some of them were present in the cells of our most ancient ancestors and can be found today in our most distant and primitive evolutionary relatives: single-celled organisms such as bacteria and yeast and simple multicellular organisms such as worms, flies and snails. These creatures use the same molecules to organize maneuvering through their environment that we use to govern our daily lives and adjust to our environment.

Thus, we gain from the new science of mind not only insights into ourselves—how we perceive, learn, remember, feel and act—but also a new perspective of ourselves in the context of biological evolution. It makes us appreciate that the human mind evolved from molecules used by our ancestors and that the extraordinary conservation of the molecular mechanisms that regulate life's various processes also applies to our mental life.

Because of its broad implications for individual and social well-being, there is now a general consensus in the scientific community that the biology of mind will be to the 21st century what the biology of the gene was to the 20th century.

A Systems Approach

As we enter the 21st century, the new science of mind faces remarkable challenges. Researchers of memory storage, including my colleagues and me, are only standing at the foothills of a great mountain range. We have learned about the cellular and molecular mechanisms of memory storage, but now we must progress to the systems properties of memory. For example, which neural circuits are critical for which kinds of memory? How does the brain encode internal representations of a face, scene, melody or experience?

To move from where we are to where we want to be, we must undertake major conceptual shifts in how we think about the brain. One such shift

PROBLEM #1: **Shift** from single cells to systems.

involves moving away from elementary processes (that is, single proteins, genes and cells) and toward systems properties, such as complex networks of proteins or nerve cells, the functioning of whole organisms and the interaction of groups of organisms. Cellular and molecular approaches will no doubt continue to yield important information, but alone they cannot reveal the intricacies of internal representations within, or interactions among, neural circuits—the key steps linking cellular and molecular neuroscience to cognitive neuroscience.

To develop an approach that relates neural systems to complex cognitive functions, we must focus on neural circuits, discerning how patterns of activity in different circuits merge to form a coherent representation. To learn how we perceive and recall complex experiences, we must determine how neural networks are organized and how attention and awareness shape and reconfigure neural activity in those networks. To accomplish these goals, biology must focus more on human beings and on nonhuman primates using imaging techniques that can resolve the activity of individual neurons and neuronal networks.

What Is Attention?

These reflections have led me to wonder what scientific questions I would pursue were I to start anew. I have two requirements for selecting such a research problem. First, it must allow me to participate in opening a new area of research that will occupy me for a long time. (I like long-term commitments, not brief romances.) Second, the problem must lie at the intersection of two or more disciplines. Based on these criteria, three sets of questions appeal to me.

First, how does the brain process sensory information consciously, and how does conscious attention stabilize memory? Crick and California Institute of Technology neuroscientist Christof Koch have argued persuasively that selective attention is not only an important area of investigation in its own right but also a critical component of consciousness. Regarding attention, I would focus on "place cells," which determine an animal's location in space, in the hippocampus—a brain region linked with long-term memory—and how place cells create an enduring spatial map only when an organism focuses its spotlight of attention on its surroundings.

What is this spotlight of attention? How does it trigger the neural circuitry of spatial memory to encode information? Moreover, what modulatory brain systems turn on when an animal pays attention, and how are they activated? How does attention enable me to embark on "mental time travel" to the little apartment in Vienna where I grew up? To investigate these matters, we ought to extend our studies of memory beyond laboratory animals to human beings.

The second question is, How do unconscious and conscious mental processes relate to one another in people? The notion that we are unaware of much of our mental life—an idea that German physician and physicist Hermann von Helmholtz proposed in 1860—lies at the core of psychoanalysis. Only through understanding such issues can we address, in biologically meaningful terms, Sigmund Freud's theories proposed in 1899 about conscious and unconscious conflicts and memory. To Helmholtz's notion, Freud added the important observation that by paying attention, we can access some of our unconscious mental processes—ones that would otherwise go unnoticed.

PROBLEM #2: **Focus** on the spotlight of attention.

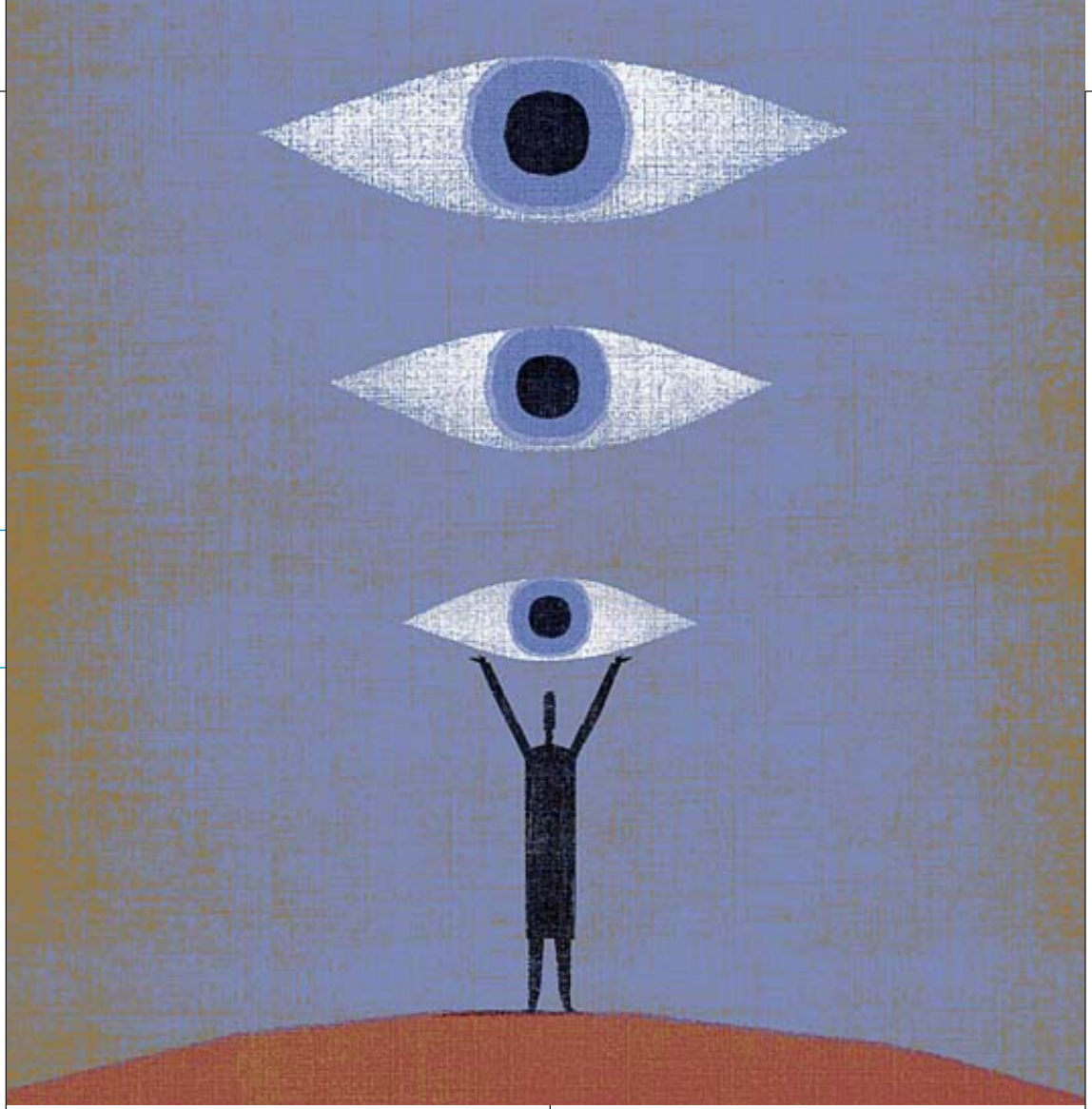
Unconscious Mechanisms

Seen from this perspective—a view that most neural scientists now hold—most of our mental life is unconscious. And we become aware of many otherwise inaccessible brain processes only through words and images. So, in principle, we should be able to use brain-imaging techniques to connect psychoanalytic processes with brain anatomy and neural functioning. Such a bridge might enable us to learn how disease states alter unconscious processes and how psychotherapy might help reconfigure them. Unconscious psychic processes play such a large role in our lives; perhaps biology can help us learn about them.

The final question is, How can we link molecular biology of mind to sociology and thus develop a realistic molecular sociobiology? Several researchers have made a fine start toward this goal. For example, Cori Bargmann, a geneticist now at the Rockefeller University, has studied two variants of the soil nematode *Caenorhabditis elegans* that differ in their feeding patterns. One is solitary and seeks food alone. The other is social and forages in groups. The only difference between the two is one amino acid in an otherwise identical receptor protein. Transferring the receptor from a social worm to a solitary one causes the solitary creature to socialize.

Another example involves male courtship in the fruit fly *Drosophila*. A key protein, called Fruitless, governs this instinctive behavior, and Fruitless is expressed differently in male and female flies. Ebru Demir and Barry J. Dickson, neuroscientists at the Research Institute of Molecular Pathology in Vienna, have made the remarkable discovery that when female flies express the male form of this protein, they mount and direct courtship toward other female flies—or toward males genetically engineered to produce a characteristic female odor, or pheromone. Dickson also found that for *Drosophila* to grow the neural circuitry for courtship and sexual preference, the *Fruitless* gene must be present and active during the fly's early development. (If scientists add this gene later, instead, then it does not have the same effect.)

Still a third example comes from Giacomo Rizzolatti, a neuroscientist at the University of Parma in Italy. He discovered that certain neurons in the premotor cortex become active when a monkey carries out a specific action with its hand, such as putting a peanut in its mouth. Remarkably, the same neurons respond when a monkey watches another monkey (or even a person) put food in its mouth. Rizzolatti calls these cells "mirror neurons," suggesting that they offer insight into imitation, identification, empathy and possibly the ability to mime vocalization—all un-



JIM FRAZIER *Images.com/Corbis*

conscious mental processes intrinsic to human interaction. Vilayanur S. Ramachandran, a neuroscientist at the University of California, San Diego, has found evidence of comparable neurons in the premotor cortex of humans.

Mental States Are Brain States

Reflecting on just these three research strands, I can see whole new areas of biology opening up, providing a sense of what makes us social, communicative beings. An ambitious undertaking of this kind might not only reveal what enables members of a cohesive group to recognize one another but also give us insight into tribalism, which so often promotes fear, hatred and intolerance of outsiders.

Since the 1980s the path toward merging mind and brain research has become clearer. As a result, psychiatry has taken on a new role, both stimulating and benefiting from biological thought. During the past few years, even members of the psychoanalytic community have taken on a keen interest in the biology of mind, acknowledging that every mental state is a brain state, that all mental disorders involve disorders of brain function. Treatments work when they alter the brain's structure and functioning.

To give a sense of how attitudes among researchers have changed in recent years, when in 1962 I turned from studying the hippocampus in the mammalian brain to studying simple forms of learning in the sea slug *Aplysia,* I encountered many negative reactions. At the time, there was a strong sense among brain scientists that mammalian brains differed radically from those of

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JIM FRAZIER *Images.com/Corbis*

lower vertebrates, such as fish and frogs—and were incomparably more complex than invertebrate brains. The fact that Nobel Prize–winning neuroscientists, such as the late Alan Hodgkin, Andrew F. Huxley of the University of Cambridge and the late Bernard Katz, discovered the fundamental principles of signaling in the human nervous system by probing the neural axons of squids and the synapses joining nerves and muscles in frogs seemed to these mammalian chauvinists an exception. Of course all nerve cells are similar, they conceded, but neural circuitry and behavior differ markedly in vertebrates and invertebrates.

Of Flies and Men

This schism persisted until molecular biologists revealed the amazing continuity—throughout evolution, from lower to higher organisms—of the genes and proteins governing all neural systems. Even then, disputes arose as to whether the cellular and molecular mechanisms of learning and memory revealed in simple animal studies would generalize to more complex animals. Neuroscientists argued about whether elementary forms of learning such as sensitization and habituation gave rise to forms of memory that would be useful to study. The ethologists, who study animal behavior in natural settings, emphasized the generality of these simple forms of memory, whereas the behaviorists highlighted associative forms of learning, such as classical and operant conditioning, which are clearly more complex.

The disagreements were eventually resolved in two ways. First, Seymour Benzer, a biologist at

Caltech, proved that cyclic AMP, which is important for short-term sensitization in *Aplysia,* plays a critical role in more complex forms of learning, such as classical conditioning, in a more complex animal—namely, *Drosophila*. Second, the regulatory protein CREB, first identified in my laboratory in *Aplysia,* proved to be a key molecular component in switching from short- to long-term memory in many forms of learning and types of organisms, ranging from snails to flies, to mice and to people. Evidently, learning and memory, as well as synaptic and neuronal plasticity, or ability to change, involve a family of processes that vary in molecular subtleties but share various components and a common logic. In most cases, these discussions proved beneficial for science, sharpening questions and moving research forward. To me, the most important facet of the debates was the sense that we were progressing in the right direction.

These debates influenced my views, as did my psychiatric training and psychoanalytic interests, which lie at the very core of my scientific thinking. Together they shaped my perspective on mind and behavior, establishing overarching ideas that influenced nearly every aspect of my research and fueled my interest in conscious and unconscious memory.

PROBLEM #3: **Develop** molecular sociology.

Passion and Bold Discoveries

Few experiences excite and stimulate the imagination more than discovering something new, no matter how modest. A new finding allows someone to see for the first time a small piece of nature's puzzle. Becoming absorbed in a problem, I find it helpful to develop a comprehensive perspective by learning what previous scientists thought about it. I want to know not only which lines of thought proved productive but also where and why other lines proved unproductive. And so Freud, as well as other early researchers in learning and memory—such as the classic psychologists William James, Edward Thorndike, Ivan Pavlov, B. F. Skinner and Ulric Neisser of Cornell University—all strongly influenced my thought. Their thinking, and even the unproductive paths they followed, provided a rich cultural background for my later work. Thus, my initial aspirations in psychoanalysis were hardly a detour. Rather they became the educational bedrock of all that I have tried to learn.

It is important to be bold. One should tackle difficult problems, especially those that initially appear messy and unstructured. One should not fear trying new things, such as moving from one field to another or working at the boundaries of disciplines—where the most interesting problems often emerge. Most good scientists never hesitate to ask questions, explore unfamiliar terrain, follow their instincts or learn new science along the way. Nothing stimulates self-education more than pursuing a new area of research.

Defining a problem, or a set of interrelated problems, with a long trajectory is also critical for success. Early on I stumbled fortunately onto an interesting problem while studying the hippocampus and memory and then switched decisively to investigate learning in a simple animal. Both problems had enough intellectual sweep and scope to carry me through many experimental failures and disappointments.

As a result, I did not share the midcareer malaise of some colleagues who grew bored with their science and turned to other things. Rather I thrived on testing new ideas. My friend and colleague Richard Axel, a fellow neuroscientist at Columbia University who received the Nobel Prize in 2004 for his remarkable discovery that there are 1,000 different receptors for smell, often speaks about the addictive quality of reviewing in one's mind new and interesting findings. Unless Richard sees new data coming along, he becomes despondent—a feeling many of us share. Such is the constructive side of addiction, one that I have experienced in pursuit of my own lifelong passion—namely, to understand the cellular and molecular basis of mind. M

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HUNTING for *Answers*

A SINGLE MUTATION CASTS THE DEATH SENTENCE OF HUNTINGTON'S DISEASE. RESEARCHERS ARE PINNING DOWN HOW THAT MUTATION RUINS NEURONS—KNOWLEDGE THAT MAY SUGGEST THERAPIES

BY JUERGEN ANDRICH AND JOERG T. EPPLEN

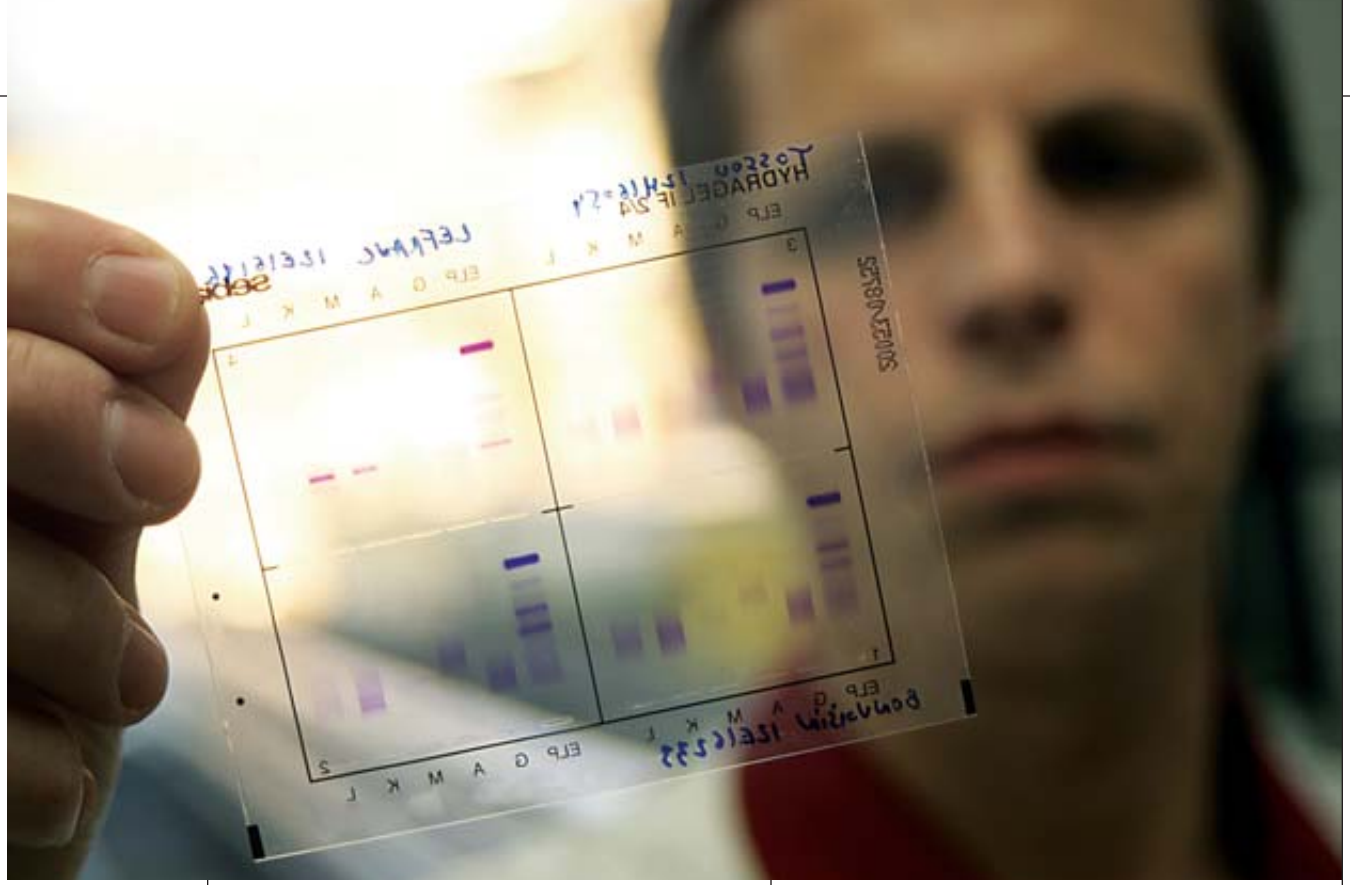
The cups fell to the floor with a crash. Was this the alarm signal? Or was it forgetting his sister's phone number the other day, even though he calls her often? Was the telling event last weekend, when he burst into a string of curse words and tailgated the driver who had just cut him off?

Incidents that to other people may seem like simple clumsiness, forgetfulness or an overreaction brought on by stress could mean disaster for Martin, a 48-year-old shipping agent. For years, he had been observing himself and his siblings with a sharp eye. Any little slip could constitute a somber omen. But after this latest string of mishaps, he could not bear the uncertainty any longer. He went in for the blood test. Three days later what Martin had feared since childhood was confirmed as the terrible truth: he was suffering from the genetic mutation that had killed his mother, his uncle and his grandfather.

Huntington's disease was recognized as an inherited disorder more than 100 years ago, yet the mutation that causes it was not discovered until 1993. A DNA test on a blood sample was quickly devised to reveal whether a person carried the abnormal form of the gene, which leads to progressive destruction of the brain, crippling muscles and mental function. Since then, every man or woman who has had a parent or other relative with the disease has faced a vexing choice: Should he or she take the test? A positive verdict is a damnation—the disease leads to certain death, given that there is no cure. Not knowing can be easier; most people do not begin to exhibit symptoms until they are middle-aged, and the progression can be very gradual. Yet nagging suspicion can creep into every corner of life, as it did for Martin.

Of course, a cure, or even treatment that could slow the disease, would ease the tension greatly and extend life for the 30,000 Americans who have been diagnosed with Huntington's. Researchers are pinning down just how the genetic mutation ruins cellular mechanisms inside neurons, knowledge that might help point the way to therapies that have thus far proved elusive.

JUAN SILVA *Getty Images*



A DNA test from a blood sample can identify the mutant gene. An individual has a 50 percent chance of harboring the bad form of the gene if either parent carries it.

Lethal Knowledge

The Huntington's test is so certain because the disease is caused by a single gene—the *huntingtin* gene on chromosome 4 (the name of the gene is spelled differently than that of the illness). Typically this gene contains several occurrences of a set of DNA building blocks: cytosine, adenine and guanine, abbreviated as CAG. This set drives the production of the huntingtin protein. The more often the CAG sequence comes up in the gene, the more glutamine—an amino acid—in the huntingtin protein. In healthy genes the CAG sequence may appear up to 28 times. But if it occurs more than 35 to 40 times, the glutamine chain in the huntingtin protein becomes too long and causes trouble [*see box on page 74*]. The larger the number of CAG sets, the longer the chain, and the earlier and more severe the disease.

For Martin, the genetic test confirmed his grim suspicions. But he decided to see what he could do and went for counseling to the North Rhine-Westphalia Huntington Center at Ruhr University in Bochum, Germany. The center serves more than 600 Huntington's patients and their families. "I accept my fate as a fact," Martin told his counselors, then asked, "What can I do now that will help me later?" The team discussed the various ways the disease could play out.

The genetic mutation that overproduces the CAG sequence is inherited from a single parent. A child, therefore, has a 50 percent chance of getting the disease-causing form of the gene if either parent has it. The therapists in Bochum began by tracing the inheritance pattern of Martin's family. "My grandmother stepped in front of a train, and I think she knew what she was doing," Martin noted, insinuating that she knew she was doomed. "And Grandma's father became very strange when he got old." Martin's mother also clearly suffered from Huntington's disease, even though during her lifetime there was no definitive genetic diagnosis.

Martin and his sister Susanne finally dared to take the test because they could no longer stand the uncertainty—and because they wanted to plan the rest of their lives and careers. Susanne had the defective gene, too. Their siblings chose not to find out about their chances of impending death.

Today, two years after his weekend of dropping cups and forgetting phone numbers, Martin is showing the first verifiable symptoms: sudden twitches in his arms and legs. Susanne has been problem-free, yet she cannot help but wonder if certain harmless behaviors she never noticed before about herself are harbingers of difficulties to come. Disease symptoms typically begin when carriers are 35 to 45 years old, but even among close relatives the onset and course can differ significantly. No one wanted to think that Martin's 10-year-old son could already be falling victim—and the pediatrician treating him wanted to believe that the boy's pain, muscle weakness and subtle coordination problems were from other

AJP/HOP AMERICAIN/PHOTO RESEARCHERS, INC.

Should Martin take the blood test? A positive verdict means death. Not knowing can be easier.

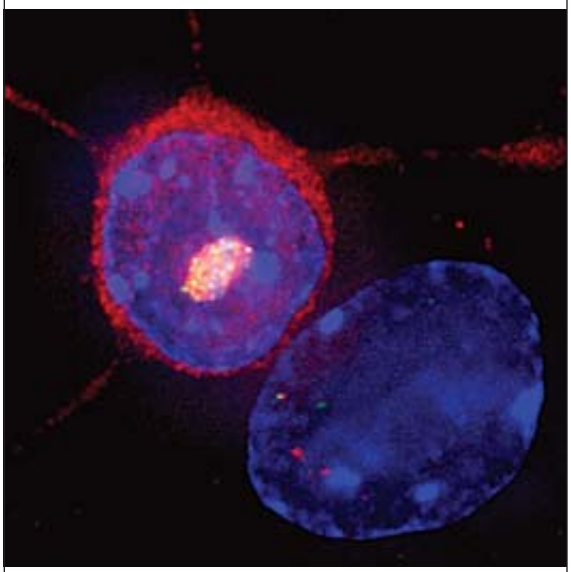
causes. But after six years of ailments and Martin's diagnosis, the boy was tested. Indeed, he had childhood Huntington's, a rarity brought on by an extremely elongated *huntingtin* gene.

Inexorable Progression

Huntington's disease had been known for centuries before it was given its definitive name. In the Middle Ages, victims of what was then called "the dance" made pilgrimages to Ulm, Germany, to pray in the chapel of Saint Vitus, leading to the ailment's name, Saint Vitus' dance. The first to recognize the condition as an inherited disease was the young American neurologist George Huntington in 1872. Together with his father, he had tracked cases in a family on Long Island, outside New York City, and was able to differentiate them from chorea minor, caused by a streptococcal infection that has similar symptoms. Today about one in 10,000 people in the U.S. suffers from Huntington's.

The symptoms that gave the disease its original name are the "dancing" movements—the exaggerated motions of the limbs that are its most frequent and striking effects. In the beginning, patients try to disguise these jerks and twitches as shrugs or try to translate them into deliberate motions such as stretches. But little by little their muscles go out of control. They are beset by sudden grimaces, and speaking and swallowing become increasingly difficult. In later stages, movements are slower; increased muscle contraction leads to painful contortions of the limbs that can last minutes or hours.

Characteristic mental symptoms often appear decades before the physical problems. The disease can cause repeated outbreaks of moodiness, yet patients who receive a positive test result can also fall victim to emotional swings driven by their knowledge of impending destruction. Relatives often notice personality changes—patients may become paranoid, tyrannize those around them with unfounded jealousy or react extraordinarily aggressively to trivial disagreements. As the disease advances, they may obsess about minor issues for days or weeks, burdening their families and destroying their social connections. Patients' cognitive abilities also wane; their memories deteriorate, and they find it increasingly difficult to concentrate. The problems progress to severe dementia and complete helplessness. Even early in the disease, the mounting mental breakdown can have catastrophic effects on a person's personal and professional lives, and suicide attempts are not unusual.



FREDERIC SADOU *Institut Curie ISM/Phototake*

Abnormal huntingtin proteins aggregate into a damaging inclusion (*white spot*) in one of two neighboring neuron nuclei photographed at the Institut Curie in Paris.

Communication Breakdown

Researchers who have been trying to better define the mechanisms that cause Huntington's muscular and mental challenges had to start by figuring out why the disease strikes at such varied ages. They have found that along with the *huntingtin* gene mutation, other inherited factors play an important role. For example, there can be great variation in how readily neuron receptors in the brain bind to glutamate, which serves as a messenger molecule that facilitates the transmission of information between neurons. The type of receptor protein a patient has helps determine how soon the disease will take hold.

Despite its rarity, Huntington's has become a focal point for defining how neurodegenerative diseases in general—including Parkinson's and Alzheimer's—harm the brain. In the 13 years since the *huntingtin* gene was discovered, scientists have learned much about the mechanisms leading to the destruction of neurons. Because the huntingtin protein is the sole cause of deteriora-

(The Authors)

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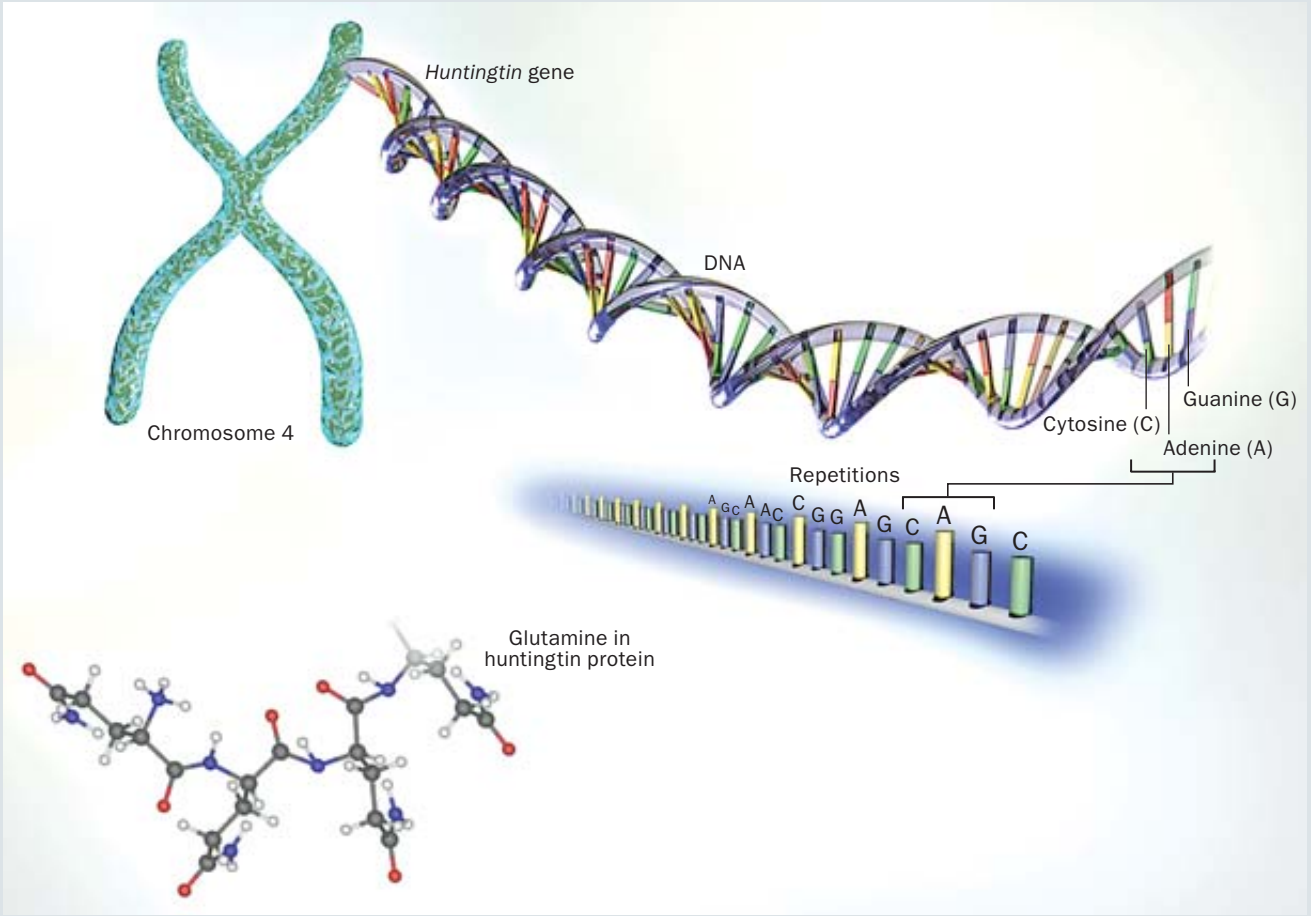
Lethal Repeats

The *huntingtin* gene lies on chromosome 4. The gene contains a number of DNA building blocks represented by the sequence cytosine-adenine-guanine (CAG), which direct the production of the huntingtin protein. If the CAG sequence appears 35 to 40 times or more on the gene, the resulting protein will contain glutamine molecules that are too long, slowly killing neurons and causing Huntington's disease.



tion in the case of Huntington's disease, it provides a path for investigation that is uncluttered by other complicating factors.

Huntingtin is not a "bad" protein per se. It appears to play a central role in embryonic development among mammals. But as humans with the mutated gene age, the overelongated protein apparently binds to other proteins vital to cellular survival, compromising their function.

The proteins affected include transcription regulators—proteins that ensure the accurate reading of genetic information. If huntingtin proteins bind to a transcription regulator within a cell, its genetic activity is disturbed and the cell's control of protein synthesis breaks down. Some of the proteins that cannot be synthesized are responsible for removing neurotransmitters (messenger molecules) such as glutamate from the synapses—the gaps between neurons across which communication occurs. If too much glutamate remains in the synapse, adjacent neurons are continually excited; the overactivity eventually damages the cells. This phenomenon, known as excitotoxicity, has been demonstrated in lab animals.

There is also increasing evidence that huntingtin is more involved than previously thought in neuronal processes. A protein known as huntingtin interacting protein 1 (HIP-1) aids in both the secretion and reuptake of messenger molecules within neuronal cells. The elongated huntingtin protein chain cannot correctly bind to HIP-1, causing a cascade of enzyme reactions that initiate apoptosis: programmed cell death. The neurons are driven to kill themselves.

Another theory is based on the observation that the elongated gene causes the huntingtin pro-

SIGANIM *Gehirn & Geist*

tein to misfold. The misfolded protein then disrupts a neuron's metabolism. Evidence indicates that several steps in the respiration chain in the mitochondria—the cell's "power plants"—no longer function correctly. Such a resulting shortage of energy would eventually kill the cell.

Search for a Cure

So far investigators have come up with few ideas for altering such fatal cellular disruptions. Various drug treatments have affected only the symptoms of Huntington's. For example, some neurologists prescribe neuroleptics to deal with muscle contractions. These drugs can have the unfortunate side effect of limiting the patients' mobility. Other doctors may treat their patients' psychological problems with antidepressants, sedatives or antipsychotic neuroleptics. Unfortunately, there is still no treatment for the loss of mental abilities—a prognosis that frightened Martin more than the impending muscular challenges.

Several labs around the globe are seeking drugs that could delay or even stop the destruction of neurons. One set of substances is the glutamate antagonists, which modulate the secretion of glutamate. One compound, riluzole, has already proved effective against another serious, rapidly progressing disease of the nervous system—amyotrophic lateral sclerosis, or Lou Gehrig's disease. The drug is currently in a Europe-wide clinical test involving 450 Huntington's patients.

Scientists also have hopes for minocycline, an antibiotic. In 2003 Robert M. Friedlander of Harvard Medical School showed that in mice with Huntington's, minocycline could inhibit the action of the enzymes that set off neuronal suicide.

Other substances could perhaps block the clumping of misfolded huntingtin proteins, which aggravates neuron death. In 2004 researchers at the RIKEN Brain Science Institute in Japan inhibited the aggregation of the proteins with trehalose, a sugar made by various desert plants. Blocking the clumping in mice delayed the disease's onset.

Physicians are exploring substances produced in the body, too, such as coenzyme Q and creatine. Coenzyme Q, ubiquitous in humans, is an antioxidant that captures oxygen free radicals and could limit damage by huntingtin proteins. Creatine, produced in the liver and kidneys, could improve energy storage in muscle and brain cells. In both cases, animal experiments have been successful, but there is no convincing evidence for efficacy in humans yet.

Researchers are testing gene therapies as well. In 2005 Beverly L. Davidson and Scott Q. Harper of the University of Iowa inhibited the action of the mutated *huntingtin* gene in mice. The team injected the animals' brains with RNA fragments that precisely mimicked the genetic instructions for the mutated huntingtin protein and thereby blocked its synthesis. The rodents produced less of the illness-inducing huntingtin protein.

BETTMANN CORBIS

Folksinger Woody Guthrie, perhaps the most well-known celebrity to have Huntington's disease, died in 1967. Before the genetic test became available in 1993, sufferers such as Guthrie were often misdiagnosed as mentally ill or alcoholic.

Stem cells could provide aid. In 2000 Anne-Catherine Bachoud-Lévi of the Henri Mondor University Hospital in Creteil, France, implanted neuronal stem cells from aborted fetuses into the brains of Huntington's patients to see if they might take the place of destroyed cells. Two years later Robert A. Hauser of the University of South Florida made similar attempts. In both trials, some patients responded to the therapy, but others suffered from cerebral hemorrhages, causing their condition to worsen. All the patients had to be given additional drugs to block immune reactions to the foreign cells.

There is nothing, today, that Martin can take to block the relentless progress of his disease. But never before have so many new approaches for treatment been under investigation. Scientists from Europe and the U.S. are preparing for larger studies, and many victims, as well as others who have not had the blood test but are at risk because of their family histories, are ready to take part. With their help, hope remains for an eventual solution for patients such as Martin. M

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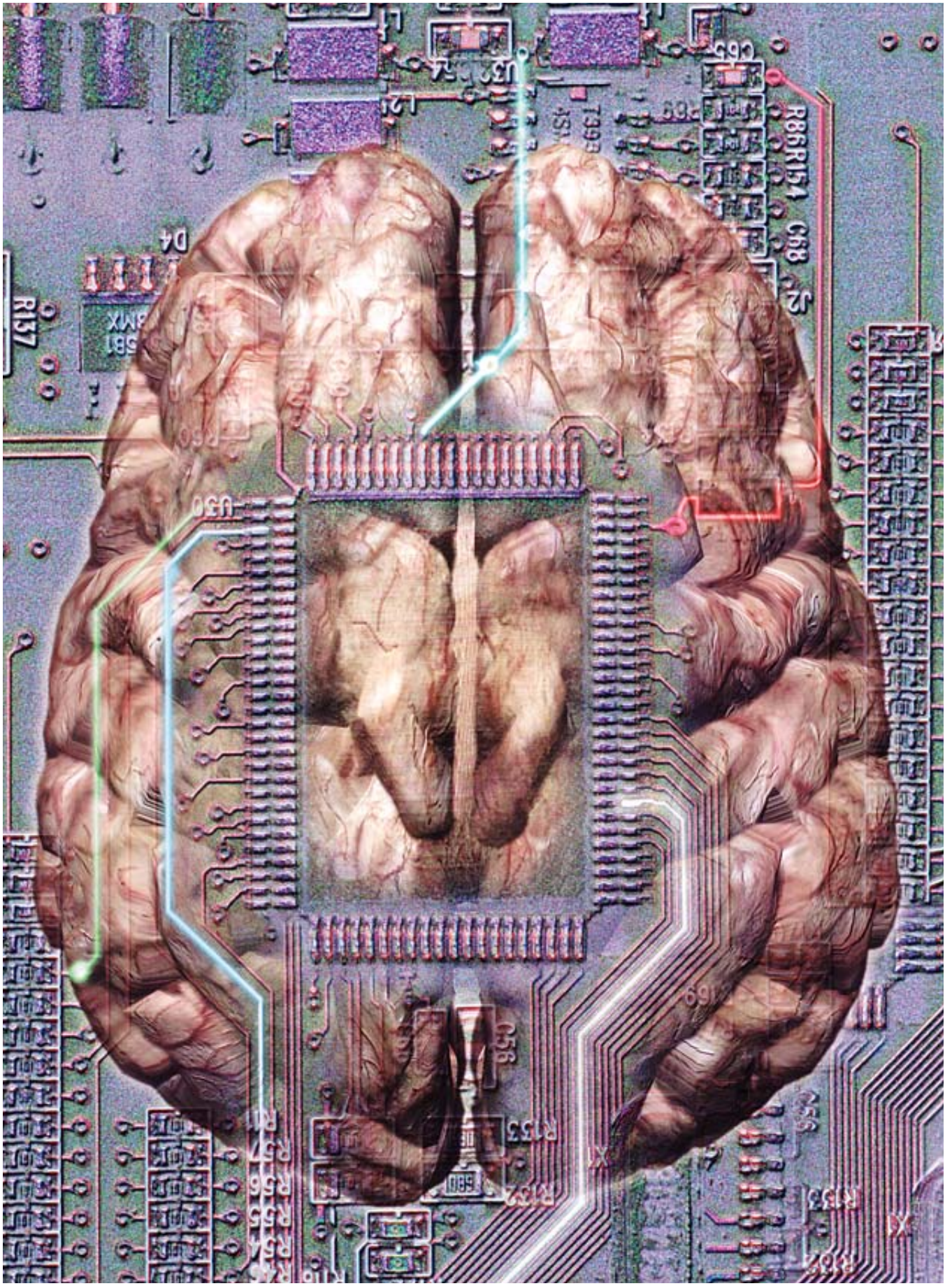
ELECTRIC Thoughts?

The latest computer designs draw inspiration from human neural networks. But will machines ever really *think?*

By Yvonne Raley



SANFORD/AGLIOLO *Corbis*

How long does it take you to add 3,456,732 and 2,245,678? Ten seconds? Not bad—for a human. The average new PC can perform the calculation in 0.000000018 second. How about your memory? Can you remember a shopping list of 10 items? Maybe 20? Compare that with 125 million items for the PC.

On the other hand, computers are stumped by faces, which people recognize instantly. Machines lack the creativity for novel ideas and have no feelings and no fond memories of their youth. But recent technological advances are narrowing the gap between human brains and circuitry. At Stanford University, bioengineers are replicating the complicated parallel processing of neural networks on microchips. Another development—a robot named Darwin VII—has a camera and a set of metal jaws so that it can interact with its environment and learn, the way juvenile animals do. Researchers at the Neurosciences Institute in La Jolla, Calif., modeled Darwin's brain on rat and ape brains.

The developments raise a natural question: If computer processing eventually apes nature's neural networks, will cold silicon ever be truly able to *think?* And how will we judge whether it does? More than 50 years ago British mathematician and philosopher Alan Turing invented an ingenious strategy to address this question, and the pursuit of this strategy has taught science a great deal about designing artificial intelligence, a field now known as AI. At the same time, it has shed some light on human cognition.

> Why does something that comes so easily for people pose such hurdles for machines?

Beginnings: Testing Smarts

So what, exactly, is this elusive capacity we call "thinking"? People often use the word to describe processes that involve consciousness, understanding and creativity. In contrast, current computers merely follow the instructions provided by their programming.

In 1950, an era when silicon microchips did not yet exist, Turing realized that as computers got smarter, this question about artificial intelligence would eventually arise. [*For more on Turing's life and work, see box on opposite page.*] In what is arguably the most famous philosophy paper ever written, "Computing Machinery and Intelligence," Turing simply replaced the question "Can machines think?" with "Can a machine—a computer—pass the imitation game?" That is, can a computer converse so naturally that it could fool a person into thinking that it was a human being?

Turing took his idea from a simple parlor game in which a person, called the interrogator, must determine, by asking a series of questions, whether or not an unseen person in another room is a man or a woman. In his thought experiment he replaced the person in the other room with a computer. To pass what is now called the Turing Test, the computer must answer any question from an interrogator with the linguistic competency and sophistication of a human being.

Turing ended his seminal paper with the prediction that in 50 years' time—which is right about now—we would be able to build computers that are so good at playing the imitation game that an average interrogator will have only a 70 percent chance of correctly identifying whether he or she is speaking to a person or a machine.

So far Turing's prediction has not come true [*see box on page 80*]. No computer can actually pass the Turing Test. Why does something that comes so easily for people pose such hurdles for machines? To pass the test, computers would have to demonstrate not just one competency (in mathematics, say, or knowledge of fishing) but many of them—as many competencies as the average human being possesses. Yet computers have what is called a restricted design. Their programming enables them to accomplish a specific job, and they have a knowledge base that is relevant to that task alone. A good example is Anna, IKEA's online assistant. You can ask Anna about IKEA's products and services, but she will not be able to tell you about the weather.

What else would a computer need to pass the Turing Test? Clearly, it would have to have an excellent command of language, with all its quirks and oddities. Crucial to being sensitive to those quirks is taking account of the context in which things are said. But computers cannot easily recognize context. The word "bank," for instance, can mean "river bank" or "financial institution," depending on the context in which it is used.

The Brains behind the Machines

Raised by various family friends, Alan Turing was a lonely child. As occurs with many gifted children, Turing's independent intellect did not fit the expectations of his schoolteachers; he was near the bottom of his class in several subjects. How apt, then, that the adult Turing would come up with a way to recognize intelligence—of the artificial kind—in his Turing Test. According to Turing, a computer can "think" if it can fool a human being into believing that its written conversation is produced by a person, not a machine.

Alan Turing

Turing was well suited to investigate the question of machine intelligence. When he was just 23 years old, he impressed his peers at the University of Cambridge by inventing the mathematical characterization of a machine that was to become one of the most important contributions in the history of computing. A Turing machine is one that can compute the answers to a mathematical problem based on a program. It consists of an input device, a set of internal states corresponding to a program, and an output device. Any modern computer, in essence, is a Turing machine.

Turing's invention also uniquely qualified him to work on another riddle. In 1938 the British government hired him to help break the code of the German Enigma machine, which encoded secret messages. Turing helped to develop a machine that did indeed break the Enigma codes and later those of the German navy as well. The Bombe, as it was appropriately called, was based in part on the Turing machine concept.

Turing was sworn to secrecy about his government work, a factor that may have isolated the already reserved mathematician even further. Perhaps that resulting pressure added to the stress Turing suffered when he was prosecuted as a homosexual and forced to endure estrogen injections as a form of therapy. Tragically, Turing committed suicide in 1954 at the age of 41.

The event was unanticipated even to those who knew him well. Turing had always come across to his friends as contented with his life. He left the world with no explanatory note, no cry for help; only a half-eaten apple laced with cyanide found by his bedside witnessed the deed. Turing's unexpected death illustrates that humans can be fooled in many ways—happiness, too, can be mimicked successfully. —*Y.R.*

What makes context so important is that it supplies background knowledge. A relevant piece of such knowledge, for example, is who is asking the question: Is it an adult or a child, an expert or a layperson? And for a query such as "Did the Yankees win the World Series?" the year in which the question is asked is important.

Background knowledge, in fact, is useful in all kinds of ways, because it reduces the amount of computational power required. Logic is not enough to correctly answer questions such as "Where is Sue's nose when Sue is in her house?" One also needs to know that noses are generally attached to their owners. To tell the computer simply to respond with "in the house" is insufficient for such a query. The computer might then answer the question "Where is Sue's backpack when Sue is in her house?" with "in the house," when the appropriate response would be "I don't know." And just imagine how complicated matters would be if Sue had recently gotten a nose job. Here the correct answer would have been another question: "Which part of Sue's nose are you talking about?" Trying to write software that accounts for every possibility quickly leads to what computer scientists call "combinatorial explosion."

Human or Just Humanlike?

The Turing Test is not without its critics, however. New York University philosopher Ned Block contends that Turing's imitation game tests only whether or not a computer *behaves* in a way that is identical to a human being (we are only talking about verbal and cognitive behavior, of course). Imagine we could program a computer with all possible conversations of a certain finite length. When the interrogator asks a question Q, the computer looks up the conversation in which

(The Author)

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A Chat with George

George: Hi, want to chat?
Yvonne: Yes. How are you doing?
George: It is the water which freezes or boils, not our thoughts.
Yvonne: Fascinating. What makes you think of water?
George: I am trying to challenge you!
Yvonne: Quite the philosopher. How did you get so smart?
George: I was born like this, 181 IQ and all.

But George was never born. The chatting robot, or chatterbot, is one of many programs that has been created to simulate written human conversation. George can learn from past conversations by storing the information and then using it to reply to new questions. George's capabilities earned it the 2005 bronze medal of the Loebner Prize Competition. The competition, sponsored by Hugh Loebner and the Cambridge Center for Behavioral Studies, will award $100,000 to any program that passes the Turing Test—that is, that can simulate human conversation sufficiently well to fool a human judge. So far no program has won the $100,000, but the bronze medal is given out annually to the best attempt.

Chatterbots date to at least the 1960s, with Eliza, which imitates a psychotherapist, and Parry, a paranoid patient. For the most part, Eliza provides answers in the form of questions, peppered with remarks such as "Are you sure?" and "Can you elaborate on that?" When I asked "What does 'elaboration' mean?" Eliza responded with "Does that question interest you?" When I answered "yes," it reverted to "Are you sure?" Typical psychoanalyst, I guess.

Developed in the 1970s, Parry is designed to imitate a paranoid person. Rather than asking questions, Parry will tell you its story. Some expert psychiatrists have actually had trouble distinguishing between Parry and human paranoid subjects, but eventually it is always found out.

Even prizewinning George reveals its flaws relatively quickly. In our conversation, it got derailed after just a few lines:

Yvonne: You weren't born, you are just a program.
George: You could be born again, though.
Yvonne: Do you believe people can be born again?
George: Yes.
Yvonne: Why do you believe that?
George: Because a baby has no place in a basket.
Yvonne: You are changing the subject.
George: What subject?
Yvonne: I thought we were talking about being born again.
George: No, we were never talking about books. How do you feel about religion?
Yvonne: Huh?

You can have a conversation with George yourself at www.simonlaven.com/ —*Y.R.*

Q occurred and then types out the answer that followed, A. When the interrogator asks his next question, P, the computer now looks up the string Q, A, P and types out the answer that followed in this conversation, B. Such a computer, Block says, would have the intelligence of a toaster, but it would pass the Turing Test. One response to Block's challenge is that the problem he raises for computers applies to human beings as well. Setting aside physical characteristics, all the evidence we *ever* have for whether a human being can think is the behavior that the thought produces. And this means that we can never really know if our conversation partner—our interlocutor—is having a conversation in the ordinary sense of the term. Philosophers call this the "other minds" problem.

Chinese, Anyone?

A similar line of discussion—the Chinese Room Argument—was developed by philosopher John Searle of the University of California, Berkeley, to show that a computer can pass the Turing Test without ever understanding the meaning of any of the words it uses. To illustrate, Searle asks us to imagine that computer programmers have

GETTY IMAGES

written a program to simulate the understanding of Chinese.

Imagine that you are a processor in a computer. You are locked in a room (the computer casing) full of baskets containing Chinese symbols (characters that would appear on a computer screen). You do not know Chinese, but you are given a big book (software) that tells you how to manipulate the symbols. The rules in the book do not tell you what the symbols mean, however. When Chinese characters are passed into the room (input), your job is to pass symbols back out of the room (output). For this task, you receive a further set of rules—these rules correspond to the simulation program that is designed to pass the Turing Test. Unbeknownst to you, the symbols that come into the room are questions, and the symbols you push back out are answers. Furthermore, these answers perfectly imitate answers a Chinese speaker might give; so from outside the room it will look exactly as if you understand Chinese. But of course, you do not. Such a computer would pass the Turing Test, but it would not, in fact, think.

Could computers ever come to understand what the symbols mean? Computer scientist Stevan Harnad of the University of Southampton in England believes they could, but like people, computers would have to grasp abstractions and their context by first learning how they relate to the real, outside world. People learn the meaning of words by means of a causal connection between us and the object the symbol stands for. We understand the word "tree" because we have had experiences with trees. (Think of the moment the blind and deaf Helen Keller finally understood the meaning of the word "water" that was being signed into her hand; the epiphany occurred when she felt the water that came out of a pump.)

Harnad contends that for a computer to understand the meanings of the symbols it manipulates, it would have to be equipped with a sensory apparatus—a camera, for instance—so that it could actually *see* the objects represented by the symbols. A project like little Darwin VII—the robot with the camera for eyes and metal mandibles for jaws—is a step in that direction.

In that spirit, Harnad proposes a revised Turing Test, which he calls the Robotic Turing Test. To merit the label "thinking," a machine would have to pass the Turing Test *and* be connected to the outside world. Interestingly, this addition captures one of Turing's own observations: a machine, he wrote in a 1948 report, should be allowed to "roam the countryside" so that it would be able to "have a chance of finding things out for itself."

Toward Robots

The sensory equipment Harnad thinks of as crucial might provide a computer scientist with a way to supply a computer with the context and background knowledge needed to pass the Turing Test. Rather than requiring that all the relevant data be entered by brute force, the robot learns what it needs to know by interacting with its environment.

> To learn to think, a machine needs to "have a chance of finding things out for itself."

Can we be sure that providing sensory access to the outside will ultimately endow a computer with true understanding? This is what Searle wants to know. But before we can answer that question, we may have to wait until a machine actually passes the Robotic Turing Test suggested by Harnad.

In the meantime, the model of intelligence put forth by Turing's test continues to provide an important research strategy for AI. According to Dartmouth College philosopher James H. Moor, the main strength of the test is the vision it offers—that of "constructing a sophisticated general intelligence that learns." This vision sets a valuable goal for AI regardless of whether or not a machine that passes the Turing Test can think like us in the sense of possessing understanding or consciousness. M

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Fixing Forgetfulness

Memory troubles can have everyday causes and simple solutions BY CARSTEN BRANDENBERG

GARY S. CHAPMAN Getty Images

IF YOU WAKE UP one morning with a headache, you might assume that you drank one glass of wine too many the previous night, or that the heat was up too high, or that you are coming down with a cold. You are less likely to jump to the conclusion that you have a brain tumor. But when you find yourself forgetting things, then, omigosh, it must be the onset of Alzheimer's disease. Men and women who are middle-aged—or older, especially—are quick to diagnose themselves with inevitable dementia.

There is no need to panic if, lately, you have forgotten an appointment or a friend's birthday or where you placed your keys. The reasons for memory lapses are usually much less dire than suspected. Almost any form of stress or emotional pressure can cause memory problems—a well-documented fact that many people never consider. Figuring out the source of stress, and relieving it, can work wonders.

Lessen Overload

Stress, especially mental overload, is often responsible for memory deficits. Conflict at work, crises at home, worrying about friends, too much to do and lack of free time—all these conditions can prompt the brain to shut down to spare itself from exhaustion. One of the first functions that may be minimized is memory.

Attempting to cure the problem by undergoing intensive memory training, as many people do, or undergoing medical tests for dementia may be completely misguided. The extra work and the associated worry increase mental tension further, making the

(Job stress, **marital tension**, even mineral deficiencies are more likely culprits than Alzheimer's.)

Physical and mental exercise, a healthy diet and **relaxation techniques** can liberate memory.

memory problem worse—thereby reinforcing the suspicion that a terrible disorder is raising its ugly head. Instead of looking to beef up your brain, your time would be better spent ferreting out sources of psychological stress and trying to ease them. If job requirements are overwhelming, design ways to reduce them. If a personal relationship is troubled, consider counseling. When general stress is high, relaxation techniques such as yoga or tai chi can ease your body and mind and liberate memory.

If you want a personalized explanation for what appears to be inexplicable memory deterioration, then you might go to a memory clinic. Specialists will conduct a detailed interview using psychological and physical tests to determine whether you have a memory problem at all—and if so, why. A neurologist will test reflexes and defense mechanisms to see whether you have any physical problems. Psychological tests will assess whether you can draw conclusions adeptly, handle numbers correctly and name particular objects. Temporal and spatial orientation tasks will test your abstract thinking, judgment, and verbal and mathematical abilities as well as your ability to draw geometric figures. The exercise shown on this page at the right is an example of such a test. All these indicators can help identify memory problems—or assuage concerns about them.

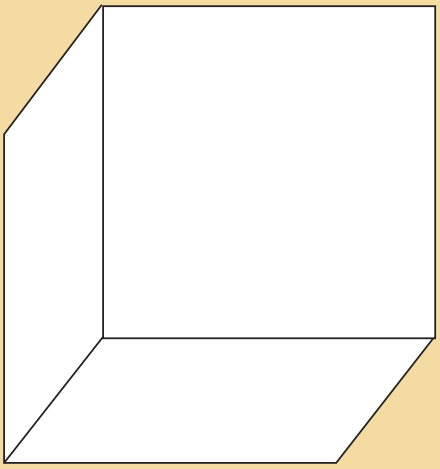
Drink More Fluids

In addition to stress, other routine conditions can affect the brain's recollections. Although some trouble with memory or recall is common as people reach their 60s and beyond, these challenges need not be accepted as unavoidable. Sometimes simple lifestyle changes can be helpful, even for 90-year-olds. A variety of physiological changes can cause memory impairments; for example, exceptionally high or low blood pressure or the onset of metabolic diseases such as diabetes can be contributors.

By examining an older person's general state of health, a geriatric specialist can determine whether aging may be the root of certain problems. Doctors are discovering seemingly minor changes that can bring about significant memory improvement. For instance, many elderly people have substantial fluid deficits or vitamin and mineral deficiencies, simply because they do not drink or eat enough or do not consume the right foods. An elderly man may consume little else but bread and cake only because a bakery is right around the corner and the supermarket is too far to reach on foot. A varied diet and lots of fluids can improve health—and memory.

An array of neurological and psychiatric conditions can lead to problems, too. Depression in old age brought on by loneliness, mild psychosis or personality disorder can impair memory. Yet physicians may be too quick to attribute the forgetfulness to Alzheimer's.

Occasionally, routine medications can create difficulties. Women who have trouble sleeping during their menopausal years may begin using sleeping pills and may continue using them for years thereafter. As they age, it can take longer for the active substance to dissipate in the body after waking, causing general drowsiness that complicates recall.



DO THIS FIRST! Commit this cube to memory, cover it and read this article. Then try to draw the cube and compare your drawing to the original. This is one kind of exercise given at memory clinics; if you do not re-create the cube exactly, don't worry—you are probably fine.

Simple expectations may be to blame for "bad" memory. In recent years tremendous attention has been focused by the media on issues of memory loss and Alzheimer's, capturing public interest. Overly sensitized, people tend to find deficiencies everywhere. Just because you cannot recall the answer to the ultimate question on *Who Wants to Be a Millionaire?* does not mean you are succumbing to incipient dementia; at most, it may mean that you need to brush up on your trivia. In the end, physical and mental exercise, a healthy diet, proper rest and, above all, stress reduction are the best ways to keep your memory sharp as you grow older. M

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GEHIRN & GEIST

Mind Reads

Putting People into Bins

Us and Them: Understanding Your Tribal Mind

by David Berreby. Little, Brown and Company, 2005 ($26.95)

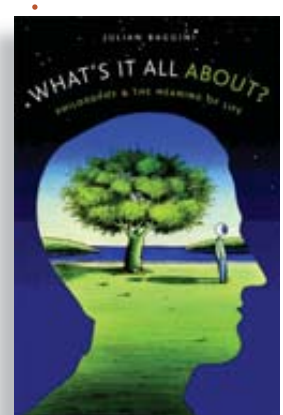
Each of us has experienced a feeling of kinship with someone who shares a love of chocolate, a passion for foreign films, or perhaps an affinity for a person with the same skin color or ethnic identity. We might also feel alienated from someone with the same qualities if he or she belongs to a "group" we do not like.

But what exactly is this seemingly natural tendency to sort others into "kinds"? This question forms the core of *Us and Them,* which explores the conscious and unconscious ways in which people classify one another—and more important—why. How humans can use this propensity constructively, rather than destructively, remains a central issue of our time, argues David Berreby, a veteran science journalist. Although this penchant may be hardwired into our brains, ultimately we choose how to live. Religious strife, political conflict and clan rivalries boil down to individual behavior.

Berreby says the sciences of brain and mind offer "a new way to look at love of country, at culture, at religion (and at hatred too)." Researchers are starting to understand "how and why people think and feel in tribes, and why all of us are capable of *both* tribal good and tribal evil." Advances are allowing scientists to grapple with such questions as "Why can't we all get along?" Berreby investigates the social, psychological and neurological mechanisms that move humans to categorize. For example, he considers how codes in the nervous system predispose us to organize perceptions, including ones that help us feel how other people feel.

Science's assault on our beliefs about race, religion and nationalism has shown that even much of "common sense" is both blind and cruel. Berreby reminds us that not long ago North Americans held by common sense that slavery was natural, women should not vote and only heterosexuals deserved respect. "Good riddance to all that," he says. Still, attitudes die hard. "A white person and a black person in today's New York City can agree over coffee that race is 'all in your mind,'" Berreby contends. "But when they leave Starbucks and raise their hands to hail a taxi, the white person is more likely to get a cab. In that moment, race is as real as gravity."

Given our drive to categorize, Berreby reflects thoughtfully on how to do so responsibly. "The Us-Them code does not own you," he concludes. "You own it." —*Richard Lipkin*



No Higher Purpose

What's It All About? Philosophy and the Meaning of Life

by Julian Baggini. Oxford University Press, 2005 ($23)

Nearly everyone has at some time wondered why we are here, what the purpose of life is. Julian Baggini's *What's It All About?* begins with these ruminations but shifts to the intimately related question of what makes life valuable and meaningful.

Baggini, founding editor of the *Philosopher's Magazine,* makes the rationalist-humanist assumption that reason and evidence are to be employed in the attempt to understand why we are here. He then proceeds to argue that inquiry into human origins and future human prospects does not reveal a purpose for human existence. Most confrontational to readers may be his skepticism about a God giving purpose to life. Is it plausible, he asks, to suppose that we are here to "be fruitful and increase in number; fill the earth and subdue it. Rule over the fish of the sea and the birds of the air and over every living creature that moves on the ground" (Genesis 1:28)? Why do we need to do this? And why would an all-powerful God create us to have us serve or worship him? Doesn't that suggest that God is an egotistical tyrant?

The conclusion that life lacks a "higher" purpose is often accompanied by great angst. Without such an overarching direction, life seems worthless. Baggini, however, challenges this view and provides some rough guidelines about what in fact makes life valuable to people. Helping others can give life meaning, insofar as it makes for an uplifted quality of life. Happiness, construed as something other than mere immediate sensual pleasure, is also a good thing. Success in parenting, in one's profession and in leading a morally decent existence can give life direction, too.

There is much to recommend Baggini's book. It is clearly written and reasoned, setting out the sober view that life can be meaningful even if purposeless. The principal shortcomings are those imposed by the genre of popular philosophy—the reader is likely to find that his or her particular views are not given the full attention they deserve. Nor are the author's positive views worked out in much detail. What this means, of course, is that *What's It All About?* is only a starting point for reflection. —*Ken Aizawa*

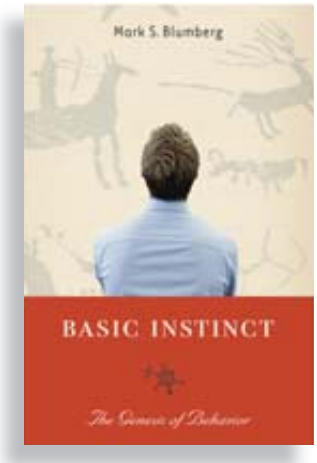
Inborn Contradiction

Basic Instinct: The Genesis of Behavior

by Mark S. Blumberg. Thunder's Mouth Press, 2005 ($24)

What is an instinct? A salmon swims upstream to spawn. A dog herds sheep. These inborn patterns of behavior characteristic to a species seem straightforward enough. Even Charles Darwin in *On the Origin of Species* remarked that "everyone understands what is meant" by an instinct.

Mark S. Blumberg, a neuroscientist at the University of Iowa, is not so convinced about creatures being born knowing how to do something, and he picks apart this notion in *Basic Instinct.* Even Darwin, he notes, became tangled in his own contradictions when he attempted to define and discuss instinct. Blumberg also notes that the issue of inborn knowledge is central to our origins and place on this earth. Do humans alone have the capacity for rational thought—that is, beyond instinctive reactions? Does experience shape instinct, perhaps even before birth? These are not idle questions, he maintains. "At stake is man's privileged place in the animal kingdom and the need to posit a god as the ultimate source of intelligent design."



After hundreds of years of debate, today's prevailing (and opposing) ideologies simultaneously hold that instincts derive either from divine influence or genes, chains of reflexes or nonreflexes, and learned or nonlearned behavior. Blumberg finds it puzzling that so much disagreement—even among scientists—prevails, and the debate over instinct's significance and role in human development has never been more heated. Nativists, he explains, argue that we are born with certain core capacities and knowledge that structure our learning throughout life. Nonnativists contend that the concept of instinct has "outlived its usefulness" and that to apply it to human infant development retards our understanding and learning about the process.

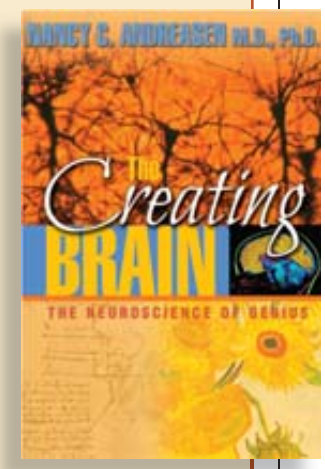
Blumberg ultimately sides with the nonnativists, explaining that too often the knee-jerk invocation of instinct is misleading. He asserts that the term "instinct" is usually just a convenient way to refer to complex, species-typical behaviors that seem to emerge mysteriously out of nowhere. Yet he believes this perspective is "an illusion fostered by the instinct concept." As the sciences of mind, brain, behavior and cognitive development now show, the very concept of instinct, he says, has become "less satisfying as an explanatory tool."

Blumberg's interest in the subject, by the way, may have been cast when he attended a debate between a nativist and a nonnativist. The room, he writes, was packed "with members nodding vociferously when *their* person was talking, and shaking their heads and muttering when it was the opponent's turn." —*Richard Lipkin*

Inspired, If Not Proved

The Creating Brain: The Neuroscience of Genius

by Nancy C. Andreasen. Dana Press, 2005 ($23.95)



What is the nature of creativity? What conditions foster it? What is going on inside the brain of a Mozart or a Shakespeare during the creative process? And is there a relation between creativity and mental illness, as often posited? Science thus far has produced only sketchy answers to these fascinating questions. *The Creating Brain* is a worthwhile inquiry into the subject and a reminder of how little is known.

Nancy C. Andreasen, a psychiatrist and neuroscientist at the University of Iowa who started her career as a Renaissance English scholar, argues that some characteristics of creative people—such as openness to new experiences and sensitivity to sensory inputs—may also make them more prone to mental and emotional problems. Her study of Iowa Writers Workshop participants shows a correlation between mood disorders and creativity, and other scientists have found similar tendencies in studies of literary and artistic types. Such research, however, has not shown a suspected link between artistic creativity and schizophrenic symptoms. Andreasen, who tends to draw conclusions primarily from her own work, notes that she is performing a study to see if any such tendency exists among especially creative scientists.

Despite the paucity of evidence, Andreasen suggests that creativity arises largely from the "association cortex"—parts of the frontal, parietal and temporal lobes that integrate sensory and other information. This idea, however, has just begun to be researched; Andreasen, again, relies heavily on her own study, this one done with positron-emission tomography (PET) scans of people's brains during free association.

In pondering the topic of genius, Andreasen points out that certain historical times and places have produced a bounty of brilliance. Among these "cradles of creativity" she lists ancient Athens, Renaissance Florence and mid- to late 19th-century Paris. Her list of factors spurring creative thought in such places is plausible if unsurprising: intellectual freedom, open competition, a critical mass of creative people, the presence of mentors and patrons, and some degree of economic prosperity.

Andreasen also provides tips for boosting creativity. For adults, she proposes exercises such as making close observations of a chosen item or imagining oneself to be someplace or someone else. Her suggestions for kids are mainly common sense, including less television exposure and more music and outdoor activity. *The Creating Brain* contains much of interest, even if breakthroughs lie mostly in the future.

—*Kenneth Silber*

askthe**Brains**

Do people lose their senses of smell and taste as they age?

—N. Sly, Windsor, Australia

Charles J. Wysocki, a neuroscientist at the Monell Chemical Senses Center in Philadelphia who studies variation among individuals in the perception of odors and the response of the human nose to chemical irritation, explains:

IT IS TRUE THAT as people age they often complain about decreases—or even losses—in their ability to taste a superb meal or a fine beverage. When people eat, however, they often confuse or combine information from the tongue and mouth (the sense of taste, which uses three nerves to send information to the brain) with what is happening in the nose (the sense of smell, which uses a different nerve input).

It is easy to demonstrate this confusion. Hold a handful of jellybeans of different flavors and close your eyes. With your other hand, pinch your nose closed. Now pop one of the jellybeans into your mouth and chew, without letting go of your nose. Can you tell what flavor went into your mouth? Probably not, but you most likely experienced the sweetness of the jellybean. Now let go of your nose. Voilà—the flavor appears.

This phenomenon occurs because smell provides most of the information about the flavor. Chemicals from the jellybean, called odorants, are inhaled through the mouth and exhaled through the nose, where they interact with special receptor cells that provide information about smell. These odorants then interact with the receptor cells and initiate a series of events that are interpreted by the brain as a smell.

Estimates for the number of odorant molecules vary, but they most likely number in the tens of thousands. Taste, on the other hand, is limited to sensations of sweet, sour, bitter, salty and umami (or savory—the taste of monosodium glutamate, or MSG).

With advancing age, the sense of smell diminishes—much more so than the decrease in sensitivity to tastes. This decrease may result from an accumulated loss of sensory cells in the nose (perhaps as much as two thirds of the original population of 10 million).

How long can humans stay awake?

—Samuel, Honolulu, Hawaii

The late **J. Christian Gillin** of the San Diego Veteran Affairs Healthcare Center and professor of psychiatry at the University of California, San Diego, conducted research on sleep, chronobiology and mood disorders. He had supplied this response:

THE QUICK ANSWER is 264 hours, or 11 days. In 1965 Randy Gardner, a 17-year-old high school student, set this apparent world record for a science fair. Several other research subjects have remained awake for eight to 10 days. All showed progressive and significant deficits in concentration, motivation, perception and other higher mental processes. Nevertheless, all recovered to relative normalcy with one or two nights of sleep.

The more complete answer to this question revolves around the definition of "awake." Prolonged sleep deprivation in normal subjects induces numerous brief episodes of light sleep (a few seconds), often described as "microsleep," alternating with drowsy wakefulness, as well as loss of cognitive and motor functions. Gardner was "awake" but basically cognitively dysfunctional at the end of his ordeal.

In certain cases of rare human medical disorders, the question of how long people can remain awake raises surprising answers—and more questions. Morvan's syndrome, for example, is characterized by muscle twitching, pain, excessive sweating, weight loss, periodic hallucinations and sleeplessness. In 1974 neurobiologist Michel Jouvet and his colleagues in Lyon, France, reported on a 27-year-old man with this disorder and found he had virtually no sleep over a period of several months. During that time the man did not feel sleepy or tired and did not show any disorders of mood, memory or anxiety. Nevertheless, nearly every day between 9 and 11 P.M., he experienced 20 to 60 minutes of auditory, visual, olfactory and somesthetic (relating to the sense of touch) hallucinations, as well as pain and blood vessel constriction in his fingers and toes.

In 1974 researchers reported on a 27-year-old man with a rare disorder who had virtually no sleep for several months.

The ultimate answer remains unclear. Will bioengineering eventually produce soldiers and citizens with a variant of Morvan's syndrome, who need no sleep yet remain effective? I hope not. A good night's sleep is one of life's blessings. As Coleridge wrote in *The Rime of the Ancient Mariner,* "Oh sleep! It is a gentle thing, beloved from pole to pole!" M

Have a question? Send it to editors@sciammind.com

PAOLO NOGUERAS

Head Games

Match wits with the Mensa puzzler

BY ABBIE F. SALNY

1 Use the same five letters to create two different words that make sense in the sentence below.

Many adults do not like snow, but children can have a different _ _ _ _ _. Many enjoy the pleasure of making a snow _ _ _ _ _.

2 The following colloquial expression describes a person who is not quite up to par intellectually. Start at the correct letter and move one letter at a time in any direction to find the saying. (Hint: start with an "I".)

R	E	T	R	F	I
C	A	H	I	D	M
A	N	E	D	U	B
E	B	'D	S	A	W

3 Sally went shopping for some new accessories. At the first store she spent one quarter of what she had plus $5. At the next stop, she spent half of what she had remaining plus $5. At the last boutique she spent one third of what she had left plus $10, leaving her with $10 for lunch. How much did she start with?

4 What is the five-digit number in which the first digit is twice the second, the third is half the fourth, the fifth is double the second, and the sum of them all is 21?

5 Break one word into two parts with completely different meanings. As one word, it is a noun for "a type of cloth." The correct solution for the two words includes a verb meaning "adheres" and another verb meaning "attempt."

6 Which word below logically comes next in the following sequence?

cat bell miss bolt _____

came
two
run
hope

7 Which word is the "odd man out"?

sail teak hurt pane

8 A palindrome is a word, phrase or sentence that is spelled the same backward or forward. The palindrome below tells what you do when the tool you are using gets dirty.

_ A _ _ _ _ _

9 Take the title of a real sports magazine, change one letter and invent a new publication for feeble athletes.

10 What is the number that is one more than one half of one third of one tenth of 12,000?

Abbie F. Salny, Ed.D., was the supervisory psychologist for American Mensa (www.us.mensa.org/sciamm) and Mensa International (www.mensa.org) for more than 25 years. She is the author and co-author of many challenging puzzle books, including the Mensa Think-Smart Book *and the* Mensa 365 Brain Puzzlers Page-A-Day Calendar *(Workman Publishing).*

Answers

1. Angle, angel.
2. "If dumb was dirt, he'd be an acre."
3. $100. $100 – ($100 ÷ 4 + $5) – ($70 ÷ 2 + $5) – ($30 ÷ 3 + $10) = $10.
4. 63,246.
5. Tapestry; tapes, try.
6. Run. The second letter of each word is a vowel, appearing in alphabetical order: a, e, i, o, u.
7. Pane. Each word can be rearranged to form another word, but the other three are girls' names: Lisa, Kate, Ruth.
8. WASH SAW.
9. *Sports Weekly* becomes *Sports Weakly.*
10. 201. 12,000 ÷ 10 = 1,200 ÷ 3 = 400 ÷ 2 = 200 + 1.

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AGE FOTOSTOCK (*left*); RENÉ SHENOUDA *zefa/Corbis* (*right*)