THE NEW GENETICS OF MENTAL ILLNESS *page 40*

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June/July 2008 www.SciAmMind.com

Don't Forget
Keys to Memory
page 48

The Creative Mind
How to release your inner genius

Avoid Mental Clutter
The Brain's Spam Filter

Bisexual Animals
What They Reveal about Us

Origins of Consciousness
Clues from Split Brains

PLUS:
Scratch This
The Science of Itching

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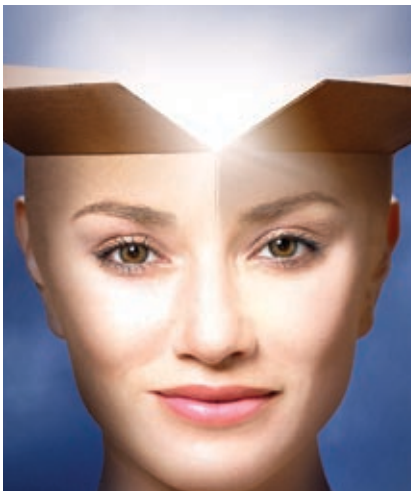

Out of the Box

Writer's block is not an affliction that I have ever suffered. So I was a little surprised at myself when I put off writing this column several times. I mulled a few options, but nothing seemed good enough to merit typing. Then it hit me: I was letting my unacknowledged fears and negativity squash my thinking. Why? Because the topic was how to tap the sources of inspiration itself—the subject of our cover story, "Let Your Creativity Soar."

My self-editing mistake was just one way we block our inner muse. But as you'll learn from our creativity experts—psychologist and contributing editor Robert Epstein, psychologist John Houtz, and poet, playwright and filmmaker Julia Cameron—*everyone* can cultivate new ideas, using a variety of techniques. Turn to page 24 to get their time-tested tips from our panel discussion.

Switching on a lightbulb is a visual cliché for creativity. But a different kind of switch, made of molecules, affects a number of other critical mental processes. Life's experiences add chemicals to the genes that control brain activity, dialing up or down the expression of various features. A special two-article section explores how these molecular mechanisms change our brains. "The New Genetics of Mental Illness," by psychiatrist Edmund S. Higgins, starting on page 40, looks at how the environment influences our susceptibility to depression, anxiety and drug addiction. "Unmasking Memory Genes," by neuroscientist Amir Levine, explains how such molecules shape memory and learning; see page 48.

How does our unified conscious experience emerge from the activity of billions of brain cells and numerous processing "modules" (brain regions associated with certain types of thought)? The mystery has long tantalized researchers. In "Spheres of Influence," neuroscientist Michael S. Gazzaniga finds some clues from his studies of split-brain patients, whose connective tissue between their two hemispheres has been separated. Are two brains better than one for learning about consciousness? Find out beginning on page 32.

Mariette DiChristina
Executive Editor
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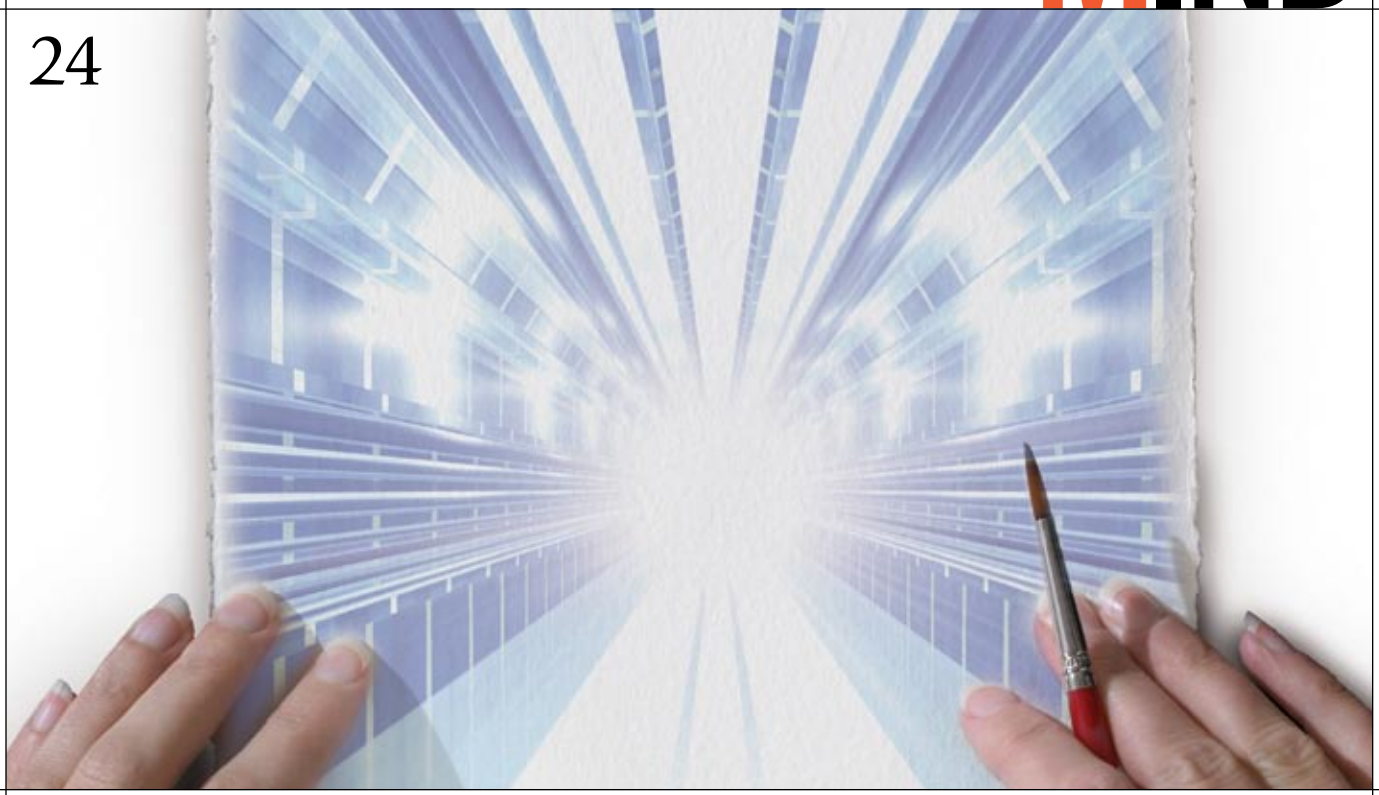
24



FEATURES

DEPARTMENTS

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KISSING THEORY

"Affairs of the Lips," by Chip Walter, suggests that the chemistry of a good kiss can predict the future of a relationship. In the "Kiss and Tell" editorial letter by Mariette DiChristina, the kiss leaves the man "speechless" and the woman with "a shivery thrill." There are undoubtedly chemicals transferred and brain areas activated, but that hardly explains the rich soul-stirring quality of a good kiss.

As a psychoanalyst, I find that the concept of incorporation goes much further in explaining the good-kiss experience than biology can. The couple's unconscious minds have been primed by attachment to incorporate the other person. In the kiss, they each take in the other's "good stuff," symbolized by each other's perceived oral quality. It is the rich lushness of the other's inner being that begins to feel augmenting and transformative to them both. They feel intensely graced by the presence of the other's qualities inside them.

This assimilation of the good other seems so instantaneously pleasurable as to be miraculous. But it is simply that when the unconscious mind incorporates the other, the act appears to the conscious mind like a magical process. Likewise, if the unconscious mind does not get enough preliminary signals of "good stuff," there will be no incorporation, and the kiss will not be magical, although it may still be erotically good.

Augustus F. Kinzel
Canaan, N.Y.

MORALITY BITES

In "When Morality Is Hard to Like," by Jorge Moll and Ricardo de Oliveira-Souza, I was intrigued by one of the test scenarios: Would it be moral to smother a crying baby to save a group of people hiding from a band of killers bent on murdering everyone? As usually posed, the choice is between the death of the baby and that of everyone in the group. But in reality, the smothered baby would lose consciousness before dying, at which point it would be safe to uncover its mouth. True, the chance of its death by accidental asphyxiation is quite real, but it is markedly less than that of death following discovery. Thus, preventing the baby from crying increases its probability of survival as well as that of the group.

This example demonstrates that studies of this type need to consider what are the alternatives that people actually think they are choosing between. The question is not just of methodological interest. Much of the brainpower spent making a difficult moral choice might go into finding a way to decide. If so, the processes of analyzing and interpreting the facts that surround and define the dilemma are of critical relevance.

Stephen M. Welch
Manhattan, Kan.

I was disturbed by David Pizarro's conclusion in "The Virtue in Being Morally Wrong" that "utilitarianism may, in the end, be the right moral theory." The decision about whether to push one man onto a trolley track to save five men farther down the tracks is a deeper question than he apparently assumes. A person making such a decision is not deciding simply if five is greater than one. He is deciding how bad he will feel if five people die versus how bad he will feel if he

pushes one man to his death. This feeling he is weighing is more than just some squishy sentimentalism—pushing that one man is equivalent to pushing the whole of human trust onto the tracks. After all, how could we function if we had to always watch our backs so as not to be sacrificed? These feelings are there for a good purpose—they evolved from a system of trust and respect that allows us to function successfully as a society.

David Butler
Mission Viejo, Calif.

WHERE THE YEARS GO

I very much enjoyed Pascal Wallisch's "An Odd Sense of Timing." According to the article, boring times seem longer when they are actually experienced but shorter when they are recalled, whereas active times seem shorter when experienced but longer when recalled.

Perhaps this explanation helps us to understand why, as we age, the days may seem to pass slowly while the years seem to fly by. Assume that there is increasingly less novelty and more similarity in our days as we get older. Then, according to the research cited, our days as we live them will seem increasingly longer, whereas our memories of those days will seem increasingly shorter. The end result is a mismatch between elapsed chronological time and the shorter-seeming psychological time that we remember as having elapsed.

Where do the years go? Apparently they are swallowed up in our memories of our less than exciting days.

Bob McCoy
San Francisco

REFUSING TO BE DUPED

In "Getting Duped," Yvonne Raley and Robert Talisse ask how the true situation in Iraq became so grossly distorted in American minds. They state that they do not think the deceptions were premeditated.

Perhaps Raley and Talisse have never heard about the White House Iraq Group, which White House Chief of Staff Andrew Card founded seven months before the invasion of Iraq. This group, chaired by Karl Rove, was created in August 2002 to market the Iraq War to America. Its escalation of rhetoric about the danger Iraq posed to the U.S. was part of the Bush administration's plan to sell the idea of a war.

The Bush administration used not only the rhetorical devices Raley and Talisse describe but also outright misrepresentation to sell the Iraq War to the American people.

Elizabeth Saenger
New York City

I was disappointed by "Getting Duped." It seems the authors were not interested in discussing the subject in any serious way but simply wanted to express their political bias.

What I got from the article is that conservatives dupe the public and, by omission, liberals do not. Tripe. By the way, the authors conveniently forgot that Representative John Murtha of Pennsylvania did call for immediate troop withdrawal, contrary to their claim that "nobody" called for such action and, therefore, Bush was invoking a "straw man." In fact, the whole article was an example of how we are often duped by others and how people dupe themselves.

Politicians may invoke a "straw man" to make their case seem stronger.

If I see any further articles like this shallow, politically biased one, I will cancel my subscription.

Paul Westbrook
via e-mail

RALEY AND TALISSE REPLY: *We received many letters accusing us of political bias based on the examples we chose, but such complaints are entirely beside the point. To charge someone with committing a fallacy is not to claim that his or her conclusion is false—in fact, it is not even to necessarily oppose the conclusion. Rather such a charge is simply to say that the argument does not support (much less demonstrate) the truth of the conclusion. So to say that, for example, President Bush has committed the "straw man" fallacy on some particular occasion is not to imply any evaluation of his position. Because nothing in the article entails a judgment about the truth of the positions promoted by those used as examples, it is difficult to make sense of the charge that the article is "biased."*

When identifying a fallacy, what matters is the form of the inference, not the content of the premises. We chose the examples in the article because we deemed them likely to be familiar to a general audience.

BOB THOMAS *Getty Images*

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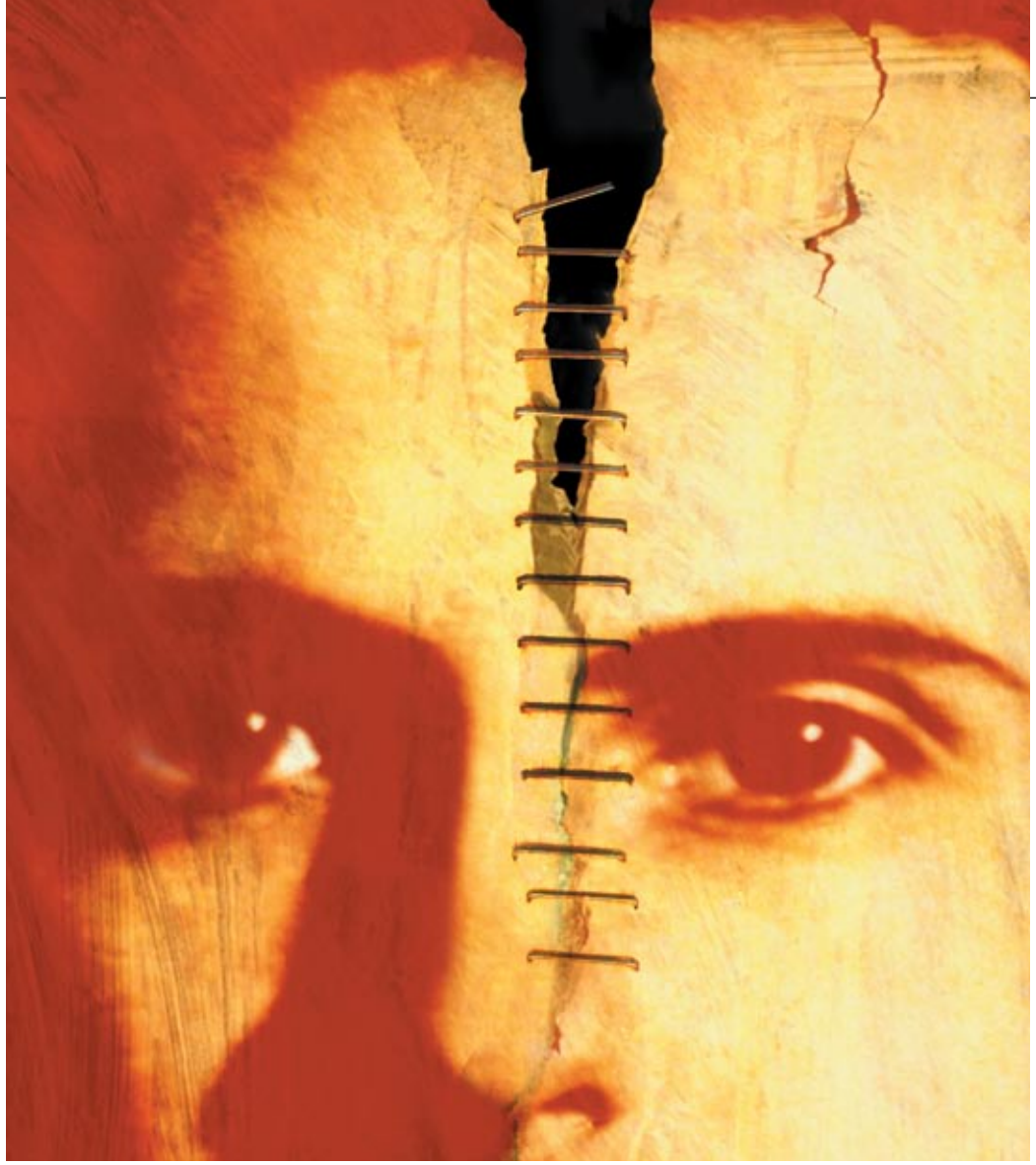


GETTY IMAGES

>> MEDICINE

A Novel Chemical Target

A drug for schizophrenia tweaks the brain's levels of glutamate

Antidepressants such as Prozac made serotonin a household word, and cocaine studies transformed dopamine into a synonym for pleasure. Now glutamate may finally find its fame, thanks to a new schizophrenia drug—the first ever to target this abundant neurotransmitter. The drug could usher in an era of better treatments for neurological ailments, including mood disorders, Alzheimer's, Parkinson's and brain damage from stroke.

Until now, clinical efforts to alter glutamate levels have failed because tinkering with this essential neurotransmitter, which excites neurons, is tricky. High concentrations of glutamate can trigger seizures or kill brain cells—and levels that dip too low can cause coma. The new agent avoids these dangers by binding only to a subset of glutamate receptors that have more nuanced effects on neurons. Researchers think it may work for schizophrenia by decreasing the abnormally high glutamate levels in certain brain areas that are associated with the disease. Restoring the glutamate balance could then reduce excessive amounts of dopamine, another key player in the disease, in a psychosis-related neuronal pathway.

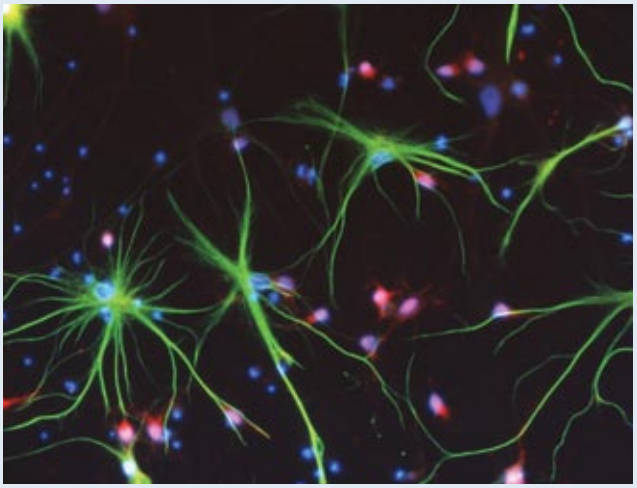
Researchers hope that aiming for glutamate will help patients who do not respond to the schizophrenia medications currently in use, which target only dopamine and serotonin. The new drug, which may reach the market in as few as three years, could also be a welcome alternative for patients who cannot tolerate the other drugs' side effects, which include involuntary repetitive movement and significant weight gain that often leads to diabetes.

Pharmaceutical companies are racing to produce more glutamate therapies. "There may be an explosion of new tools" targeting glutamate, says Darryle Schoepp, a Merck scientist who developed the novel drug while working at Eli Lilly. —*Susannah F. Locke*

>> NEUROSCIENCE

The Other Brain Cells

Glia are turning out to be much more than passive bystanders



Neurons have always been the stars of brain research, but scientists are now realizing that nonneuronal cells known as glia—which make up around 90 percent of cells in the brain—are not the mild-mannered understudies they appeared to be. Some glia may even fire electrical signals, a finding that overturns a central dogma of neuroscience that holds that neurons are the only cells in the brain with such signaling ability.

Last winter, when neuroscientists at University College London examined glia known as oligodendrocyte precursor cells (OPCs), they were astounded to find that, just like neurons, one subtype fired electrical signals in response to electrical stimulation. Before this study little was known about the function of OPCs, says study leader Ragnhildur Karadottir, except that they could develop into new oligodendrocytes, a type of glial cell that forms an insulating sheath around neurons like the rubber on an electrical cord.

"We were very surprised," Karadottir says. "The first thing one learns in neuroscience is that neurons fire action potentials and glia do not." The researchers suspect that, in these glia, action potentials—the rapid electric currents that travel along nerves—might serve as a signal to insulate an active neuron.

Other recent findings are further eroding the idea that glia merely provide food and support to neurons. Scientists have known for years that glial cells play an integral role at the neuromuscular junction, where nerves meet muscle in the body. But glia in the brain are much more difficult to study because they are harder to isolate, image and grow in the lab.

So a number of scientists are focusing on alternative ways to study glia. This winter a group of researchers at Stanford University compared the active genes of neurons, oligodendrocytes and astrocytes, the star-shaped glial cells that fill the spaces between neurons. Some of the astrocyte genes they found are important for phagocytosis, a crucial biological process by which healthy cells engulf and destroy bacteria or dying cells. This genetic footprint may indicate that astrocytes help to keep the brain clean of dying cells and scar tissue, says John Cahoy, the graduate student who led the study.

Many of the newly identified genes are completely unknown, however, and Cahoy says that his research on glia is just a start. As neuroscientists refine their understanding of the brain, they are realizing that cognition is even more complex than anybody imagined. "We're just opening the door on understanding how glial cells interact with neurons," Cahoy says. (For more on the role of glia in the brain, see "The Forgotten Brain Emerges," by Claudia Krebs, Kerstin Hüttmann and Christian Steinhäuser; SCIENTIFIC AMERICAN MIND, December 2004.)

—Katherine Leitzell

>> THE SEXES

She Never Forgets a Face

Women's memories get personal

Do women remember better than men do? Research shows that females may have an advantage when it comes to episodic memory, a type of long-term memory based on personal experiences. A Swedish team of psychologists showed, for example, that women are better on average than men at remembering faces, particularly female faces. These findings may have an evolutionary explanation that is rooted in female-female competition, says David C. Geary, a psychologist at the University of Missouri–Columbia who was not involved with the study. "Women certainly fought and continue to fight over the best guys … those with good genes and resources to invest in kids," Geary says. Remembering details of personal experiences is important for monitoring and maneuvering relationships, including disrupting the social and romantic ties of other women who are competitors, he says. Previous studies have shown that women also have a superior memory for verbal information, which they may use to dissect a person's underlying motives or intentions—a skill that, according to Geary, "seems to elude many men."

—Nicole Branan

NANCY KEDERSHA U.C.L.A./SPL/Photo Researchers, Inc. (top); CORBIS (bottom)

>> COGNITION

Learning with Language

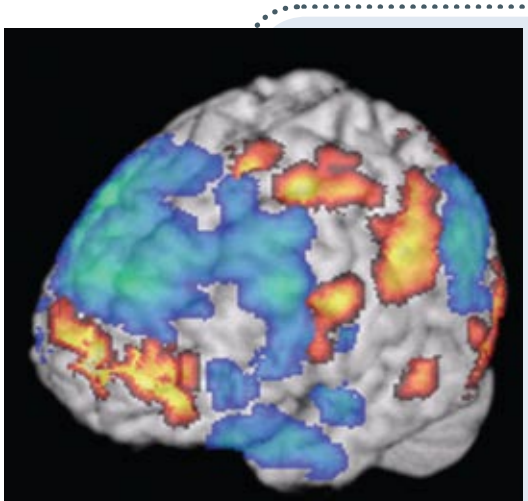
Words do more than convey information

Everyone knows that language is a great tool for communication, but scholars have debated for centuries whether it also plays an important role in learning. A new study supports this notion by showing that linguistic information boosts people's ability to sort objects.

A team led by Gary Lupyan, then at Carnegie Mellon University, asked volunteers to categorize 16 "aliens" that appeared on a computer screen as good guys or bad guys. All the aliens looked different, but half of them shared subtle features that distinguished them from the other half. Participants heard either a bell or a buzz to indicate whether their choice was correct or incorrect. But half of the volunteers received extra information: they also saw the word "leebish" or "grecious" appear on the screen, depending on which group the aliens belonged to. Those who received the linguistic cues learned to tell the difference between friend and foe much faster even though the nonsense words provided unnecessary information. And to rule out the idea that *any* additional cue might speed up learning, the researchers also tried giving the subjects nonlingual information about where the aliens lived; this hint had no effect. The results indicate that the words acted "as a glue," connecting the objects in each category, says Lupyan, who is now at Cornell University.

Related work by Lupyan and others has shown that language also affects visual processing. For example, when people are asked to rapidly find a 5 among 2s on a computer screen, they are able to pick out the target number more quickly when they hear the words "find the five" than when they hear static.

These findings reveal clues about how language might have evolved in our ancestors, Lupyan says. If language were only good for communication, then it would have value to users only if it were understood by others and, therefore, would have had to evolve as a group trait. "But if language also helps individuals think," he says, "then we can entertain other possibilities about its evolution, because people didn't actually have to understand each other fully for language to be a useful trait." —*Nicole Branan*



Jazz improvisation excited self-expression areas (*activation indicated by orange*) and suppressed self-control regions (*blue*).

>> ART

The Roots of Creativity

Improvising a jazz tune puts the brain in an altered state

Jazz greats have said that spinning off an improvised tune is like entering another world, and a new study has provided that world's first map. Researchers at the National Institutes of Health gave six professional jazz pianists a few days to memorize a never-before-seen tune. The musicians then tickled the ivories while being scanned by an MRI machine, playing the novel composition and an improvisation in the same key. As compared with the memorized melody, the improvised jam elicited stronger activity in the medial prefrontal cortex, a part of the brain active in autobiographical storytelling, among other varieties of self-expression. Supporting the altered-state notion, activity dipped in the dorsolateral prefrontal cortex (an area linked to planning and self-censorship), which, the researchers point out, is similar to what happens during dreams. They note that the same pattern might show up in all kinds of improvisations, from solving problems on the fly to riffing on a topic of high interest—such as, say, your favorite jazz musicians.

—*JR Minkel*

GETTY IMAGES (*top*); COURTESY OF CHARLES J. LIMB *Johns Hopkins Hospital* (*bottom*)

>> NEUROECONOMICS

Smokers' Choice

Certain people make decisions differently

Smokers tend to resist antismoking efforts that rely on "rational" approaches such as taxes, and researchers have pointed to confounding influences, including social factors and addiction. But differences in smokers' decision-making processes may also be at play.

A recent study from the Baylor College of Medicine found that smokers and nonsmokers react differently to news of how much they could have made in a stock-market game. The feedback was purely incidental: it offered no financial incentive to adjust one's investment strategy, yet nonsmokers were swayed by what might have been and changed their tactics. Smokers ignored the input, even though they processed the information in the same part of the brain as their nonsmoking peers did.

The study does not address whether smokers' behavior is a cause or an effect of their addictions but rather adds to a growing list of ways in which human beings sometimes ignore reason when it comes to decision making. In the book *Predictably Irrational* (HarperCollins, 2008), behavioral economist Dan Ariely of the Massachusetts Institute of Technology catalogues a bevy of errors, biases and otherwise illogical human behavior. Other behavioral economists are doing the same on the premise that these absurdities are understandable, and they are just beginning to team up with neuroscientists to try to tease out the roots of decision-making biases in the brain.

The hope is that this knowledge will one day inform policy. To combat smoking, for example, policymakers could "use evidence of what brain areas are active during the [decision-making] process to design other strategies" more nuanced than taxation, says behavioral economist Colin Camerer of the California Institute of Technology.

The field of neuroeconomics is in its infancy, however. Neuroscientists agree with behavioral economists that in the future it will be possible to use our irrationalities to our advantage, but as for whether their work could soon steer policy, "I think it's just too early" to make a decision, Ariely says.

—Lucas Laursen

GETTY IMAGES (*top*); MITSUHIKO IMAMORI *Minden Pictures* (*bottom*)

>> EVOLUTION

Big Brains Dominate

Waspish clues to human smarts

Experts have long suspected that complex social interaction drove the evolution of large brains in humans. Now a study in wasps supports and refines that theory: it seems that dominant individuals have larger brain regions responsible for higher-order cognitive processes.

Biologists at the University of Washington observed the behavior of paper wasps (*Mischocyttarus mastigorphorus*) in the Costa Rican rain forest and then measured the size of their brains. The researchers found that the so-called mushroom bodies, the lobes that underlie learning and memory in insects, were larger in dominant wasps than in their subordinate peers.

Mushroom bodies are the insect equivalent of the human neocortex, the outer layer of our brain, which handles complex cognition. Scientists have already established that the neocortex and the mushroom bodies are larger in social species such as humans and wasps, as compared with solitary animals such as bears and lone spiders. The new study suggests that competition for rank may have been a key factor in the evolution of this intelligence.

—Peter Sergo

BRAIN BITS

- **The "runner's high"** phenomenon may be widely known, but until now there was no evidence (other than athletes' anecdotes) that the effect actually exists. Neuroscientists at the University of Bonn in Germany finally confirmed with a new type of PET scan that strenuous exercise indeed releases a flood of endorphins in the brain, likely causing the widely reported euphoria that follows a hard workout.

- **Anticipating** a good laugh whisks away stress, say scientists at Loma Linda University. The researchers told one group of men that they would be watching a funny video; a second group was offered some magazines. As suspected, the group that got the comedy had much lower levels of stress hormones such as cortisol than the magazine crowd did. Most surprising: the video viewers' stress levels dropped before the film had even begun.

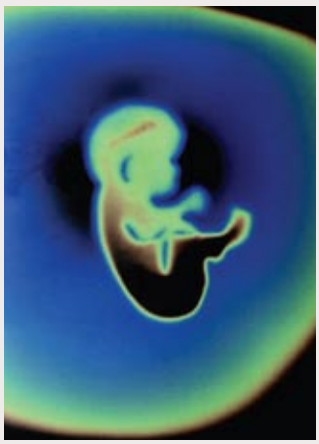
- **The dreaded** "sex talk" has long been an awkward tradition for moms and dads, but a growing body of research shows that many such conversations are better than one. The latest study, published in the March issue of *Pediatrics,* found that when parents repeatedly brought up sexual topics, their adolescent children reported feeling closer to them and more comfortable talking with them about personal issues. Previous studies have shown that kids who have closer relationships with their parents have sex later in life and are more likely to use contraception.

>> DEVELOPMENT

Autism and Antibodies

Could mom's overzealous immune system put her child at risk?

Every 18 minutes in the U.S., a baby who will acquire autism is born. Despite its widespread prevalence, scientists do not know what causes the developmental disorder—an array of genetic and environmental factors are probably involved. One such variable, a new study suggests, might be the womb: mothers of autistic children may produce immune proteins that react with and potentially harm their babies' brains during pregnancy.



Past studies have linked autism to the immune system—especially to autoimmune reactions, in which the body's defenses mistakenly attack native tissue. Autistic people are more likely than healthy subjects to make antibodies against their own brain cells, and autoimmune disorders such as type 1 diabetes are more common in mothers of autistic kids. Harvey Singer, a pediatric neurologist at Johns Hopkins University, wondered whether mothers of autistics might have passed aberrant antibodies to their children during pregnancy.

Singer and his colleagues collected blood samples from 100 mothers of children with moderate to severe autism and 100 mothers of healthy children. They extracted only the antibodies that could cross the placenta during pregnancy, then tested these antibodies against proteins from human fetal brain tissue. The team found that the blood from the mothers of autistic children reacted more strongly than that of the mothers of normal children against at least two fetal brain proteins. The two groups of mothers had reactions similar to each other against the other proteins.

"These immune factors may help turn on or trigger some potential underlying problem," Singer speculates. He does not yet know, however, the role the brain proteins play during development or whether the maternal antibodies actually influence their function. The team plans to investigate these questions by injecting human maternal antibodies into pregnant mice to see if their offspring show developmental problems. —*Melinda Wenner*

Mothers of autistic kids are more likely to have anti-brain immune particles in their blood.

>> HEALTH

So Lonely It Hurts

Chronic loneliness alters gene activity and leads to illness

Doctors have known for a long time that feeling lonely can make you physically sick, but until now they did not know why. The answer may be in our genes.

Researcher Steven Cole of the University of California, Los Angeles, and his colleagues there and at other institutions found that chronic loneliness triggers a change in gene activity. The initial results published last year showed that people who scored in the top 15 percent of the U.C.L.A. Loneliness Scale, a self-administered psychiatric questionnaire for measuring the emotion, exhibited increased gene activity linked to inflammation and reduced gene activity associated with antibody production and antiviral responses. These patterns of gene expression were specific to loneliness, not to other negative feelings such as depression.

But what could cause these changes? In a new study of 1,023 Taiwanese adults, Cole analyzed data from a variety of lonely people and found that the hormone cortisol was not doing its job of suppressing the genes associated with inflammation. Inflammation is a known risk factor for a variety of serious illnesses, such as heart disease and cancer. Recent animal studies from Cole's group confirm the link: cortisol receptors stopped working in rhesus monkeys that were socially stressed.

Yet questions still remain. Cole and his colleagues are now working with patients in Chicago to try to determine how different degrees of loneliness affect health. Do all lonely people suffer some damage, or is there some threshold at which feeling isolated starts affecting the body? "We are just touching the tip of the iceberg" in our understanding of loneliness, says University of Chicago team member John Cacioppo.

—*Victoria Stern*

GETTY IMAGES (*top*); ERIC McNATT *Jupiterimages* (*bottom*)

GETTY IMAGES

>> IMAGING

Can You Read My Mind?

With a brain scanner, researchers can guess what you see

Legions of science-fiction authors have imagined a future that includes mind-reading technology. Although the ability to play back memories like a movie remains a distant dream, a new study has taken a provocative step in that direction by decoding neural signals for images.

Neuroscientist Kendrick Kay and his colleagues at the University of California, Berkeley, were able to successfully determine which of a large group of never-before-seen photographs a subject was viewing based purely on functional MRI data. By analyzing fMRI scans of viewers as they looked at thousands of images, Kay's team created a computer model that uses picture elements such as angles and brightness to predict the neural activity elicited by a novel black-and-white photograph. Then the researchers scanned subjects while showing them new snapshots. Most of the time Kay's model could single out which image the subject was viewing by matching its prediction of brain activity to the actual activity measured by the fMRI scanner, although very similar pictures tended to baffle the program.

Kay's reproduction of the age-old "pick a card, any card" trick is intriguing to visual neuroscience researchers because of his algorithm's versatility. Perhaps more interesting to science-fiction buffs is Kay's opinion that someday his algorithm might perform "at least some degree of [image] reconstruction" based on fMRI data. Starting from brain activity alone, his model should be able to deduce, for example, an image's overall brightness. The team has not yet studied the model in this capacity, however; Kay says it is too early to gauge exactly how much information the program can glean from a brain scan.

As for truly reading people's thoughts, Kay does not foresee anything of that nature in this century. Technological improvement, he explains, may yield piles of brain data. Without sufficient insight into the brain's workings, however, we will have no idea what it all means.

—Christopher Intagliata

>> TECHNOLOGY

Quieting the Brain

Aiming at tinnitus's roots

Twelve million Americans seek medical relief from the perpetual whooshing, ringing or roaring noise of tinnitus, but there is currently no cure. Treatments such as electrical shocks, pills and sound therapy have had only limited success. But as researchers learn more about the causes of tinnitus—and its devastating emotional toll—they are discovering better options.

Researchers at Neuromonics in Bethlehem, Pa., have developed a new iPod-like device called Neuromonics Oasis, which tackles each tinnitus sufferer's unique combination of emotional and auditory symptoms. The portable music player delivers New Age and baroque tunes, which serve a double purpose: the music provides psychological relief from the agony of hearing phantom noise, and it addresses the complex neurological roots of tinnitus.

When ear damage or normal aging mutes certain sound frequencies, some experts believe the brain becomes hyperactive as it strains to hear those missing data. "The brain wants a signal," explains neuroscientist Richard Salvi of the University at Buffalo, "so it starts turning up the volume." The Neuromonics system boosts the intensity of musical frequencies at which a user has poor hearing, fulfilling the brain's need for input. The device also attempts to train users to tune out their tinnitus—like tuning out the humming fridge—by slowly lowering the music's volume over several months of treatment. As the music transitions from continuously covering up the "brain static" to intermittently obscuring and revealing it with sonic peaks and troughs, the brain gradually habituates by ignoring the tinnitus as well as the repetitive music accompanying it.

The Neuromonics device has been successful in more than 2,000 tinnitus patients so far, but it is not without critics. Neurologist Jack Wazen, who is conducting clinical trials with the device at the Silverstein Institute in Sarasota, Fla., noted that only half his tinnitus patients can afford its $3,500 to $6,000 price tag. And as with other treatments, Neuromonics is not for everyone. Marc Fagelson, an audiologist at East Tennessee State University, says, "It doesn't work for musicians, because they don't like the way it sounds. But for most people who weren't weaned on the Sex Pistols, it is a well-designed package." —*Christopher Intagliata*

>> PSYCHIATRY

Moody Blood

Testing for depression

If only mood rings really worked. With no easy test for mood disorders, doctors must rely on patients' subjective reports of their emotional states to make a diagnosis. But help may be on the way—researchers have discovered markers of depression and mania in blood, taking a significant step toward developing a blood test for mood.

A team of molecular psychiatrists led by Alexander Niculescu of the Indiana University School of Medicine extracted RNA—genetic material that turns genes on and off—from the blood of people with bipolar disorder. The researchers identified 10 genes that display different patterns of activity during episodes of depression and mania. "We were pleased and surprised to get a blood readout that correlates with symptoms of the illness and things that happen in the brain," Niculescu says. The changes in genetic activity indicate high and low moods with 60 to 80 percent accuracy.

Five of the genes are involved with myelin, the white matter that insulates neurons and facilitates their communication. Myelin deficits have been associated with schizophrenia and alcoholism, but whether they are a cause or a symptom of these diseases is unknown. Nevertheless, such deficits could serve as a red flag.

"To find particular biomarkers for mental illness is very significant," says Akira Sawa of Johns Hopkins University, who is searching for similar signposts of schizophrenia.

Broader studies must be done to assess how time, gender and medications may influence gene expression, but Niculescu expects a blood test for mood disorders to be available within about five years. "Having an objective test for a disease state, its severity and especially its response to treatment would be a big step forward," he says. —*Melissa Mahony*

TIM VERNON *LTH NHS Trust/Photo Researchers, Inc. (top)*; ADAMSMITH *Getty Images (bottom)*

ALVARO LEIVA *age fotostock*

>> BUSINESS

The Cubicle Bully

Worse than sexual harassment?

Most people think of bullies as a playground issue for schoolchildren. Adult bullying in the workplace, however, can be extremely harmful to its victims—even more so than sexual harassment—and it may be far more common than most people realize, according to new research.

Business researchers Sandy Hershcovis of the University of Manitoba and Julian Barling of Queen's University in Ontario combined and analyzed 111 studies on workplace social dynamics. They discovered that as compared with workers who have experienced sexual harassment, victims of bullying report feeling angrier and more stressed at work—and are more likely to quit their job.

Workplace bullying, which includes ostracizing co-workers, spreading office gossip, and insulting people about their job performance or private life, is also more prevalent than sexual harassment. According to the Workplace Bullying Institute (WBI), a nonprofit organization that advocates for victims' rights, 37 percent of U.S. employees have been bullied at their job, as opposed to 8 to 10 percent who have been sexually harassed.

Psychologist Gary Namie, director of the WBI, thinks the lack of legal consequences is one reason bullying causes more harm than sexual harassment does—its victims often suffer without receiving much help or sympathy. "Bullying situations are minimized as 'mere personality conflicts,' and targets feel delegitimized," Namie says. Hershcovis thinks the simplest solution is for companies to take things into their own hands: "Implementing [company] policy and enforcing it is the best way" to stop bullying, she says. *—Jane N. Kim*

>> SATIETY

Faux Sugar: Bittersweet

Artificial sweeteners may hinder a diet more than they help

Splenda is not satisfying—at least according to the brain. A new study found that even when the palate cannot distinguish between the artificial sweetener and sugar, our brain knows the difference.

At the University of California, San Diego, 12 women underwent functional MRI while sipping water sweetened with either real sugar (sucrose) or Splenda (sucralose). Sweeteners, real or artificial, bind to and stimulate receptors on the taste buds, which then signal the brain via the cranial nerve. Although both sugar and Splenda initiate the same taste and pleasure pathways in the brain—and the subjects could not tell the solutions apart—the sugar activated pleasure-related brain regions more extensively than the Splenda did. In particular, "the real thing, the sugar, elicits a much greater response in the insula," says the study's lead author, psychiatrist Guido Frank, now at the University of Colorado at Denver. The insula, involved with taste, also plays a role

in enjoyment by connecting regions in the reward system that encode the sensation of pleasantness.

Although Splenda elicits less overall activity within the brain, the researchers were surprised to find that the artificial sweetener seems to inspire more communication between these regions. "Looking at the connection between the taste areas, Splenda is stronger," Frank says. He suggests that when we taste Splenda, the reward system becomes activated but not satiated. "Our hypothesis is that Splenda has less of a feedback mechanism to stop the craving, to get satisfied."

If that theory plays out, there could be implications for those who use artificial sweeteners as a weight-control aid. Recent research indeed suggests a correlation between artificial sweetener intake and compromised health. In one large survey, diet soda consumption was found to be associated with elevated cardiovascular and metabolic disease risk. A different study reveals a possible mechanism behind this effect: rats that were fed artificially sweetened yogurt in addition to their regular feed ended up eating more and gaining more weight than rats that ate yogurt with real sugar. The study's authors suggest that exposure to an artificial sweetener may undermine the brain's ability to track calories and to determine when to stop eating.

"There is good evidence that the brain responds differently to artificial sweeteners, and you should take that into account when designing weight-loss programs," Frank says. The team plans to extend this research to elucidate mechanisms that underlie eating disorders. —*Lisa Conti*

>> MEMORY

Put the Kid on the Stand

Children may make fewer memory errors when recalling an event

In court, many people assume that adult witnesses are more reliable than children. This bias may be unfair, according to a growing number of studies. Although adults remember a greater amount of accurate information, they tend to focus on the meaning of an event, which leads to more "false memory" mistakes—they recall something that makes sense in context but is actually a detail fabricated by their brain. Children, the new research shows, do not make such errors as often.

Although studies have shown this trait in kids before, critics sometimes blame the study methods, which rely on word lists. When adults read the words "dream," "pajamas" and "bed," they often mistakenly remember seeing the word "sleep." Children do not make these meaning-based inferences as often, but skeptics suggest that this result can be attributed to the fact that kids simply may not be familiar with some of the words they are asked to recall or recognize, such as "surgeon" or "physician."

Researchers at the University of Tennessee at Chattanooga and other institutions countered these criticisms by using word lists generated by second-grade children. They then found that other second graders did not make many false-memory errors, fifth graders sometimes resembled adults and sometimes the younger children—depending on the task—and by eighth grade the kids were thinking like grown-ups.

Younger kids "don't seem to view the world in quite the connected way that adults do," says psychologist Richard Metzger, lead author of the study. The findings answered what was "going to be a nagging question" about whether the results in children were real, says Charles Brainerd, a psychologist at Cornell University who evaluated Metzger's research as part of a review of more than 30 studies of false memory in children. Many psychologists hope this type of research will bolster the credibility of children's testimony in court. —*Rachel Mahan*

JUPITERIMAGES (*top*); AGE FOTOSTOCK (*bottom*)

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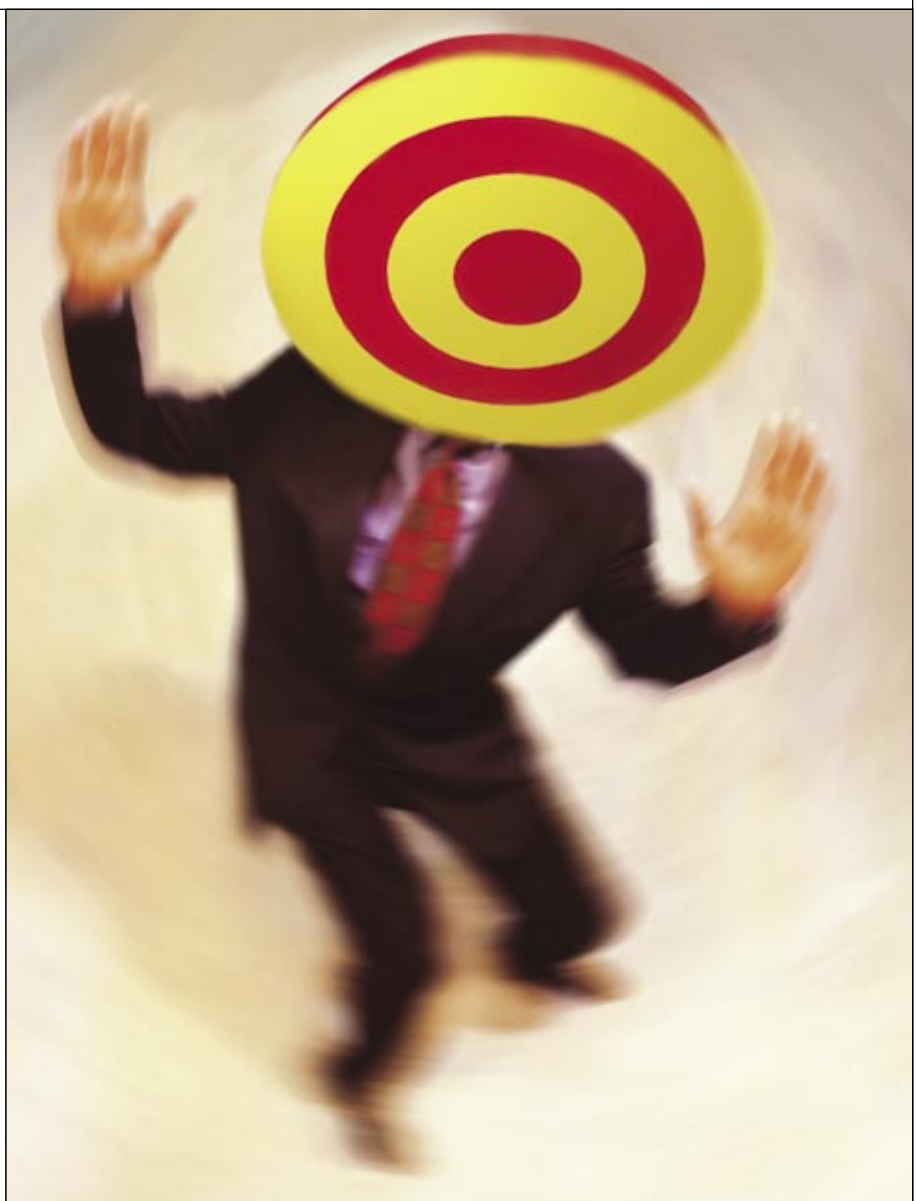
Character Attacks

A new theory parses fair from unfair uses of the ad hominem

BY YVONNE RALEY



A DOCTOR tells her patient to lose weight, and the patient thinks: "If my doctor really believed that, she wouldn't be so fat." A movie aficionado pans the latest Tom Cruise flick because Cruise is a Scientologist. A homeowner ignores a neighbor's advice on lawn care because the neighbor is a … you name it: Democrat, Republican, Christian or atheist. These examples illustrate classic uses of ad hominem attacks, in which an argument is rejected, or advanced, based on a personal characteristic of an individual rather than on reasons for or against the claim itself.

Putting the focus on the arguer or person being discussed can distract us from the issues that matter. Rather than concentrating on an individual's character, we should, in these cases, be asking ourselves questions such as, Is the doctor's advice medically sound? Is the Cruise film entertaining? Is the neighbor's lawn healthy? Meanwhile ad hominem attacks can also unfairly discredit an individual, especially because such critiques are often effective.

Although ad hominem arguments have long been considered errors in reasoning, a recent analysis suggests that this is not always the case. In his new book, *Media Argumentation: Dialectic, Persuasion, and Rhetoric*, University of Winnipeg philosopher Douglas Walton proposes that fallacies such as the ad hominem are better understood as perversions or corruptions of perfectly good arguments. Regarding the ad hominem, Walton contends that although such attacks are usually fallacious, they can be legitimate when a character critique is directly or indirectly related to the point being articulated.

If Walton is right, distinguishing clearly between these cases is important to evaluating the validity of statements people make to us about others. Good or fair uses of ad hominem critiques should, in fact, persuade us, whereas unwarranted uses should not.

Corruptions

Which ad hominem arguments should we aim to ignore? In the so-

(Ad hominem attacks can be **legitimate** when a character critique is related to the point being made.)

BARROS & BARROS *Getty Images*

called abusive ad hominem, someone argues that because a person has a bad character, we should not accept that person's claims. For instance, during the presidential campaign of 1800, John Adams was called "a fool, a gross hypocrite and an unprincipled oppressor." His rival, Thomas Jefferson, on the other hand, was deemed "an uncivilized atheist, anti-American, a tool for the godless French." Accusations like these can easily foreclose on intelligent political discourse about what might make either candidate a good president.

Another illegitimate form of the ad hominem is the tu quoque, or "you, too" version, which is an attempt to discredit a person's claims because the person has failed to follow his or her own advice. The example of the overweight doctor prescribing weight loss falls into this category. Its use is unfair because, after all, there are good reasons for losing weight, and the fact that a doctor has not managed to heed her own advice should not dissuade others from trying to follow it.

The Cruise attack, on the other hand, exemplifies "poisoning the well," another brand of ad hominem attacks in which the character assault is launched before the listener has a chance to form his or her own opinion on a subject—in this case, Cruise's film. If successful, the reminder that Cruise is affiliated with Scientology will bias the listener against the movie. This partiality is unjustified, because Cruise's religious affiliation is not germane to his acting abilities or the entertainment value of his movie.

Fair Use

What types of ad hominems might then be justified? Walton argues that an ad hominem is valid when the claims made about a person's character or actions are relevant to the conclusions being drawn. Consider, for example, former New York governor Eliot Spitzer, who was caught on a wiretap arranging to hire a prostitute for $4,300. Because this behavior ran counter to Spitzer's anticorruption platform, its unveiling would prevent Spitzer from governing successfully; thus, criticizing this aspect of his character was relevant and fair. In an earlier scandal, in 1987, televangelist Jimmy Swaggart was seen at a motel with a prostitute. Because his behavior undercut his preaching and status as a Christian role model, a character attack based on this incident would have been spot-on.

In another case, when President Bill Clinton fibbed on national television about his affair with White House intern Monica Lewinsky, accusations that he was a liar were not entirely unjust. Although a supporter might argue that Clinton's sex life was not directly relevant to his ability to govern, his ability to adhere to the truth could certainly be, and his willingness to lie on this occasion could call into question the veracity of his remarks on other subjects.

Of course, we should not discount everything any person says, no matter how badly he or she has been discredited. The fact that a person lies or behaves improperly on one occasion does not mean that he or she lies or behaves inappropriately all the time. Again, a critique of a person's character should not prevent further examination of the arguments at hand. After all, which position is right is usually independent of a person's character or conduct.

Being aware of how the ad hominem attack works can help us evaluate which instances of its use we should ignore and which we should consider. Ask yourself: How relevant is a political candidate's character or action to his or her ability to perform in office? How pertinent is any person's past or group affiliation to the claims that person makes or to that individual's expertise in a specific domain? If the character-based attacks are not relevant to these larger issues, then they are best ignored. Instead we should attend to what is really important: What is a person asserting? Why does he or she offer a particular view, and is the view defensible? M

Consider: How **pertinent** is a politician's personality or behavior to his or her ability to perform in office?

Former New York governor Eliot Spitzer.

MARY ALTAFFER *AP Photo*

YVONNE RALEY is assistant professor of philosophy at Felician College in Lodi, N.J., where she teaches critical reasoning, among other subjects.

(Further Reading)

- **Media Argumentation: Dialectic, Persuasion, and Rhetoric.** Douglas Walton. Cambridge University Press, 2007.
- **Becoming a Critical Thinker: A User Friendly Manual.** Fifth edition. Sherry Diestler. Prentice Hall, 2008.

Sliding Stripes

A few simple experiments untangle the mysteries behind the Barber Pole Illusion

BY VILAYANUR S. RAMACHANDRAN AND DIANE ROGERS-RAMACHANDRAN

EARLY GESTALT psychologists—including Stuart Anstis of the University of California, San Diego, and the late Hans Wallach—were intrigued by what they referred to as the Barber Pole Illusion (*a*). A vertical cylinder with spiraling red and white stripes painted on its surface is made to spin on its long axis. Even though the stripes are actually moving horizontally, around the pole, they appear to move vertically (up or down the pole, depending on direction of spin).

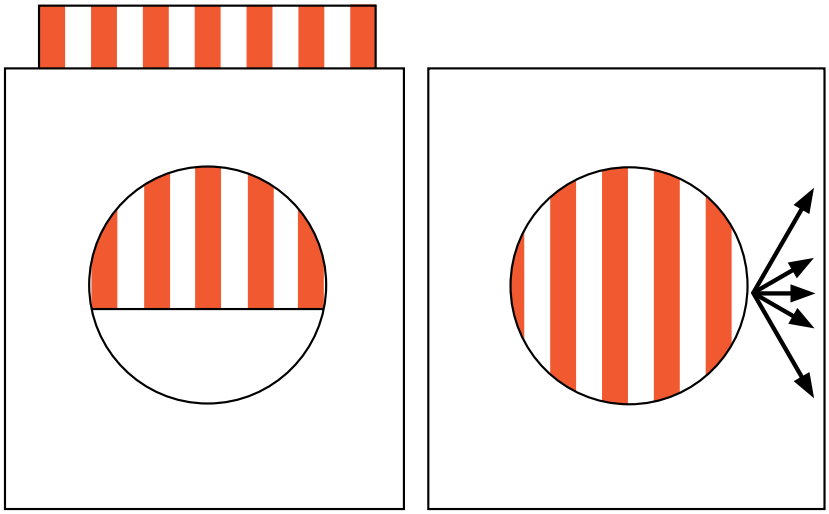
The illusion is a powerful demonstration of the point we have made repeatedly in this column—perception does not mimic physics. It involves the brain's interpretation—derived from an image on the retina located at the back of the eye—to pass judgment on what is happening out there in the world. But what causes the illusion?

Let us consider a simpler case: a card painted with vertical stripes moving horizontally behind a circular aperture (*b*). Here the outer margins of the striped card are shown schematically to make it clear what is going on behind the aperture. They would not be visible, however, when the actual display is viewed. You can make this simple setup at home by cutting from a large piece of cardboard a circular aperture, say one to two inches in diameter. Then use a second, smaller cardboard with vertical stripes, alternating white and red, about four to six stripes to an inch. Have someone else move the striped card back and forth along any axis while you look at the stripes within the aperture and judge their direction of motion.

As the Barber Pole Illusion demonstrates yet again, perception does not **mimic physics**.

JUPITERIMAGES

Even though the visual stimulus itself is ambiguous, **your perception** of it is not.



b

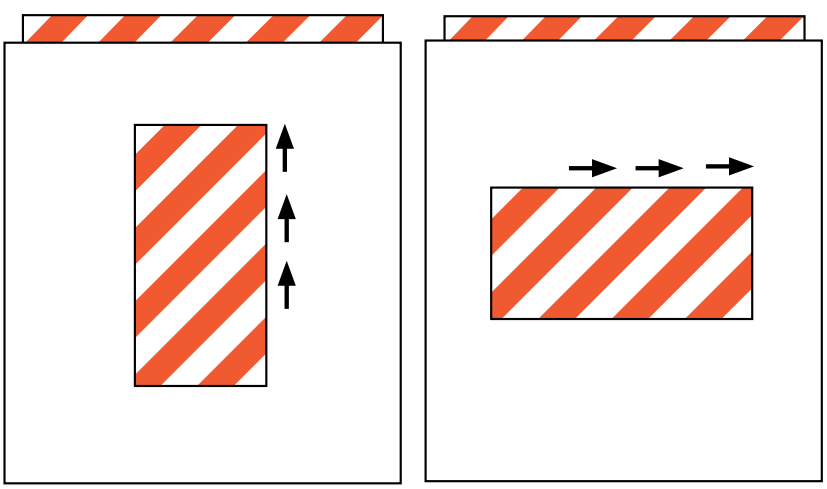
If the striped cardboard is moved horizontally, then, not surprisingly, you will see the stripes moving horizontally. But if the stripes were actually moving *diagonally* at a faster speed, the stimulus on the retina would be exactly the same. In fact, there is a family of vectors (that is, directional movements) of varying speeds and orientations that would all produce the same changing image on the retina. This family of vectors is indicated in *b* by arrows of different lengths, which represent speed and direction. Yet even though the stimulus itself is ambiguous, your perception is not; you always see the stripes moving orthogonally to their orientation; it seems to be the default for our perception, other things being equal. You do not see the stripes moving diagonally at a higher speed. The brain solves the so-called aperture problem by assuming a default.

Inside the Box

Now let us reconsider a stimulus like the barber pole—that is, one in which the aperture is rectangular and vertical, and the stripes are diagonally oriented (*c*). As you try the same experiment with this new setup, you might expect that the default perception will be the same—of motion perpendicular to the stripes' orientation. But it is not; you do not see diagonal motion. Instead, these stripes invariably appear to move vertically along the aperture's long axis (as in the barber pole). Why?

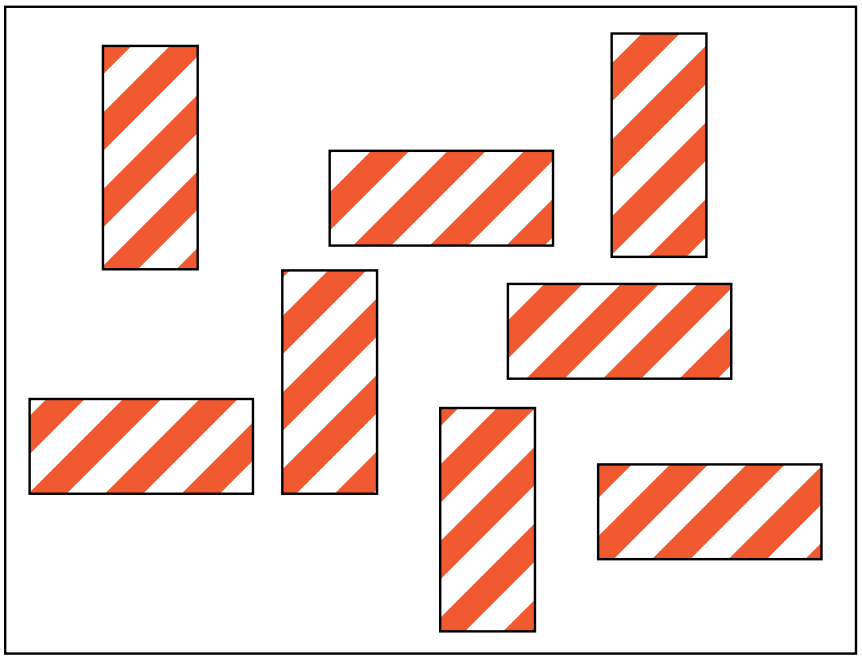
One reason may be that there is an additional factor at work in this case. Notice that even though the direction (and velocity) the stripes move in is still ambiguous, the tips (or sharp endpoints) of the lines are moving unambiguously upward along the long axis of the aperture (or cylinder, in the case of a real barber pole). The motion of these "terminators" may help disambiguate the direction of movement; the tips "drag" the stripes in a single upward direction, an effect that some researchers refer to as "motion capture." This phenomenon explains the Barber Pole Illusion. You might say that unambigious motion tips off the brain and dictates that the entire stripe pattern be seen moving (*arrows in c*) along the length of the pole, whether that pole is horizontal or vertical.

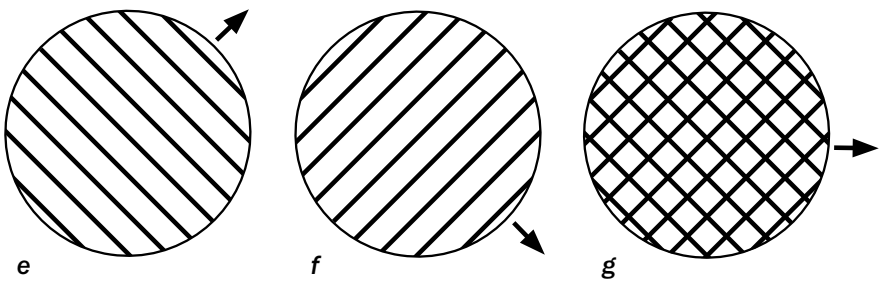
We can challenge the visual system by creating a display such as *d*, which is made of a randomly scattered group of vertical and horizontal apertures behind *all* of which stripes are moving diagonally. If you focus on any one of the openings, you will see either horizontally or vertically moving stripes, as expected. But with a bit of effort, you can make yourself see the entire display as a "whole." In that case, you perceive the *tout ensemble* as a single large diagonally moving set of stripes seen through a giant opaque card from which horizontal and vertical apertures have been cut out in random locations. Your visual system "thinks" this perception is a more economical description of the data than is the vision of independent barber poles scattered in the world in precisely this manner by some mad Martian intent on confusing you. Your immunity to



c

Your immunity to seeing independent barber poles implies some **fairly complex** visual-system rules.





seeing independent barber poles implies that some fairly complex rules of image segmentation (including "completion" of the striped surface behind horizontal and vertical windows) must be wired into the visual system.

Where Constraints Intersect

Or take another example. In *e* you will tend to see motion 45 degrees up and to the right, and in *f* 45 degrees down and to the right, as indicated by the arrows.

Now what if you superimpose the two? Do you see them sliding past each other at right angles? The answer is no; you see the plaid moving horizontally (*indicated by arrow in g*). Perception researchers Edward H. Adelson of the Massachusetts Institute of Technology and J. Anthony Movshon of New York University have done some clever experiments to show that, contrary to naive intuition, this effect does not happen simply by averaging the vectors of the two stripes. It happens because of a principle they dubbed "intersection of constraints." Each grating's motion is compatible with a family of vectors, and the region of overlap—where the two families overlap—is taken as the "true" direction of motion. Intriguingly, motion-sensitive cells in areas of the brain (including one called MT) at work early in the visual hierarchy of motion processing respond to the direction of each grating separately ("component motion"), whereas cells at a higher level respond to the overall direction of the plaid ("plaid motion"). It is as though the cells were integrating the output of the component sensitive cells by deploying the intersection-of-constraints algorithm.

There is an alternative model to the intersection of constraints. Notice in *g* that even though the motion of the component stripes is ambiguous the intersections between the lines are moving unambiguously horizontally. These crossover points might "capture" and drag along the gratings horizontally (analogous to the role of the sharp tips in the vertical aperture or barber pole).

At present, no compelling reason exists to choose one model over the other; the former (intersection of constraints) is more mathematically elegant and might appeal to a cosmologist, whereas the latter (a messy "shortcut") might appeal to a biologist.

The original barber pole pattern is supposed to depict blood and bandages, harking back to an era when barbers were also surgeons. Little did they realize that the illusion could provide such razor-sharp insights into human motion perception. M

VILAYANUR S. RAMACHANDRAN and DIANE ROGERS-RAMACHANDRAN are at the Center for Brain and Cognition at the University of California, San Diego. They serve on *Scientific American Mind*'s board of advisers.

(Further Reading)

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- **Transparency and Coherence in Human Motion Perception.** G. R. Stoner, T. D. Albright and V.S. Ramachandran in *Nature,* Vol. 344, pages 153–155; March 8, 1990.

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(calendar)

June

13 If you spill some salt and walk under a ladder at the Exploratorium's new **Superstition Obstacle Course**, you won't have to knock on wood—you'll be conducting these rituals as you learn why our brain is evolutionarily primed to concoct superstitions and how these beliefs shape our actions, emotions and judgment. The course of breakable mirrors and cracked sidewalks is a temporary addition to the science museum's permanent "Mind" collection.
San Francisco
www.exploratorium.edu

13 When a wheelchair-bound radio journalist meets a healthy woman who envies his paralysis in the movie ***Quid Pro Quo***, he finds his own identity challenged as he uncovers the reasons behind her seemingly strange desire. (Learn more about the real-life diagnosis of body integrity identity disorder in "Amputee Envy," by Sabine Mueller; SciAm Mind, December 2007/January 2008.)
Magnolia Pictures
www.magpictures.com

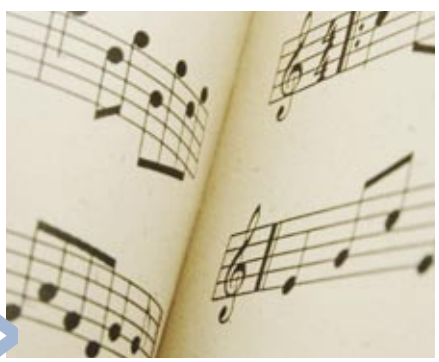
25–28 Explore music's roots and effects in our brain at the third triennial **Neurosciences and Music** conference. Discover how musical study enhances intellect, why music can act as a pain reliever and where disorders such as amusia (the inability to perceive tone or rhythm) arise in the brain. At night, conduct your own musical investigations at the Montreal International Jazz Festival, which neatly coincides with the conference.
Montreal
www.fondazione-mariani.org

26–29 As brain-imaging technology becomes more advanced, scientists are inching closer to literally reading people's minds—and many of them are becoming concerned with the ethics involved in wielding such power. Join in the discussion at the **Society for Philosophy and Psychology's 34th Annual Meeting**, featuring a symposium on neuroethics.
Philadelphia
www.socphilpsych.org

July

23 Although language may be uniquely human, some of its underlying genes are also found in songbirds. In this episode of **NOVA scienceNOW**, a weekly science newsmagazine broadcast Wednesday nights, find out how studying the brains of zebra finches has given scientists a better understanding of how children learn to speak. Watch the segment online if you miss it on the air.
PBS
www.pbs.org/nova/sciencenow

24 On this date in 1824 the *Harrisburg Pennsylvanian* newspaper conducted **the first public opinion poll**, which correctly predicted that military man Andrew Jackson would win the popular vote over Secretary of State John Quincy Adams in the presidential election. (When no candidate got the electoral college majority, however, the House of Representatives later declared Adams president.) Over the past two centuries, social scientists have greatly improved their sampling methods—the first poll was conducted only in Delaware—and opinion polling has since assumed an integral role in American democracy.



Seeing Is **Believing**

Engage your brain in some unusual perceptual activities at these summer art exhibitions:

June 29

Salvador Dalí's interest in the mysteries of the mind is clear in his art; take, for example, his dream sequence in Alfred Hitchcock's psychological thriller *Spellbound*. Examine the vivid oil paintings and sketches Dalí created to depict the movie protagonist's psychosis as part of the Museum of Modern Art's new exhibit: **Dalí: Painting and Film**.
New York City
www.moma.org

July 18

Long before computer-generated three-dimensional illusions, visual artists were already fascinated with the idea that 2-D pictures could exploit the quirks of the visual perception system to suggest movement or depth. In **Op Art Revisited**, the Albright-Knox Art Gallery showcases images from the 1960s movement known as op art, short for "optical art," in which artists employed geometric patterns to trick our susceptible brain into seeing what is not really there.
Buffalo, N.Y.
www.albrightknox.org/exhibitions

Through September

Take 20,736 colored spools of thread, abundant lengths of aluminum chain and a crystal ball. What do you get? Leonardo da Vinci's *The Last Supper* in **Interpretations: Devorah Sperber**, a traveling exhibit currently at the Massachusetts Museum of Contemporary Art. Inspired by the way our brain corrects for the retina's inverted view of the world, Sperber's seemingly abstract collages instantly coalesce into sharp, recognizable masterpieces when viewed through clear spheres.
North Adams, Mass.
www.massmoca.org

CHRIS BOYDELL *Australian Picture Library/Corbis (zebra finch)*; LYNDA SCHEMANSKY *age fotostock (sheet music)*; *SURPRISE, SURPRISE*, BY TIM BAVINGTON, 2003 ACRYLIC ON CANVAS, COLLECTION ALBRIGHT-KNOX ART GALLERY, GEORGE B. AND JENNY R. MATHEWS FUND, 2003 (*Op Art Revisited*)

Compiled by Christopher Intagliata and Karen Schrock. Send items to editors@SciAmMind.com

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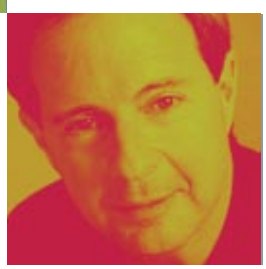
Let Your Creativity Soar

IN A DISCUSSION WITH *SCIENTIFIC AMERICAN MIND* EXECUTIVE EDITOR MARIETTE DiCHRISTINA, THREE NOTED EXPERTS ON CREATIVITY, EACH WITH A VERY DIFFERENT PERSPECTIVE AND BACKGROUND, REVEAL POWERFUL WAYS TO UNLEASH YOUR CREATIVE SELF

MARIETTE DiCHRISTINA is executive editor of *Scientific American Mind* and *Scientific American*. She has been a journalist for more than 20 years.

JOHN HOUTZ is a psychologist and professor at Fordham University. His most recent book is *The Educational Psychology of Creativity* (Hampton Press, 2002).

JULIA CAMERON is an award-winning poet, playwright and filmmaker. Her book *The Artist's Way* (Jeremy P. Tarcher/Putnam, 2002) has sold more than three million copies worldwide. Her latest book is *The Writing Diet*.



ROBERT EPSTEIN is a visiting scholar at the University of California, San Diego. Contributing editor for *Scientific American Mind* and former editor in chief of *Psychology Today*, Epstein has written several books on creativity, including *The Big Book of Creativity Games* (McGraw-Hill, 2000).

MARIETTE DiCHRISTINA: Let's start by talking about what has drawn each of you to the study of creativity. What's so fascinating about it?

JOHN HOUTZ: There's so much power in a new idea taking shape and changing the way people live and act. Often the rest of us are in awe, or we are even afraid of a new idea, and sometimes our fears spur us to learn more about it. In addition to what some academics call Big Creativity or "Big C"—profound ideas that sometimes change the world—there is what we call the "little c" type of creativity: the everyday problem solving that we all do. The bottom line is that we'd all like to be more creative. We'd all like to be able to solve our problems in a better way. We don't like being frustrated. We don't like having obstacles in our path.

JULIA CAMERON: What drew me to working on my creativity was running into a couple of bumps. I had had a blessed decade in my 20s, and then when I got to my 30s I felt thwarted. I was writing movies and selling them to studios, but they weren't getting made. I needed to find a way to maintain equilibrium and optimism in the face of creative despair. I fought my despair with what I call "morning pages"—three pages of longhand writing about anything: "I don't like the way Fred talked to me at the office"; "I need to get the car checked"; "I forgot to buy kitty litter." They don't look like they have anything to do with creativity, but in fact, as we put these worries, which are sort of a daily soundtrack for most of us,

COURTESY OF MARIETTE DiCHRISTINA, JOHN HOUTZ, JULIA CAMERON AND ROBERT EPSTEIN

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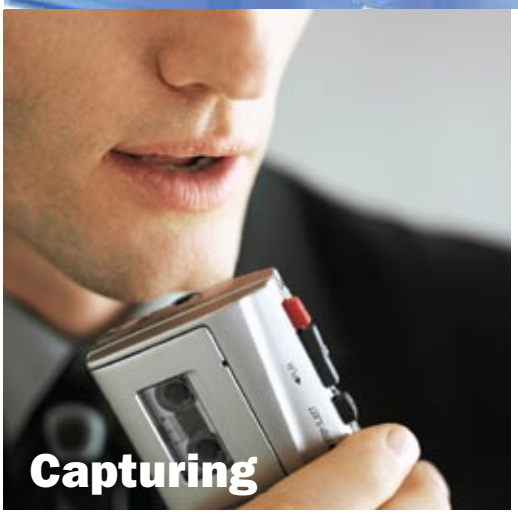
THE RIGHT TOOLS

According to Epstein, there are four "core competencies" of creative expression. People need to learn to preserve their new ideas (capturing), surround themselves with interesting people and things (surrounding), tackle tough problems (challenging), and expand their knowledge (broadening).



down on the page, we are suddenly much more alert, aware, focused and available to the moment. And we begin to see that we have many creative choices. As I wrote those pages, new ideas began to walk in. Over time, I began to share the morning-pages technique with other people.

ROBERT EPSTEIN: My interest in creativity started in a peculiar way—while I was working with pigeons at Harvard in the 1970s. I was intrigued by the fact that they always did things I hadn't taught them, and I wanted to know where the new behavior was coming from. I began teaching them different things systematically and then placing them in new situations and watching new behavior emerge. There was an orderly relation between what I had taught and the new behavior, and eventually I discovered principles or laws that allowed me to predict the new behavior, literally moment to moment. Eventually I began similar research with children, and then with adult humans, and found that those laws, somewhat tweaked, were still helpful. I came to believe that the creative process in individuals is orderly and predictable every moment in time. At some point I developed tests to see whether people have the competencies they need for expressing creativity, and then I developed games and exercises to boost creativity. I think that the fact that creativity is orderly is good news, because it means we can all tap into this rich potential we all have.

CAMERON: I, too, have found the creative process to be teachable and trackable. I teach people three simple tools, and anyone using those tools has what might be called an awakening. They become much more alert; they become much more friendly in interacting with people—much less threatened by change.

HOUTZ: I think that some of the techniques Julia teaches are similar to the competencies Robert has uncovered. Perhaps, Robert, you might explain what those competencies are.

EPSTEIN: There are four different skill sets, or competencies, that I've found are essential for creative expression. The first and most important competency is "capturing"—preserving new ideas as they occur to you and doing so without judging them. Your morning pages, Ju-

FAST FACTS

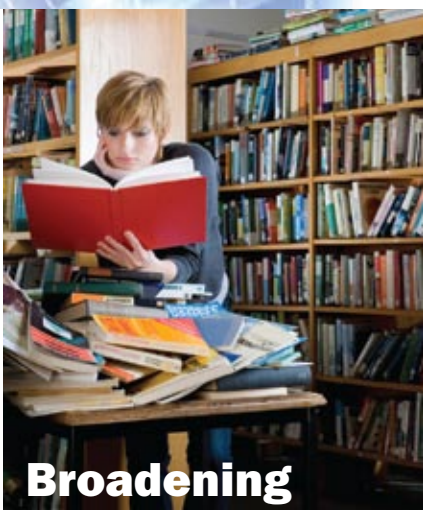
Unleashing Creativity

1» **Creativity is not a gift from the muses only granted to certain people. Rather it is something that anyone can cultivate, using a variety of methods.**

2» **The experts in the panel discussion offer simple ways to stimulate and capture new ideas—while countering negative thoughts and habits that block novel thinking.**

3» **The lessons apply not only to adults: encouraging open-ended problem solving can help foster creativity in children as well.**

GETTY IMAGES (*left*); ANTONY NAGELMANN Getty Images (*right*)



GETTY IMAGES (*left* and *right*)

lia, are a perfect example of a capturing technique. There are many ways to capture new ideas. Otto Loewi won a Nobel Prize for work based on an idea about cell biology that he almost failed to capture. He had the idea in his sleep, woke up and scribbled the idea on a pad but found the next morning that he couldn't read his notes or remember the idea. When the idea turned up in his dreams the following night, he used a better capturing technique: he put on his pants and went straight to his lab!

The second competency is called "challenging"—giving ourselves tough problems to solve. In tough situations, multiple behaviors compete with one another, and their interconnections create new behaviors and ideas. The third area is "broadening." The more diverse your knowledge, the more interesting the interconnections—so you can boost your creativity simply by learning interesting new things. And the last competency is "surrounding," which has to do with how you manage your physical and social environments. The more interesting and diverse the things and the people around you, the more interesting your own ideas become.

CAMERON: I've mentioned the morning pages, which sounds like your capturing, and the second technique I teach everybody—the artist "date" or "outing," I call it—is to take an adventure once a week, which probably involves both broadening and challenging. The third tool is to walk out the door for 20 minutes or so and see what happens to your thinking. When people walk, they often begin to integrate the insights and intuitions that they have had through morning pages and outings.

HOUTZ: I think if we want everyone to have a way to be more creative, we have to convey the message that they have to work at it; creativity isn't necessarily going to come naturally. And what strikes me about Julia is her high productivity. Creative people are productive. They may have lots of ideas that don't work, but the point is that they have lots of ideas. So if people want to be more creative—and to be effective problem solvers—they're going to have to be disciplined like Julia is.

DiCHRISTINA: I was talking with a couple of attorneys about creativity, and one of them said, "Well, some people just have more than others, don't they?" Could we talk about why so few people express creativity?

EPSTEIN: When children are very young, they all express creativity, but by the end of the first grade, very few do so. This is because of socialization. They learn in school to stay on task and to stop daydreaming and asking silly questions. As a result, the expression of new ideas is largely shut down. We end up leaving creative expression to the misfits—the people who can't be socialized. It's a tragedy.

CAMERON: I sometimes ask people to list 10 traits they think artists have. They say things like "artists are broke," "artists are crazy," "artists are drug-addicted" and "artists are drunk." Doesn't

THEY HAVE TO WORK AT IT; CREATIVITY ISN'T NECESSARILY GOING TO COME NATURALLY.

OBSTACLES

Creativity is shut down in most people by early socialization, leaving it to "misfits," according to the panelists. But everyone has roughly equal potential to express creativity, given the right skills.

this make you want to rush right out and become an artist? We have a mythology in America around creativity that's very, very negative. As a result, when young people tell their parents, "I'd love to be a writer," their parents respond, "Oh, darling, don't you think you might need something to fall back on?" We're also trained to believe that some people are born knowing they're artists and that they are the "real" artists, the ones who give us the Big C creativity. In other words, we have a mythology about artistry that tends to be very daunting.

HOUTZ: I think that comes from some of the studies of Big C creativity. When we look at individuals who have had a tremendous impact on some field, for whatever reason, they often turn out to be unstable or living a wild life—the misfits, as Robert said. That's very unfortunate. But there also are real obstacles for creative people. Julia, you mentioned that many of your creative projects were failing at one point. People who want to be more creative have to realize that many new ideas will at first meet great obstacles. When Robert talked about "challenge," you could read that word "challenge" in two ways. You need to challenge yourself, that's true, but you also have to realize that the world out there—society, the audience for your new idea—will perhaps need a lot of time to get used to it and may initially not want to reward you. It's important not to become discouraged. You have to keep at it!

An expanded version of this discussion—along with three other articles on creativity from *Scientific American Mind* is available in the audiobook *Brainstorm: Using Science to Spark Maximum Creativity.* It will be published July 22, 2008, by Macmillan Audio, unabridged on CD and as a digital download. Available wherever books are sold.

CAMERON: When I first gave the manuscript for *The Artist's Way* to my literary agent at William Morris, she said, "Oh, Julia, *no one* is going to be interested in this." So Mark Bryan and I self-published the book by photocopying it at a little communist bookstore and selling a few copies at a time. Emma Lively and I have been working for eight years on a musical that is only now getting its lucky break.

You have to put up with dry spells and keep creating in the face of them.

EPSTEIN: When I do seminars on creativity, I teach stress-management techniques to help people cope with the rejection that goes hand in hand with creativity. You have to learn not to fear failure and even to rejoice in it. When I'm failing, I say to myself, "I'm in good company. I'm in the company of some of the most creative and productive people in the world."

NICHOLAS PRIOR *Getty Images (left)*; PANORAMIC IMAGES/GETTY IMAGES *(right)*

HOUTZ: The creative individual thinks of failure as a new opportunity: "Okay, why did I fail? What was wrong? Let me try to do something else. Let me go forward with it."

EPSTEIN: In the laboratory, failure also produces a phenomenon called resurgence—the emergence of behaviors that used to be effective in that situation—that leads to a competition among behaviors and to new interconnections. In other words, failure actually stimulates creativity directly. It really is valuable.

CAMERON: You also need to be able to take criticism. When I write a novel, I send it to about 10 people whom I consider very trusted readers. They come back to me with their criticisms, and I write another draft. Sometimes I write as many as seven drafts of a work before it goes forward into the world.

HOUTZ: There's also a stereotype that creativity is just involved in the generation of ideas. But after the ideas are generated, you then have to evaluate them, sift through them, embellish them, repair them, revise them and get them tested, which all means that the creative process is actually quite complex.

EPSTEIN: But you've got to capture now and evaluate later. A big mistake people make is to start visualizing the criticism or the feedback while they're still generating. That can shut you right down.

CAMERON: Morning pages allow you to bypass the censor, because there's no wrong way to do the pages. You just keep writing. They allow you to take risks freely with your ideas.

DICHRISTINA: There's another dynamic here, too, John, which I'm hoping you can speak to: the group dynamic of creativity. People often play different roles in the creative process, don't they?

HOUTZ: A key factor here is personality, which has been researched extensively. Some personality characteristics seem to close off the expression of new ideas. Other personality characteristics encourage that expression.

EPSTEIN: I've found that no matter what their personality, people can learn skills that boost creative output. I also doubt that there's any real difference between the little c and the Big C types of creativity. If you write enough morning pages, now and then some Big C items have a chance of creeping into the little c list—no matter what your personality.

HOUTZ: We may all have the same potential or at least the potential to be better, but if we know about our strengths and weaknesses, then we can better capitalize on our strengths, and we also know what we need to work on.

EPSTEIN: No question about that. Getting back to Mariette's question about groups, let me give you an example of an exercise I do with people that boosts group creativity. It's called "the shifting game." In this exercise, half of my teams stay together for 15 minutes to generate names for a new cola. The other teams work together for five minutes, then shift out of the group to work on the problem individually, then come together for the last five minutes. Even with all the moving around, the shifting teams produce twice as many ideas as the nonshifting ones. This happens, I think, because groups inhibit a lot of creative expression. Dominant people tend to do most of the talking, for one thing. But when people shift, everyone ends up working on the problem.

THE CREATIVE INDIVIDUAL THINKS OF FAILURE AS A NEW OPPORTUNITY.

THERE IS NO REASON WHY WE CAN'T DEVELOP MORE CREATIVE PROBLEM SOLVERS FROM NURSERY SCHOOL ON UP.

DICHRISTINA: Don't many people believe they're not creative at all? What can you do about that?

EPSTEIN: Sometimes that's a permission issue. Many of us feel like we need permission to be creative, maybe because of a teacher who shut us down when we were young—like my eighth grade English teacher! One thing I like to do with people is to give them permission to have a daydream. We all just close our eyes and daydream together. It can be quite a liberating experience. Virtually everyone has amazing daydreams and dreams, and those can be used to boost creative output. In fact, when you really start letting yourself go, you can end up with *too many* ideas. Your own output can overwhelm you, and you can get stuck!

HOUTZ: What might be some tools to help people that have the problem Robert just described?

CAMERON: I have a tool that's called "blasting through blocks." It's very simply sitting down with a piece of paper and writing down all of your angers and fears related to finishing a project. Sometimes they're very petty: I'm afraid I'll finish it, and no one will think it's any good; I'm afraid I'll finish it, and *I* won't think it's any good; I'm afraid I'll finish it, and it will be good, but no one will recognize that. Just getting those reservations on a sheet of paper and maybe sharing them with someone can give you the freedom to go back to work on the project.

DICHRISTINA: How about the idea of taking breaks to promote creativity? There's the old adage about sleeping on something. Isn't a lot of creativity about being mindful of those times and paying attention?

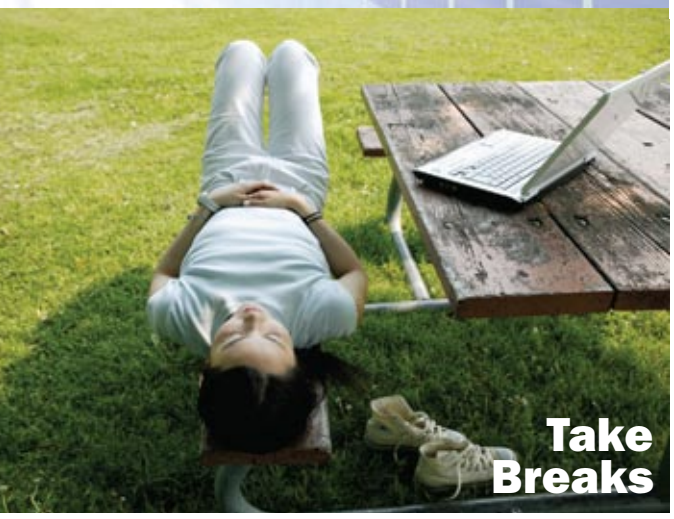
EPSTEIN: Absolutely, but you can also be strategic about how you're going to use those breaks. Salvador Dalí made deliberate use of his naps to get ideas for his art, for example. While relaxing on a sofa, he'd hold a spoon out over the edge and place a plate on the floor beneath the spoon. Just as he'd drift off to sleep, his hand would relax and the spoon would fall. The sound of the spoon hitting the plate would awaken him, at which point he'd grab a pad and sketch out interesting images he might have seen in the semisleep state. Thomas Edison used a similar technique to get ideas for his inventions. And the good news here is that we all experience this state—the so-called hypnagogic state. Think about how deliberate Dalí and Edison were or about how deliberate Julia's techniques are. You don't need to leave creativity to chance.

DICHRISTINA: I think many people make the mistake of believing that there's just no time to be creative, even to do something simple like paying attention to your thoughts and capturing them.

EPSTEIN: Well, high tech is making this easier, fortunately. These days all you have to do to capture an idea is to pick up your PDA or memo recorder or even just to leave a message for yourself on your voice mail. You can even capture new melodies that way.

HOUTZ: This is where one's style or various personality traits might come into play. If I'm an in-

GETTY IMAGES (*left*); MANFRED BAUMANN *age fotostock* (*right*)



SHIO GUCHI Getty Images

BOOST YOUR IDEAS

To boost your creative output, think and behave like creative people do: don't let criticism stop you from expressing your ideas and do not fear failure. Take breaks and learn to use them strategically; use daydreams as sources of new ideas.

ternal person, I might enjoy the reflectivity and the quiet time and the incubation time. If I'm an external person, I might take my strength from interactions with others in a dynamic group that's giving and taking and making lots of noise.

DICHRISTINA: How about fostering creativity and maintaining it in children? What tips do you have for educators and parents?

EPSTEIN: Well, all four of the basic creativity competencies can be taught to children. But when I've suggested to teachers that they set aside a few minutes each week for creativity training, these days they tell me that's impossible. This is an area where I see our society moving in the wrong direction—toward an obsession with raising scores on standardized tests.

CAMERON: I think that creativity is contagious and that the best thing we can do for children is to model for them what it's like to be a creative individual.

HOUTZ: There is no legitimate reason why we can't develop more creative problem solvers from nursery school on up. There are many techniques that could be introduced into the curriculum alongside the content domains. But, as Robert said, the emphasis right now is more political than educational.

DICHRISTINA: How might we be able to challenge our children in small ways so that we're at least keeping creativity alive at home?

EPSTEIN: One thing I like to do is make all problems open-ended. Never say, give me three ideas for this; always say, give me *at least* three. When tasks are open-ended, a lot more ideas are generated. I also like to use what I call "ultimate" problems with kids. Those are problems that have no real solutions. Children have great fun with problems like those. Ask them questions like "How could you get a dog to fly?" or "How could you make the sky a different color?" You can also supply your kids with idea boxes and folders—special places for putting drawings and poems and scraps of anything new. That encourages capturing on an ongoing basis and tells children that their new ideas have value.

HOUTZ: It's also important to give children permission to make decisions rather than always making decisions for them.

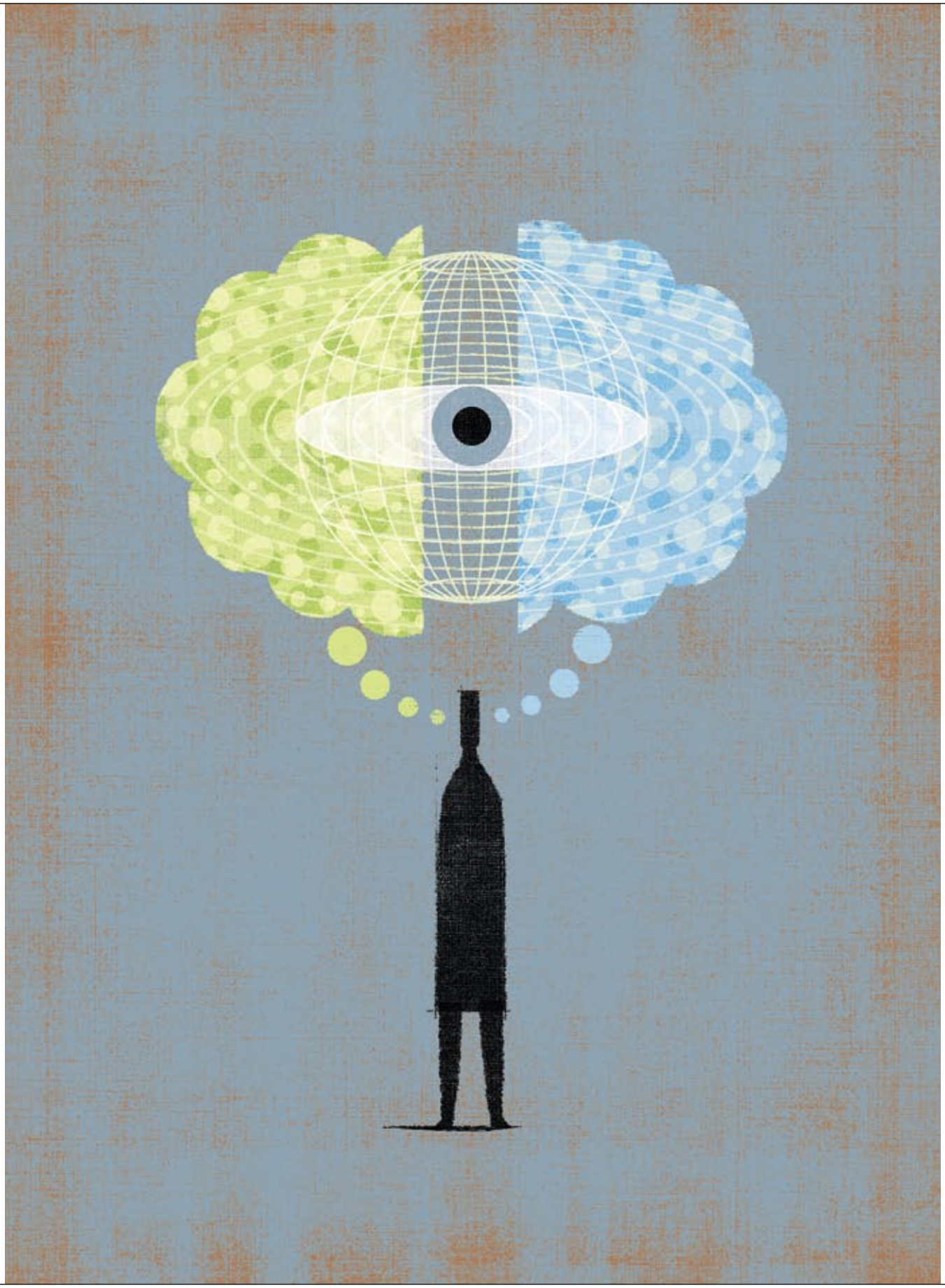
DICHRISTINA: When my children have a question that I might be able to answer, I sometimes instead say, "Why don't we find out?" Then I guide them through a process of discovering the answer for themselves. They sometimes find amazing ways to get there. Are we leaving anything out?

EPSTEIN: Maybe just that there's something both humbling and exhilarating about generating a new idea. I'm looking at Julia Cameron's eyes right now, trying to imagine the extraordinary things she's put on paper that have never been seen before by anyone in human history. I believe everyone has that kind of potential. Imagine that. M

Test Your Creative Competencies

To get a quick fix on your creativity competencies, take the Epstein Creativity Competencies Inventory at http://MyCreativitySkills.com

If you are a manager or teacher, see if you have the skills you need to stimulate creativity in other people at http://MyCreativitySkills.com/managers



JIM FRAZIER

Spheres of INFLUENCE

SPLIT-BRAIN PATIENTS—WHOSE TWO HEMISPHERES ARE SEPARATED SURGICALLY—PROVIDE FASCINATING CLUES TO HOW A UNITARY SENSE OF CONSCIOUSNESS EMERGES FROM THE FURIOUS ACTIVITY OF BILLIONS OF BRAIN CELLS BY MICHAEL S. GAZZANIGA

The human brain has approximately 100 billion neurons, and each, on average, connects to about 1,000 other neurons. A quick multiplication reveals that there are 100 trillion synaptical connections. So how is all this input getting spliced and integrated into a coherent package? How do we get order out of this chaos of connections? Even though it may not always seem so, our consciousness is rather kicked back and relaxed when you think about all the input with which the brain is being bombarded and all the processing that is going on. In fact, it is as if our consciousness is out on the golf course like the CEO of a big company while all the underlings are working. It occasionally listens to some chatter, makes a decision and then is out sunning itself.

We have gotten some clues about how consciousness emerges from studying "split brain" patients. The surgical procedure to cut the corpus callosum is a last ditch treatment effort for patients with severe intractable epilepsy for whom no other treatments have worked. Very few patients have had this surgery, and it is done even more rarely now because of improved medications and other modes of treatment. In fact, there have only been 10 split-brain patients who have been well tested. William Van Wagenen, a Rochester, N.Y., neurosurgeon, performed the procedure for the first time in 1940, following the observation that one of his patients with severe seizures got relief after developing a tumor in his corpus callosum. Epileptic seizures are caused by abnormal electrical discharges that in some people spread from one hemisphere to the other. It was thought that if the connection between the two sides of the brain were cut, then the electrical impulses causing the seizures would not spread from one side of the brain to the other.

The great fear was what the side effects of the surgery might be. Would it create a split personality with two brains in one head?

In fact, the treatment was a great success. Most patients' seizure activity decreased 60 to 70 percent, and they felt just fine: no split personality, no split consciousness. Most seemed completely unaware of any changes in their mental processes. This was great, but puzzling nonetheless. Why don't split-brain patients have dual consciousness? Why aren't the two halves of the brain conflicting over which half is in charge? Is one half in charge? Are consciousness and the sense of self actually located in one half of the brain?

Split-brain patients will do subtle things to compensate for their loss of brain connectivity. They may move their heads to feed visual information to both hemispheres, or talk out loud for the same purpose, or make symbolic hand movements. Only under experimental conditions, when we eliminate cross cueing, does the disconnection between the two hemispheres become apparent. We are then able to demonstrate the different abilities of the two hemispheres.

Before we see what is separated after this surgery, we need to understand what continues to be shared. There are subcortical pathways that remain intact. Both hemispheres of the split-brain patient are still connected to a common brain stem, so both sides receive much of the same sensory and proprioceptive information automatically coding the body's position in space. Both hemispheres can initiate eye movements, and the brain stem supports similar arousal levels, so both sides sleep and wake up at the same time.

JIM FRAZIER *theispot.com*

There also appears to be only one integrated spatial-attention system, which continues to be unifocal after the brain has been split. Attention cannot be distributed to two spatially disparate locations. The left brain is not attentive to the blackboard while the right brain is checking out the hot dude in the next row. Emotional stimuli presented to one hemisphere will still affect the judgment of the other hemisphere.

You may have been taught in anatomy lectures that the right hemisphere of the brain controls the left half of the body and that the left hemisphere controls the right half of the body. Of course, things are not quite that simple. For instance, both hemispheres can guide the facial and proximal muscles, such as those in the upper arms and legs, but the separate hemispheres have control over the distal muscles (those farthest from the center of the body), so that the left hemisphere controls the right hand. Although both hemispheres can generate spontaneous facial expressions, only the dominant left hemisphere can do so voluntarily. Because half the optic nerve crosses from one side of the brain to the other at the optic chiasm, the information from the parts of both eyes that attend to the right visual field is processed in the left hemisphere, and vice versa. This information does not cross over from one disconnected hemisphere to the other. If the left visual field sees something in isolation from the right, only the right side of the brain has access to that visual information.

It has also been known since the first studies by French neuroanatomist Paul Broca that our language areas are usually located in the left hemisphere (with exceptions in a few left-handed people). A split-brain patient's left hemisphere and language center have no access to the information that is being fed to the right brain. Bearing these things in mind, we have designed ways of testing split-brain patients to better understand what is going on in the separate hemispheres and have verified and learned that the left hemisphere is specialized for language, speech and intelligent behavior, whereas the right is specialized for such tasks as recognizing upright faces, focusing attention and making perceptual distinctions.

Where attention is concerned, the hemispheres interact quite differently in their control of reflexive and voluntary attention processes. There is a limited amount of overall available attention. The evidence suggests that reflexive (bottom-up) attention-orienting happens independently in the two hemispheres, whereas voluntary attention-orienting involves hemispheric competition with control preferentially lateralized to the left hemisphere. The right hemisphere, however, attends to the entire visual field, whereas the left hemisphere attends only to the right field. When the right inferior parietal lobe is damaged, the left parietal lobe remains intact.

WHY DON'T SPLIT-BRAIN PATIENTS HAVE DUAL CONSCIOUSNESS? WHY AREN'T THE TWO HALVES OF THE BRAIN CONFLICTING OVER WHICH HALF IS IN CHARGE? IS ONE HALF IN CHARGE?

Yet the left parietal lobe directs its visual attention only to the right side of the body. There is no brain area paying attention to what is going on in the left visual field. The question that is left is, Why doesn't this bother the patient? I'm getting there....

Left Hemisphere and Intelligence

After the human cerebral hemispheres have been disconnected, the verbal IQ of a patient remains intact, and so does his problem-solving capacity. There may be some deficits in free-recall capacity and in other performance measures, but isolating essentially half of the cortex from the dominant left hemisphere causes no major change in cognitive functions. The left hemisphere remains unchanged from its preoperative capacity, yet the largely disconnected, same-size right

FAST FACTS

Lessons from Split Brains

1» **A singular feeling of consciousness emerges from the chaos of 100 trillion neural connections. How?**

2» **"Split brain" patients—whose two hemispheres have been surgically sundered—have given scientists some ideas about how these semi-independent processing modules normally work together to create a unified experience.**

3» **The two hemispheres approach problem-solving situations in complementary ways, with the right able to maintain an accurate record of events and the left focusing on interpretation of those events.**

hemisphere is seriously impoverished in cognitive tasks. Although the right hemisphere remains superior to the isolated left hemisphere for some perceptual and attentional skills, and perhaps also emotions, it is poor at problem solving and many other mental activities.

The difference between the two hemispheres in problem solving is captured in a probability-guessing experiment. We have subjects try to guess which of two events will happen next: Will it be a red light or a green light? Each event has a different probability of occurrence (for example, a red light appears 75 percent of the time, and a green 25 percent of the time), but the order of occurrence of the events is entirely random.

There are two possible strategies one can use: frequency matching or maximizing. Frequency matching would involve guessing red 75 percent of the time and guessing green 25 percent of the time. The problem with that strategy is that because the order of occurrence is entirely random it can result in a great deal of error—being correct only 50 percent of the time—although it could result in being correct 100 percent of the time as well. The second strategy, maximizing, involves simply guessing red every time. That ensures an accuracy rate of 75 percent because red appears 75 percent of the time. Animals such as rats and goldfish maximize. The "house" in Las Vegas maximizes. Humans, on the other hand, match. The result is that nonhuman animals perform better than humans in this task.

Use of this suboptimal strategy by people has been attributed to a propensity to try to find patterns in sequences of events even when they are told that the sequences are random. At Dartmouth College, psychologists George Wolford, Michael Miller and I tested the two hemispheres of split-brain patients to see if the different sides used the same or different strategies. We found that the left hemisphere used the frequency-matching strategy, whereas the right hemisphere maximized! Our interpretation was that the right hemisphere's accuracy was higher than the left's because the right hemisphere approaches the task in the simplest possible manner with no attempt to form complicated hypotheses about the task.

More recent tests have even more interesting findings. They have shown the right hemisphere does frequency-match when presented with stimuli for which it is specialized, such as in facial recognition, and the left hemisphere, which is not a specialist in this task, responds randomly. This division of labor suggests that one hemisphere cedes control of a task to the other hemisphere, if the other hemisphere specializes in that task. The left hemisphere, on the other hand, engages in the human tendency to find order in chaos and persists in forming hypotheses about the sequence of events even in the face of evidence that no pattern exists: slot machines, for instance. Why does the left hemisphere do this even when it can be nonadaptive?

THE LEFT BRAIN, OBSERVING THE LEFT HAND'S RESPONSE WITHOUT THE KNOWLEDGE OF WHY IT HAS PICKED THAT ITEM, HAS TO EXPLAIN IT. IT WILL NOT SAY, "I DON'T KNOW."

Know-It-All Left Hemisphere

Several years ago we observed something about the left hemisphere that was very interesting: we had elicited from the disconnected right hemisphere how it deals with behaviors about which it had no information. We showed a split-brain patient two pictures: a chicken claw was shown to his right visual field, so only the left hemisphere saw that, and a snow scene was shown to the left visual field, so the only right hemisphere saw that. He was then asked to choose from an array of pictures placed in full view in front of him. Of the pictures placed in front of the subject, the shovel was chosen with the left hand and the chicken with the right. When asked why he chose these items, his left hemisphere speech center replied, "Oh, that's simple. The chicken claw goes with the chicken, and you need a shovel to clean out the chicken shed." Here the left brain, observing the left hand's response without the knowledge of why it has picked that item, has to explain it. It will not say, "I don't know." Instead it interprets that response in a context consistent with what it knows, and all it knows is "chicken claw." It knows nothing about the snow scene, but it has got to explain that shovel in the left hand. It has to create order out of its behavior. We called this left-hemisphere process "the interpreter."

We also tried the same type of test with mood shifts. We showed a command to the right hemisphere to laugh. The patient began to laugh. Then we asked the patient why she was laughing. The

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speech center in the left hemisphere had no knowledge of why its person was laughing, but out would come an answer anyway: "You guys are so funny!" When we triggered a negative mood in the right hemisphere by a visual stimulus, the patient denied seeing anything but suddenly said that she was upset and that it was the experimenter who was upsetting her. She *felt* the emotional response to the stimulus—all the autonomic results—but had no idea what caused it. Ah, lack of knowledge is of no importance, the left brain will find a solution. Order must be made. The first plausible explanation will do: the experimenter did it! The left-brain interpreter makes sense out of all the other processes. It takes all the input that is coming in and puts it together in a makes-sense story, even though it may be completely wrong.

The Interpreter and Consciousness

So here we are, back to the leading question of the article. Why do we feel unified when we are made up of a gazillion modules? Decades of split-brain research have revealed the specialized functions of the two hemispheres and have provided insights into specialization within each hemisphere. The answer may lie in the left-hemisphere interpreter and its drive to seek explanations for why events occur.

In 1962 Stanley Schachter of Columbia Uni-

(The Author)

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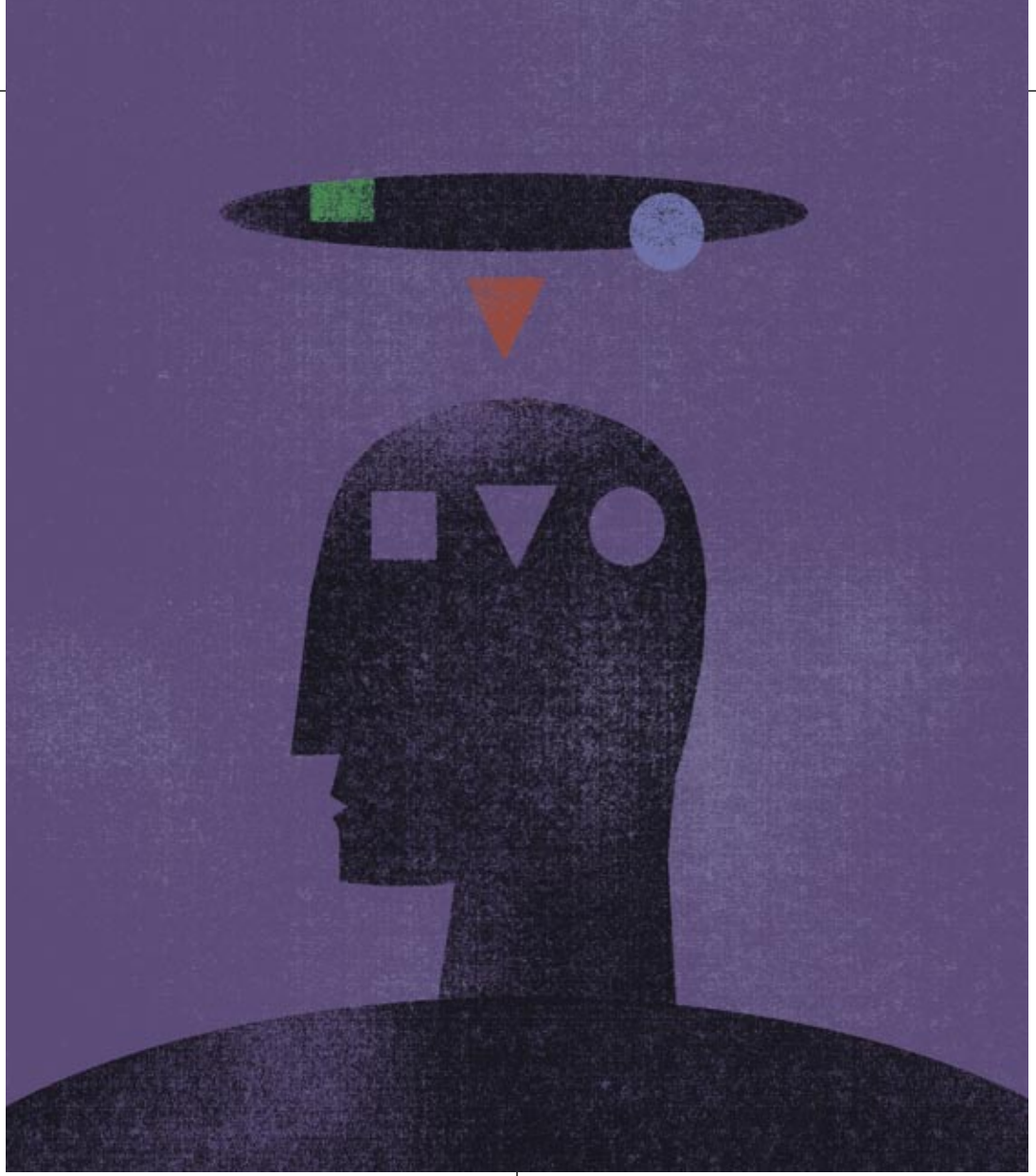


JIM FRAZIER *Corbis*

versity and Jerome E. Singer of Pennsylvania State University injected epinephrine into subjects participating in a research experiment. Epinephrine activates the sympathetic nervous system, and the result is an increased heart rate, hand tremors and facial flushing. The subjects were then put into contact with a confederate who behaved in either a euphoric or an angry manner. The subjects who were informed about the effects of the epinephrine attributed symptoms such as a racing heart to the drug. The subjects who were not informed, however, attributed their autonomic arousal to the environment. Those who were paired with the euphoric confederate reported being elated and those with the angry confederate reported being angry. This finding illustrates the human tendency to generate explanations for events. When aroused, we are driven to explain why. If there is an obvious explanation, we accept it, as did the group informed about the effects of epinephrine. When there is not an obvious explanation, the left brain generates one. This is a powerful mechanism; once seen, it makes one wonder how often we are victims of spurious emotional-cognitive correlations. ("I am feeling good! I must really like this guy!" As he is thinking: "Ah, the chocolate is working!")

Although the left hemisphere seems driven to interpret events, the right hemisphere shows no such tendency. A reconsideration of hemispheric-memory differences suggests why this dichotomy might be adaptive. When a person is asked to decide whether a series of items appeared in a study set or not, his or her right hemisphere is able to identify correctly items that have been seen previously and to reject new items. "Yes, there was the plastic fork, the pencil, the can opener and the orange." The left hemisphere, however, tends to falsely recognize new items when they are similar

to previously presented items, presumably because they fit into the schema it has constructed. "Yes, the fork (but it is a silver one and not plastic), the pencil (although this one is mechanical, and the other was not), the can opener and the orange." This finding is consistent with the hypothesis that the left-hemisphere interpreter constructs theories to assimilate perceived information into a comprehensible whole.

By going beyond simply observing events to asking why they happened, a brain can cope with such events more effectively should they happen again. In doing so, however, the process of elaborating (story-making) has a deleterious effect on the accuracy of perceptual recognition, as it does with verbal and visual material. Accuracy remains high in the right hemisphere, however, because it does not engage in these interpretive processes. The advantage of having such a dual system is obvious. The right hemisphere maintains an accurate record of events, leaving the left hemisphere free to elaborate and make inferences about the material presented. In an intact brain, the two systems complement each other, allowing elaborative processing without sacrificing veracity.

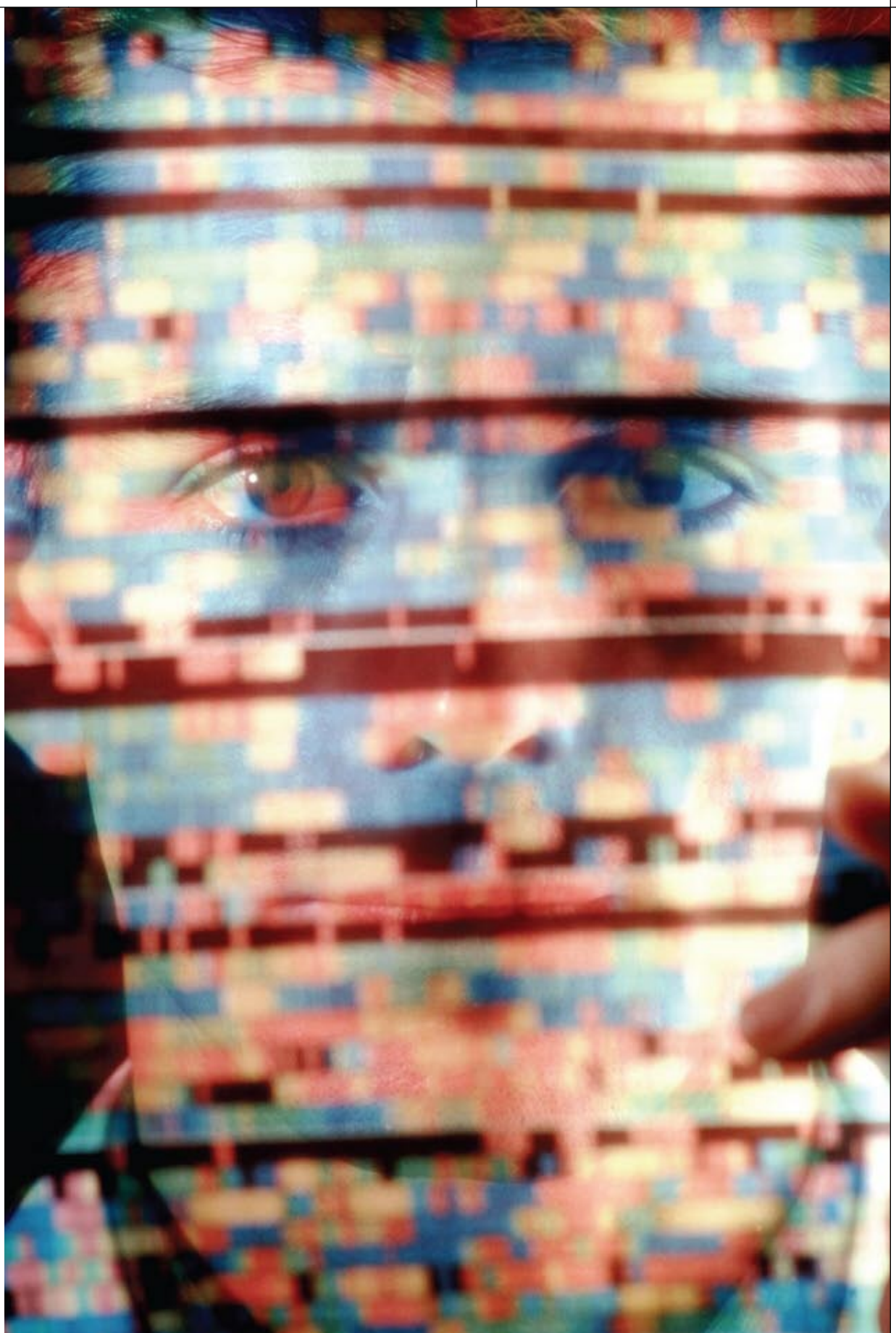
The probability-guessing paradigm also demonstrates why an interpreter in one hemisphere and not the other would be adaptive. The two hemispheres approach problem-solving situations in two different ways. The right hemisphere bases its judgments on simple frequency information, whereas the left relies on the formation of elaborate hypotheses. Sometimes it is just a random coincidence. In the case of random events, the right hemisphere's strategy is clearly advantageous, and the left hemisphere's tendency to create nonsensical theories about random sequences is detrimental to performance. This is what happens when you build a theory on a single anecdotal situation: "I vomited all night. It must have been the food was bad at that new restaurant where I ate dinner." This hypothesis would be good if everyone who ate what you ate became ill, but not if it happened to just one person. It may have been the flu or your lunch. In many situations, however, there is an underlying pattern, and in these situations the left hemisphere's drive to create order from apparent chaos would be the best strategy. Coincidences do happen, but sometimes there really is a conspiracy. In an intact brain, both these cognitive styles are available and can be implemented depending on the situation.

The difference in the way the two hemispheres approach the world might also provide some clues about the nature of human consciousness. In the media, split-brain patients have been described as having two brains. The patients themselves, however, claim that they do not feel any different after the surgery than they did before. They do not have any sense of the dual consciousness implied by the notion of having two brains. How is it that two isolated hemispheres give rise to a single consciousness? The left-hemisphere interpreter may be the answer. The interpreter is driven to generate explanations and hypotheses regardless of circumstances. The left hemisphere of split-brain patients does not hesitate to offer explanations for behaviors that are generated by the right hemisphere. In neurologically intact individuals, the interpreter does not hesitate to generate spurious explanations for sympathetic nervous system arousal. In these ways, the left-hemisphere interpreter may generate a feeling in all of us that we are integrated and unified.

THE DIFFERENCE IN THE WAY THE TWO HEMISPHERES APPROACH THE WORLD MIGHT ALSO PROVIDE SOME CLUES ABOUT THE NATURE OF HUMAN CONSCIOUSNESS.

A split-brain patient, a human who has had the two halves of his or her brain disconnected from each other, does not find one side of the brain missing the other. The left brain has lost all consciousness about the mental processes managed by the right brain, and vice versa. We don't miss what we no longer have access to. The emergent conscious state arises out of each side's capacity and probably through neural circuits local to the capacity in question. If they are disconnected or damaged, there is no underlying circuitry from which the emergent property arises.

Each of the thousands if not millions of conscious moments that we have reflects one of our networks being "up for duty." These networks are all over the place, not in one specific location. When one finishes, the next one pops up, and the pipe organ–like device plays its tune all day long. What makes emergent human consciousness so vibrant is that our pipe organ has lots of tunes to play, whereas the rat's (for instance) has few. And the more we know, the richer the concert. M



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The New Genetics of Mental Illness

Life's experiences add molecular switches to the genes that control our brain activity, affecting how susceptible we are to depression, anxiety and drug addiction

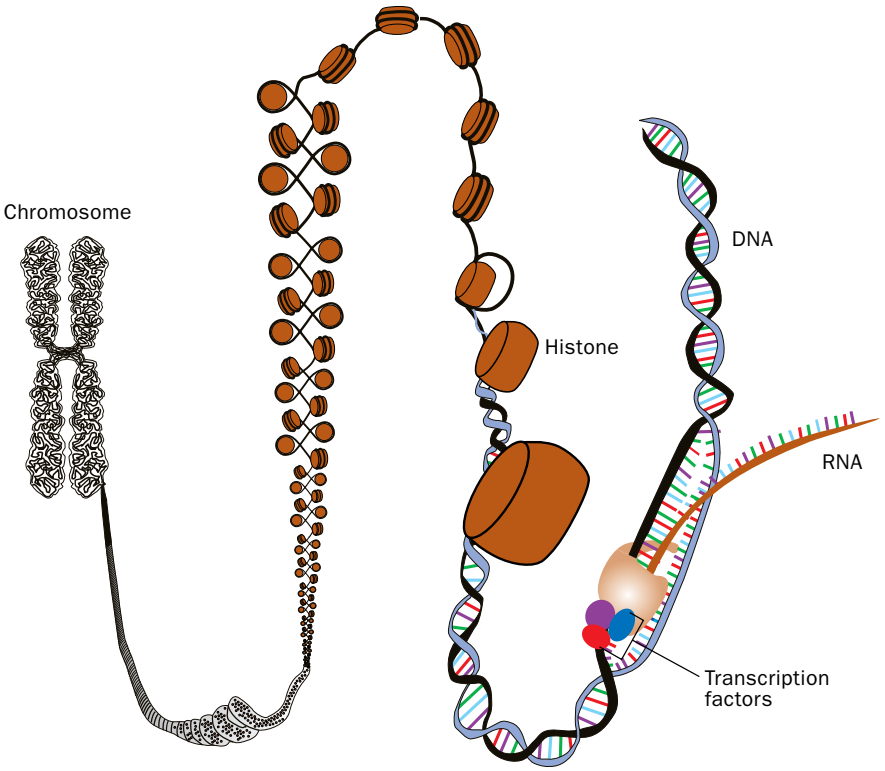
By Edmund S. Higgins

Throughout history shamans, clerics and physicians have tried to pin down what goes awry when a person slips into sadness, insanity or psychosis. Theorists have variously blamed mental illness on an imbalance of bodily fluids, the movement of planets, unconscious mental conflict and unfortunate life experiences. Today many researchers believe that psychiatric disorders arise in large part from a person's genetic makeup. Genes, after all, are the blueprints for the proteins that create and control the brain.

And yet genetics cannot be the whole story: identical twins, who have virtually the same DNA, do not always develop the same mental disorders. For example, if one identical twin acquires schizophrenia, the other stands just a 50 percent chance of also suffering from the disease. Indeed, abundant data suggest that psychiatric ailments typically result from a complex

Unraveling the Chromosome

In the nucleus of every cell, the DNA in chromosomes is tightly wound around proteins, called histones, to make its considerable length fit inside the cell. DNA's protein packaging also controls the expression of genes. For a gene to be expressed, a chromosome must unravel so that a complex of proteins, including so-called transcription factors, can attach to the appropriate section of the DNA and create an RNA molecule. This RNA is then translated into a protein (*not shown*).



interplay between the environment and a number of different genes [see "The Character Code," by Turhan Canli; Scientific American Mind, February/March 2008]. But only recently have scientists begun to grasp how the environment affects the brain to produce psychological changes.

FAST FACTS

Doctoring DNA

1» Experiences can literally change a person's mind by chemically coating the DNA that controls its function. Instead of tinkering with the genetic code, the coating alters gene expression, shutting down or revving up the construction of proteins that affect a person's mental state.

2» A female rat's nurturing behavior bolsters emotional resilience in her pups by boosting the expression of a gene that modulates anxiety. Distressing events can turn off the expression of a neuronal growth protein by epigenetic mechanisms and thereby trigger depression.

3» Epigenetic changes may also underlie the pathology of schizophrenia and drug addiction.

Ushering in a new conception of mental illness, researchers are discovering that life experience can literally change a person's mind by chemically coating the DNA that controls its function—but in a way that does not alter the genetic code. Rather the experience of trauma, drug abuse or lack of affection somehow causes satellite molecules to latch onto a person's DNA. Instead of tinkering with the basic essence of a gene, these molecular hangers-on alter gene expression, shutting down or revving up the construction of proteins that affect an individual's mental state, the way the speed of an assembly line affects production and, ultimately, the company's bottom line.

Investigators in this new field, called epigenetics ("epi" meaning "above" or "beyond"), have discovered that a mother rat's nurturing behavior can bolster emotional resilience in her pups by boosting the expression of a gene that modulates stress and anxiety. Distressing events, on the other hand, seem to turn off the expression of a neuronal growth protein by epigenetic mechanisms, thereby promoting depression.

Recent work similarly suggests that epigenetic changes may also underlie the pathology of drug addiction and schizophrenia as well as the retain-

EDMUND S. HIGGINS

ing of long-term memories [see "Unmasking Memory Genes," by Amir Levine, on page 48].

Identifying such molecular mishaps on the road to mental illness may enable scientists to develop a host of new treatments for psychiatric diseases. Future drugs might, for example, be designed to pharmacologically scrub DNA to eliminate the molecular alterations that led to the slide into schizophrenia, depression, anxiety or drug addiction.

Expressive Genes

Our genes, embedded in the DNA at the center of every cell in the body, form the blueprints for proteins, the cellular workhorses. Protein molecules build and maintain our brains and our bodies, shaping our personalities as well as our physical characteristics. The study of genetics is largely a discipline of correlating changes in the genetic code—that is, in its sequence of chemical units (A, T, C and G)—with changes in a person's or animal's appearance or behavior.

But to have an effect, a gene must actually be used as a template for a protein. In this process, called gene expression, various (previously fabricated) proteins attach to the DNA and use it to transcribe an intermediate molecule termed RNA, which is then translated into a protein. A cell does not transcribe and translate every gene, however. Each cell in an individual contains the same genes, but different cells use different subsets of them. Such selective gene expression is what makes a liver cell, say, different from a brain cell. Similarly, a person could take on different physical or emotional characteristics if gene expression were to change in his or her cells.

How might this happen? The primary mechanism for silencing a gene involves preventing the necessary molecular machinery from accessing it. Like a long wire wound into a Slinky toy, the DNA molecule is tightly coiled—much of it around protein "spools," or histones—a necessary measure if its considerable length is to fit inside a cell's nucleus [*see box on opposite page*]. In its condensed state, DNA cannot be actively used as a protein template. To be expressed, a gene's DNA segment must be unraveled and exposed.

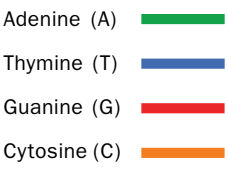
Epigenetic mechanisms ease or block access to a cell's genes, thereby controlling gene expression. Such mechanisms include the addition or removal of molecules to or from the DNA or histones. For instance, attaching so-called methyl groups, which consist of a carbon atom attached to three hydrogen atoms (CH_3), to DNA limits access by physically hampering the ability of the transcription machinery to bind to that DNA, thus silencing or at least quieting the gene. On the other hand, affixing acetyl groups ($COCH_3$) to the histones expands the chromosome's structure, facilitating gene expression [*see box below*]. Experimenters are increasingly finding that such chemical changes can occur in response to par-

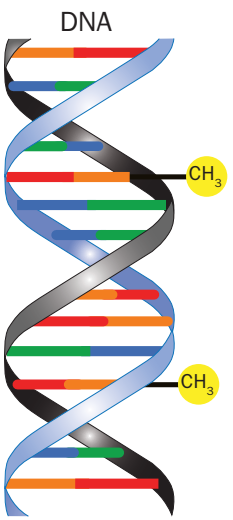
Beyond Genetics

Epigenetics is the study of certain kinds of chemical switches that turn genes on or off, thereby altering gene expression (how actively a gene is used to make protein).

Genetics

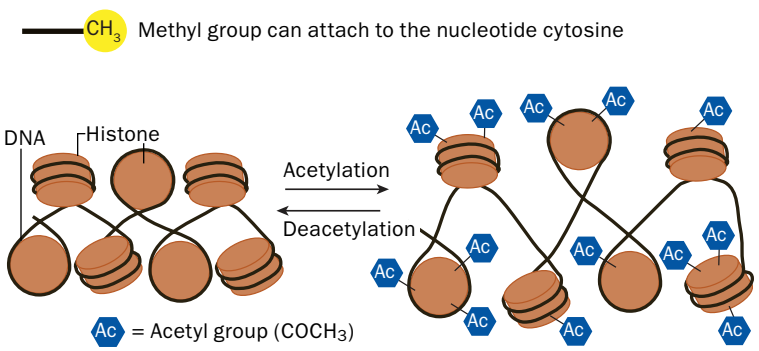
Changes in the genetic code—the sequence of nucleotides A, T, C and G in DNA—affect appearance and behavior.





Epigenetics

Some chemical changes alter gene expression without affecting the genetic code. For example, affixing methyl groups to DNA inhibits gene expression, whereas adding acetyl groups to proteins called histones loosens chromosome structure, making the underlying genes easier to transcribe.



EDMUND S. HIGGINS

Certain parenting practices that profoundly shape a child's mental health may do so by altering DNA.

ticular life experiences, and some of these modifications influence a person's mental stability.

Product of Parenting

Certain parenting practices can profoundly shape a child's emotional development and mental health—and some evidence suggests they can do so through epigenetics. For example, women with a history of childhood sexual and physical abuse have an exaggerated stress response: the amount of the stress hormone cortisol in their blood becomes abnormally elevated in the face of even minor stresses, such as speaking and performing mental arithmetic in front of an audience for 10 minutes. On the other hand, children who receive a lot of normal physical affection and care may end up more emotionally resilient and less prone to stress as adults than those who receive less attention and nurturing—at least that is what some animal studies suggest.

Children who receive a lot of affection and attention may be less prone to stress as adults.

TARA MOORE *Getty Images*

In 1997 neuroscientist Michael J. Meaney of McGill University and his colleagues compared the stress response of rats whose mothers had vigorously licked and groomed them during the first 10 days of their lives with that of rats whose mothers rarely licked and groomed them as pups. Meaney and his co-workers found that the progeny of high lickers and groomers displayed less anxiety and stress than the pups of low lickers and groomers when they were confined to a small plastic tube for 20 minutes. Levels of the rat stress hormone, corticosterone, shot up noticeably higher and stayed elevated for longer in the rodents that had low-licking and low-grooming mothers than they did in the animals whose mothers had been high lickers and groomers.

But how did affection and nurturing, or the lack thereof, shape the rat pups' physiological reaction to stress? When a person or animal perceives a threat, the cognitive and emotional parts of the brain alert the hypothalamus, an almond-size structure at the base of the brain. The hypothalamus then sends chemical signals to the adrenal glands, by way of another gland called the pituitary, telling them to release cortisol or (in a rat) corticosterone. That hormone then eventually provides feedback to the hypothalamus, binding to specialized molecular receptors on neurons there, to inhibit further activity [*see box on opposite page*]. This feedback loop prevents the body from producing an overly intense and extended reaction to stress. In the anxious rats, however, that loop apparently did not work well, so the hypothalamus remained active and continued to trigger corticosterone release in response to the stress of confinement.

Meaney and his colleagues wondered whether the problem in these rats could be traced back to the corticosterone receptors in the hypothalamus. If a rat's brain lacked them, the researchers reasoned, that deficit might create a glitch in the feedback system. So Meaney, along with graduate student Ian Weaver, now at the University of Toronto, and others took a closer look at the gene for this corticosterone receptor in rats that received either a lot or very little licking and grooming from their mothers.

In 2004 Meaney's team reported that the corticosterone receptor gene in the pups of the low lickers and groomers bore many more methyl groups than did the same gene in their better-cared-for counterparts. As a result, the pups that received less nurturing only sluggishly expressed this gene and thus produced fewer corticosterone receptors in the hypothalamus. The lack of receptors weakened the ability of corticosterone to calm the hypothalamus after a stressful event, exaggerating the stress response and making for overly stressed and anxious rodents. On the oth-

er hand, the nurturing behavior of the high-licking and high-grooming mothers kept their pups' corticosterone receptor gene relatively clear of methyl groups, and these pups were thus better able to handle stress as adults.

Dialing Down Depression

Another epigenetic modification may play a critical role in the development of depression. Although many people conceptualize depression as a chemical imbalance, nobody knows the exact mechanism for the disorder. Some investigators now theorize that depression can result from insufficient quantities of growth factor proteins such as brain-derived neurotrophic factor (BDNF), which, like other growth factors, sustains and nourishes nerve cells. In a 2006 study researchers found that concentrations of BDNF were abnormally low in the blood of depressed women. What is more, treatment with antidepressants brought the amount of BDNF in these women's bloodstreams back to normal. Likewise, other experiments demonstrate that treatments such as antidepressant medications, electroconvulsive therapy (ECT) and exercise increase concentrations of BDNF in the brains of rodents.

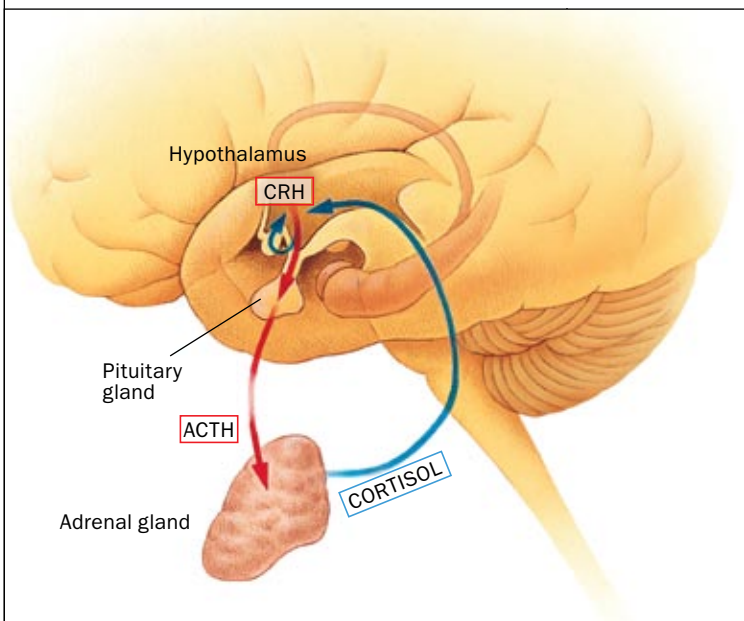
Until recently, no one knew the molecular mechanism of the BDNF depletion, but in the early part of this decade psychiatrist and neuroscientist Eric J. Nestler of the University of Texas Southwestern Medical Center at Dallas and his colleagues theorized that distressing experiences might alter the DNA that codes for BDNF. In a 2006 study Nestler and his colleagues paired "bully" mice with smaller mice in cages for five minutes a day. Face to face with their bully, the smaller mice acted anxious and submissive: they squeaked, cowered and tried to get out of the cage.

The scientists put a stop to the encounter by separating the two mice by a wire mesh, which still enabled the smaller mouse to smell the bully until the next go-round. After 10 days of such treatment, the small rodents acted defeated: like depressed humans, they would not interact with other mice and displayed unusual anxiety in novel settings, standing stock-still rather than exploring them. These mice also had abnormally low levels of BDNF in their brains.

To find out how bullying might lower BDNF concentrations, the researchers examined the gene for BDNF in cells from the hippocampus in the brains of both bullied and better-treated mice. They found a greater density of methyl groups on histones near the BDNF gene in the defeated mice than in normal mice, suggesting that the threatening experiences had chemically closed off the BDNF gene, silencing the blueprint and squelching production of BDNF. What is more, treating the defeated mice with an antidepressant, imipramine, every day for a month boosted production of BDNF (and alleviated the depression), apparently by adding acetyl groups to the BDNF gene.

Other depression treatments may have a similar effect on the BDNF gene. For example, in a 2004 study Nestler's team found that ECT, when applied to depressed rodents, also increased acetylation of the histones around the BDNF gene.

Stress Response System



When a person faces a frightening or stressful situation, cognitive and emotional brain areas (*not shown*) alert the hypothalamus, which secretes corticotropin-releasing hormone (CRH) into the blood vessels that feed the pituitary gland. In response to the CRH, the pituitary releases adrenocorticotropic hormone (ACTH) into the bloodstream—and that substance prompts the adrenal glands to secrete the stress hormone cortisol. Cortisol not only prepares the body to confront or flee a challenge, it also acts on the hypothalamus to dampen the stress response. The effectiveness of this feedback may depend on epigenetic changes in the gene for the cortisol receptor in the hypothalamus.

(The Author)

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ROBERTO OSTI

Neuroscientists speculate that psychotherapy might have the same effect, but no one knows because no one has yet developed effective talk therapy for a rodent.

Branching Out

Epigenetic mechanisms also may lie at the root of our addictions to substances such as alcohol and illicit drugs. Drug addiction is probably fueled by genetic factors; that is, genetically susceptible individuals are more easily addicted than others. But the use of a substance is necessary to switch the brain to an addicted state, and epigenetics likely plays a role in that transformation.

Addictive drugs exert their insidious effects by hijacking the brain's reward centers, including a midbrain structure called the nucleus accumbens. This structure normally responds to ordinary delights, including eating and sex, but a drug of abuse such as cocaine can corrupt the brain's reward circuitry such that the drug becomes a person's sole source of pleasure [see "New Weapons against Cocaine Addiction," by Peter Sergo; Scientific American Mind, April/May 2008]. At the cellular level, the nucleus accumbens of cocaine-dependent rodents contains neurons that appear "bushier," with more branches, or dendritic spines, that connect to other neurons, than those of animals that have never been exposed to cocaine. Drug abuse seems to spur this branching, which may abnormally enrich the communication between neurons in the brain's reward circuitry.

One protein that may be stimulating the cellular changes is cyclin-dependent kinase-5 (Cdk5), an enzyme that seems to be involved in adjusting how well two neurons communicate at junctions called synapses. In 2003 Nestler and his colleagues reported that injecting rats with a drug that inhibits the activity of Cdk5 reduced cocaine's effect on neuronal branching: the rats' nucleus accumbens neurons sprouted fewer branches and thus appeared less bushy. The study authors concluded that "cocaine-induced proliferation of dendritic spines in [the] nucleus accumbens is dependent on the activity of cyclin-dependent kinase-5."

In 2004 Nestler, along with University of Texas Southwestern Medical Center neuroscientist Arvind Kumar and others, reported that rats that were chronically exposed to cocaine had more than four times as many acetyl groups (which loosen the chromosome structure and make genes more accessible) on the histone at the *Cdk5* gene as compared with rats that imbibed a saline solution. The cocaine exposure thus appeared to boost the expression of the *Cdk5* gene, raising production of the Cdk5 protein, which in turn stimulated or enabled the growth of neuronal connections in the nucleus accumbens. Such an epigenetic change may therefore contribute to addictive behavior.

Making Connections

In contrast to the obvious environmental contributors to drug addiction, the causes of the hallucinations, apathy and distorted thinking characteristic of schizophrenia remain relatively opaque. At the cellular level, investigators have noted an anomaly in brains of deceased schizophrenics: the neurons in some of their cognitive and visual brain regions are smaller, thinner and less densely connected with other neurons than are their counterparts in people who had been mentally healthy. Although no one is sure what might account for this anatomical curiosity, it could arise in part from aberrations in certain proteins critical for modulating or forming neuronal connections. One such protein is reelin, an enzyme that acts on the structural matrix of molecules that stretches between neurons.

Researchers have found reelin concentrations to be about 50 percent reduced in various regions of the brains of deceased patients who suffered from schizophrenia [*see illustration on opposite page*]. In 2005 two scientific teams simultaneously reported a probable cause for the reelin deficit. In one of these studies molecular biologist Dennis R. Grayson and his colleagues at the University of Illinois at Chicago compared the gene for reelin in brain tissue from 15 deceased schizophrenia patients with the same gene in the brains of 15 people who had not been mentally ill. The

After repeated encounters with "bully" mice, smaller mice may display behaviors akin to those of depressed humans. Epigenetic alterations affecting a gene for a nerve growth substance are likely to partly underlie this change in mental state.

COURTESY OF ERIC J. NESTLER

Combating stress and anxiety might be partly a matter of cleansing DNA of its epigenetic markings.

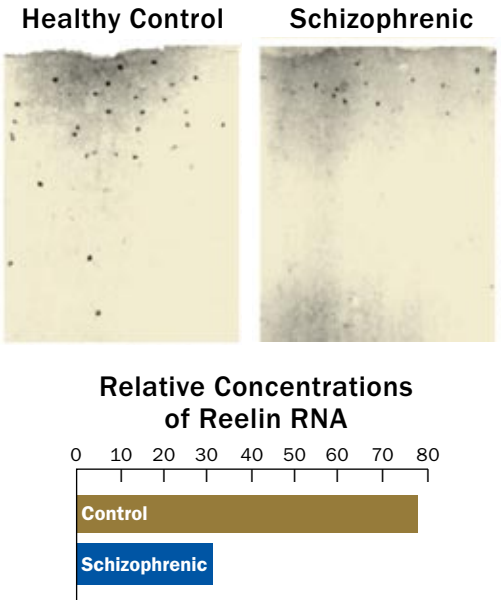
experimenters detected a greater number of methyl groups attached to the reelin gene in tissue from a region at the back of the schizophrenic brains as compared with tissue from the normal brains, suggesting that schizophrenia could arise from an epigenetic change that depresses reelin gene expression. Although psychiatrist Ming Tsuang of the University of California, San Diego, and his colleagues obtained similar results, two other groups of scientists later failed to find an association between reelin gene methylation and schizophrenia.

Even if reelin gene methylation is one cause of schizophrenia, no one knows what environmental factors might produce this chemical perturbation of the DNA. Scientists are similarly unsure how diminished production of reelin might lead to schizophrenia. A lack of reelin, which participates in neuronal migration and the remodeling of neuronal connections, could render neurons incapable of forming the ordinary number of links with other neurons—but how this might lead to symptoms such as hallucinations is unclear. Nevertheless, accumulating evidence suggests that excess methylation of DNA in the brains of schizophrenics is not limited to reelin but extends to various other genes involved in neural communication and brain development. Thus, DNA methylation, spurred by unknown environmental occurrences, may play an important role in the development of schizophrenia.

Chemical Erasers

Researchers hope that illuminating the molecular path between experience and mental illness will ultimately pave the way toward better treatments for psychiatric disorders. Early work already suggests that combating stress and anxiety, at least in rats, might be partly a matter of cleansing DNA of its epigenetic markings.

In their 2004 paper Weaver, Meaney and their colleagues administered a histone deacetylase inhibitor—a compound that both boosts the number of acetyl groups and thins out methyl groups on chromosomes—to rats that had been raised by low-licking and low-grooming mothers. Meaney's group found that this treatment erased the emotional fallout from the rats' deficient upbringing. The treated rats were no longer especially anxious when they were trapped in the tube: their stress hormone levels paralleled those of rats raised by high-licking and high-grooming mothers.



Concentrations of an enzyme called reelin (*dark spots on images*) involved in the remodeling of neuronal connections are about 50 percent lower in the brains of schizophrenics. The reduction may stem from epigenetic alterations of the gene for reelin, providing a possible clue to one cause of schizophrenia.

Eventually scientists might test a similar treatment in humans with intractable psychiatric disorders. Doctors might also advise patients at risk for mental disorders to engage in behaviors—say, changing their diet (which can alter gene expression in mice and thereby determine traits such as fur color), undergoing psychotherapy or taking medication—that could *prevent* deleterious epigenetic alterations to their DNA. A methylation antagonist blocker might, for example, help reduce the frequency or severity of post-traumatic stress disorder in rape and trauma victims. It might even be able to limit the psychological effects of combat in soldiers. Even though such therapies remain futuristic, the latest insights into the epigenetics of mental disorders are already prompting new notions about how the events and experiences of our lives can alter our minds. M

SOURCE: "DECREASE IN REELIN AND GLUTAMIC ACID DECARBOXYLASE67 (GAD67) EXPRESSION IN SCHIZOPHRENIA AND BIPOLAR DISORDER: A POSTMORTEM BRAIN STUDY," BY A. GUIDOTTI ET AL., IN *ARCHIVES OF GENERAL PSYCHIATRY*, VOL. 57, NO. 11; 2000

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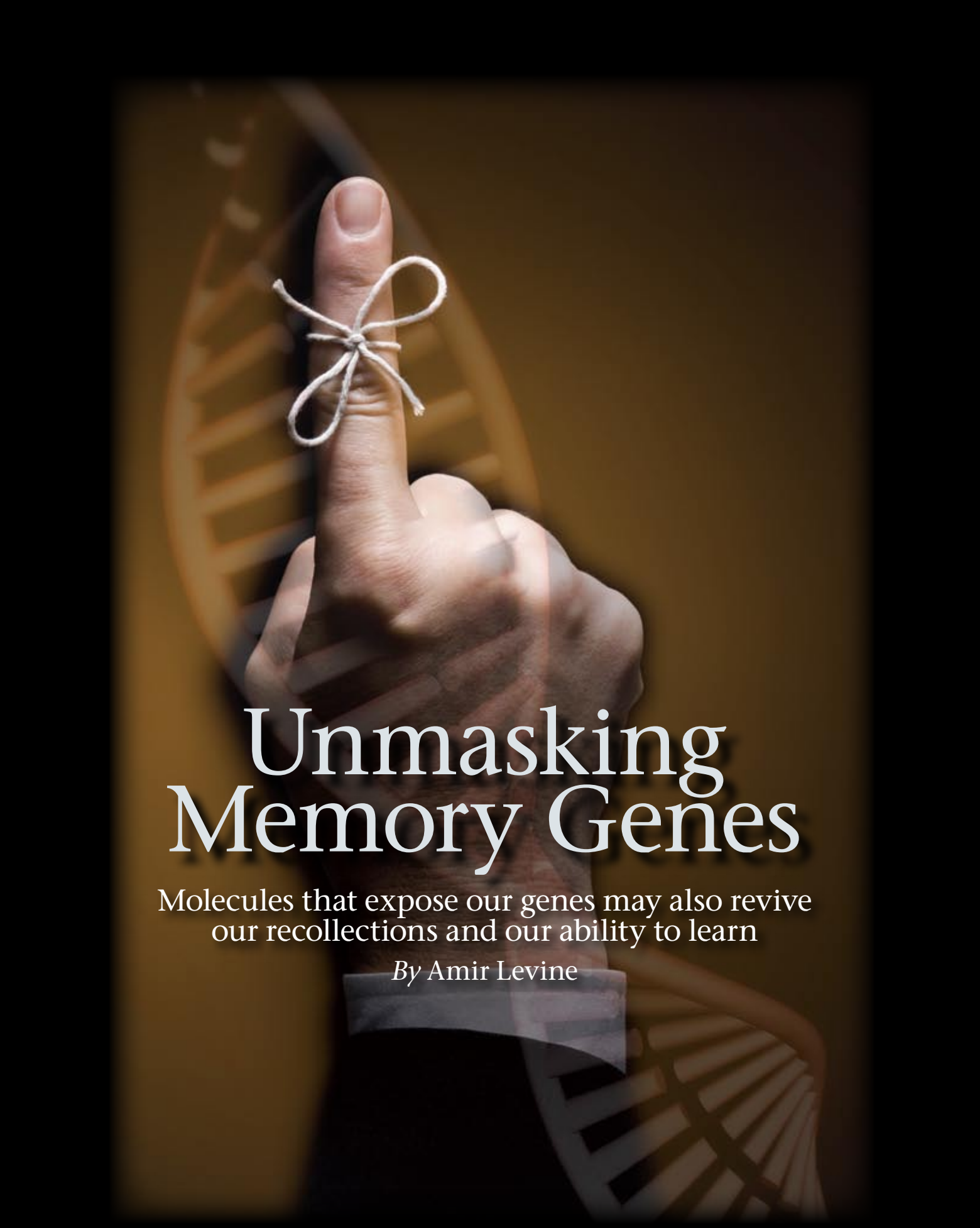


Unmasking Memory Genes

Molecules that expose our genes may also revive our recollections and our ability to learn

By Amir Levine

In Rainbows End, *by Vernor Vinge, a 2006 science-fiction novel set in the near future, modern medicine brings a talented Chinese-American poet, Robert Gu, back from end-stage Alzheimer's disease. Before treatment, Gu is bedridden and can neither talk nor remember his children. After the therapy, his memory returns, although he develops a different set of talents.* Flowers for Algernon, *the 1959 short story by Daniel Keyes, entertains a related fantasy in which a futuristic treatment transforms Charlie, a mentally retarded man, into a genius.*

Though fanciful, both these works echo research hinting that certain chemical treatments can reinvigorate the ability to learn and remember even in the face of brain damage or innate mental deficits. The studies—so far done in mice and sea slugs—indicate that the key to such cognitive improvements lies in epigenetics, the study of changes in DNA that do not affect the genetic code. Instead these chemical changes influence gene expression—that is, how actively the gene is used to make protein. Such alterations, it turns out, can have a profound impact on long-term memory. A drug compound, or even an environmental manipulation, that acts as a kind of volume knob for gene expression could someday help treat memory disorders and facilitate learning.

Gene expression is, after all, critical to memory formation. As a person learns and a memory takes shape, ebbs and flows in the activity of neurons incite the synthesis of new proteins, which help to cement or create connections between nerve cells. In this process, genes are first transcribed into RNA, which is then translated into protein [*see illustration on next page*].

Gene expression is strictly regulated. In chromosomes inside cells, DNA wraps around proteins called histones that serve as packaging material. In places where this packaging is looser, the underlying genes are accessible to the proteins that transcribe them, whereas tightly packaged DNA cannot be transcribed [see "The New Genetics of Mental Illness," by Edmund S. Higgins, on page 40]. Certain chemical changes to DNA or histones can loosen or tighten this chromosome structure and thereby enable or thwart the expression of memory genes.

Recently biologists have found that loosening part of a chromosome using drugs, or environments that provide more intellectual stimulation, can improve learning and memory in cognitively impaired animals. If such effects can be extended to humans, future therapies for memory disorders might work by altering DNA packaging in specific ways.

Rescuing Recollections

In the past few years several scientific teams have revealed that making a memory requires enzymes called histone acetyltransferases (HATs). HATs attach chemical units called acetyl groups to histones, thereby opening up DNA and facilitating gene expression. These enzymes counteract the activities of histone deacetylases, or HDACs, which remove acetyl groups from histones and condense DNA.

One 2004 study, for example, points to the importance of HATs in a mouse's ability to remember objects and locations. Neuroscientist Mark Mayford of the Scripps Research Institute in La Jolla, Calif., and his colleagues engineered mice with an abnormal gene for a HAT called CREB binding protein. The inserted gene produced CREB binding protein devoid of all HAT activity, eliminating its capacity to stick acetyl groups onto histones near important memory genes. (They engineered the defect so that it appeared only in adulthood and did not affect development.)

These mice displayed distinct memory deficits—they had difficulty recognizing familiar objects and recalling the path to a hidden platform in a water maze—suggesting that normal memo-

FAST FACTS

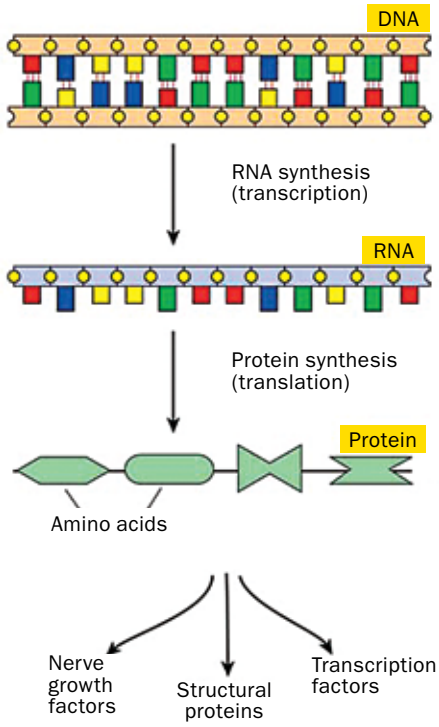
Molecules of the Mind

1» **Chemical treatments can reinvigorate learning and memory in rodents, even in the face of brain damage or inborn mental deficits.**

2» **One route to cognitive improvement lies in epigenetics, the study of changes in DNA that do not affect the genetic code but instead influence gene expression—that is, how actively the gene is used to make protein.**

3» **Future therapies for memory disorders might work by altering DNA in ways that facilitate gene expression.**

AGE FOTOSTOCK (*DNA*); JUPITERIMAGES (*hand*)



During protein synthesis, a complex of (previously fabricated) proteins (*not shown*) reads a segment of DNA, using it to produce RNA, in a process known as transcription. Another set of molecules cooperates to translate the RNA into a protein, made up of linked amino acids. Cellular proteins may participate in cell growth, cell structure or transcription of DNA, among other functions.

ry requires the capacity to attach a sufficient number of acetyl groups to histones. And to prove that the memory impairment resulted from a lack of HAT activity, the researchers showed they could abolish the cognitive deficit by compensating for the molecular one. Gene-altered mice performed normally on the object memory test after receiving a chemical that inhibits HDACs, the enzymes that remove acetyl groups, and therefore boosts the number of acetyl groups bound to histones.

But could such a drug recover memories in other situations? Certain clinical phenomena show that memory loss is not always permanent. When patients emerge from anesthesia after receiving electric shock treatment for depression, their memory returns in stages. At first they remember nothing; then childhood memories emerge, and, within minutes, memory lane takes patients to the present, indicating that recollections can indeed reappear after they might seem to have vanished.

Animal experiments now indicate that retrieving lost memories might even be possible after severe neuronal damage—and that epigenetic mechanisms are central to this recovery. Neuroscientist Li-Huei Tsai of the Massachusetts Institute of Technology and the Howard Hughes Medical Institute and her colleagues genetically engineered a group of mice to develop an Alzheimer's-like dementia when the scientists gave them the antibiotic doxycycline: the antibiotic flipped the genetically programmed dementia switch to the "on" position at the desired time.

While the mice were still cognitively healthy, the scientists taught them to associate an electric shock with a particular chamber so that the mice froze in fear whenever they were in the chamber. When the researchers administered doxycycline to some of the mice, however, those rodents suffered brain damage and memory loss and forgot their fear, frequently failing to freeze in the chamber. In contrast, mice that did not get the antibiotic froze as much as they ever had.

In an attempt to restore the memory in the brain-damaged mice, the investigators injected some of them daily for four weeks with a chemical that inhibits the acetyl-removing HDACs, a process that invigorates HATs and unwraps DNA from its protein packaging. In 2007 Tsai's team reported that the epigenetic treatment restored the fear memory in the mice that received it and that no such memory reappeared in the mice that had been injected with an inert saline solution. Changing the packaging of DNA and reinvigorating gene expression somehow unmasked this simple fear memory—probably, the researchers speculate, by spawning new connections between healthy neurons rather than by repairing damaged ones.

The M.I.T. group also came up with a drug-free way to restore the obliterated fear memory: changing the rodents' environment. Enriching the surroundings—giving the mice new toys to play with and running wheels that enabled them to exercise—similarly increased the number of acetyl groups on histones, apparently revving up the expression of memory genes just as the HDAC inhibitors did. Such a finding may help explain why scholars, who presumably live in an intellectually enriched world, are less susceptible to Alzheimer's. A mentally stimulating job may be a form of environmental enrichment for humans, alleviating the effects of neurodegenerative processes in people by loosening chromosome structure.

Correcting Cognition

If medicine can revive memory after brain degeneration, could it also ameliorate inborn mental deficiencies such as those the fictional character Charlie displays in *Flowers for Algernon*? In a study published in 2004, biologist Angel Barco, then at the College of Physicians and Surgeons at

EDMUND S. HIGGINS

(The Author)

AMIR LEVINE is a psychiatrist and neuroscientist at Columbia University. He is currently investigating the epigenetics of addiction and memory.

A drug that chemically uncoils DNA restored the forgotten fear of a shock in brain-damaged mice.

Columbia University, and his colleagues tested this hypothesis in mice that had a genetic disorder resembling Rubinstein-Taybi syndrome, which in humans leads to mental retardation as well as skeletal abnormalities such as facial deformities and broad thumbs.

Underlying this syndrome is a mutation in the gene for CREB binding protein. A defect in one of a person's two copies of the gene renders its protein nonfunctional; in such cases, cells generally produce only half the normal amount of protein. The resulting deficit in CREB binding protein activity seems to stymie the gene expression necessary for long-term memories to form, among its other effects. Similar to what Mayford's group saw in their HAT-deficient adult mice, Barco's team confirmed that mice born with a defective gene for CREB binding protein (and displaying classic Rubinstein-Taybi-like traits) have poor long-term memory. In their experiments, the mutant rodents had trouble recollecting having been shocked in a particular environment or after hearing a tone. They froze less often than normal mice did when they were exposed to the setting or sound that had been paired with the shock.

Mice with the CREB binding protein deficit displayed no such cognitive problems, however, if they received an HDAC inhibitor three hours before their training sessions with the shock, suggesting that the deficit can be reversed by loosening DNA's protein packaging—even if this unraveling occurs belatedly, in adulthood. Such findings hint that the remodeling of this DNA wrapping might help improve cognition even in the face of ingrained developmental deficits, presumably by facilitating the expression of important memory genes. In Rubinstein-Taybi syndrome, such fixes may directly compensate for the low rates of acetylation that result from the lack of functional CREB binding protein.

Other molecules affecting DNA's wrapping are also involved in memory and learning. The sea slug *Aplysia,* for instance, contains a pair of compounds called polyADP-ribose (PAR) and PAR polymerase (PARP), the enzyme that attaches PAR to DNA's protein packaging. This enzyme facilitates transcription by stacking PAR molecules on histones as well as on various proteins involved in the reading of the DNA template.

To study the role of this enzyme in memory and learning, the late neurobiologist James H. Schwartz of Columbia University and his colleagues tempted *Aplysia* with a seaweed these creatures love and that the researchers had deviously encased in a cotton mesh, making the seaweed impossible for the slug to eat. The slugs learned that the seaweed was inedible and stopped trying to get it, eliciting the formation of a long-term memory, which required protein synthesis. But when the scientists treated some sea slugs with a compound that inhibits the PARP enzyme shortly before showing them the covered seaweed, the mollusks failed to remember that the food was inaccessible: the next day they still attempted to eat it. Thus, PARP seems to be an essential memory enzyme, suggesting that chemically enhancing its effects could be yet another avenue for bolstering memory in humans, who also bear a version of this protein.

Such work, along with the rodent studies, reveals the tremendous potential of epigenetic alterations to mold memories and, in the future, to reverse cognitive disorders as diverse as Alzheimer's and mental retardation. A better understanding of the systems that modify the packaging of DNA may help us one day make science-fiction stories such as *Rainbows End* and *Flowers for Algernon* a reality. M

In the sea slug *Aplysia,* an enzyme called PARP enables memory formation by loosening the structure of chromosomes.

CHRIS NEWBERT *Minden Pictures*

(Further Reading)

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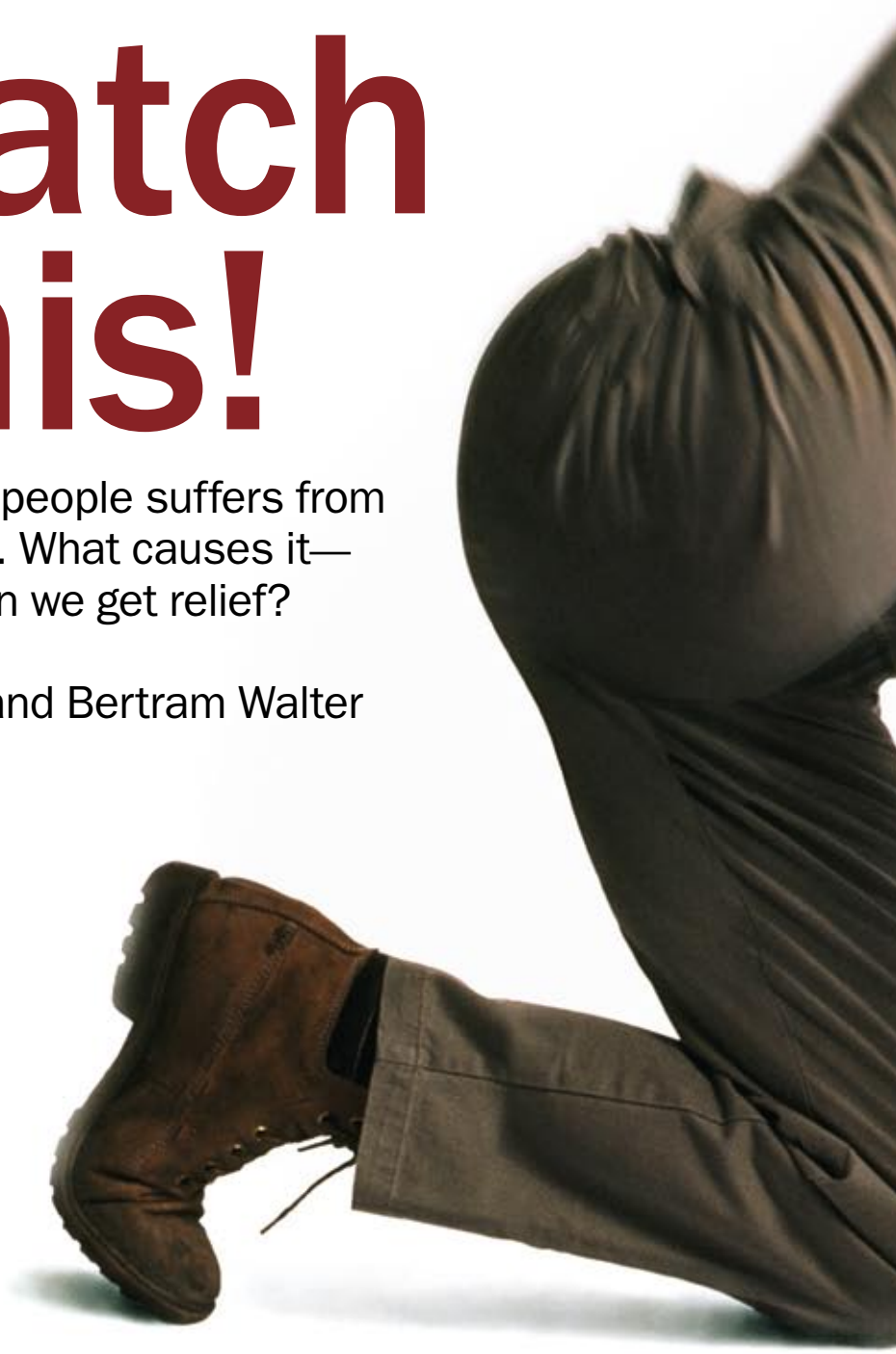
Scratch This!

About one in 10 people suffers from chronic itching. What causes it—and how can we get relief?

By Uwe Gieler and Bertram Walter



Warning: just reading this article might make your skin crawl.

Thinking about itching, seeing people scratch, looking at pictures of bedbugs or other itch inducers—all can bring on an irresistible urge to flick away that irksome feeling.

But itching—"pruritus," to physicians—is more than an occasional nuisance. The sensation, which arises from an irritation of the nerve cells along the skin, serves as a helpful warning about potential hazards such as insects or foreign materials—and scratching is often a simple and effective method for dealing with them. Itching is also the main symptom of many skin diseases and appears in some systemic conditions, such as chronic renal disease, cirrhosis and some types of cancer.

Whereas a quick skin scrape has its pleasures, constant itching can become an agony if underlying conditions are not treated. According to estimates, 8 to 10 percent of people worldwide endure chronic itching, and it is the most frequent complaint confronted by dermatologists. The sensation's sources, however, have been mysterious and poorly understood.

Long overlooked as a milder form of pain, itching is now gaining a new appreciation in the research community because of its complexity and its significance to thousands of sufferers. In addition to physical causes such as skin conditions or allergies, the source of that tingling torment has a strong mental component. Scientists are now probing the phenomenon's underpinnings with imaging technology and other means—even down to the molecular level.

Glossary
Four Reasons to Scratch

The medical field groups itching sources into four categories:

- **Pruritoceptive**, which results from dry, inflamed or otherwise damaged skin and is mediated by the messenger substance histamine, as in cases of insect bites, hives, neurodermatitis and psoriasis
- **Neuropathic**, which arises in diseases of the nerve fibers, such as multiple sclerosis, shingles and chicken pox
- **Neurogenic**, which originates in the central nervous system
- **Somatoform** (formerly psychogenic), which has no physical cause

A New Understanding

Itching's sources have puzzled people for ages. In the second century A.D., for instance, Greek physician Galen observed that itching might arise from an underlying condition not related to the skin. German physician Samuel Hafenreffer defined itching almost 350 years ago as an unpleasant perception on the skin that subsequently triggers the need to scratch. Napoleon famously experienced severe itching, as did physician Jean-Paul Marat, an intellectual leader during the French Revolution.

As little as 10 years ago the medical profession viewed itching as pain's little brother. After all, the logic went, the sensation courses along the same nerve paths to the brain as pain does, except that the intensity of the irritation is less severe. This notion was based on, among other

FAST FACTS
Why We Itch

1» **Itching is a subjective, unpleasant sensation on the skin that induces the need to scratch. It is symptomatic of numerous dermatological and other diseases, and it may have varied causes.**

2» **Previously researchers believed that itching could be traced back to the same neuronal circuits as pain. Today it is clear that it is mediated by its own nerve paths.**

3» **A variety of drugs such as antihistamines and certain psychoactive substances may help relieve discomfort—as can a cool environment.**

HOWARD BERMAN *Getty Images (preceding pages)*

SUSUMU NISHINAGA *SPL/Photo Researchers, Inc.* (*pollen*); GETTY IMAGES (*stressed man*); TIM FLACH *Getty Images* (*bedbug*); GETTY IMAGES (*snowflake*)

things, the observation that pain switches off itching. According to so-called intensity theory, weak neuronal stimulation causes itching, whereas stronger stimulation leads to pain.

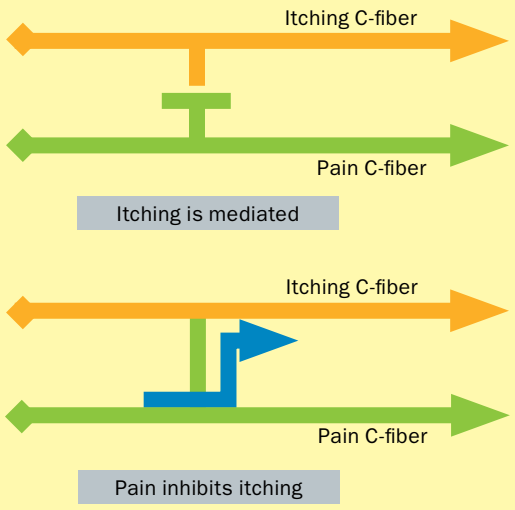
In 1997, however, neurophysiologist Martin Schmelz, then at the University of Erlangen-Nuremberg in Germany, proved that the need to scratch reaches the spinal cord from the skin via independent nerve fibers called polymodal C-fibers. These C-fibers seem to be identical to those that signal pain, but they transmit only itching sensations. Signals conveying skin irritation travel down the nerve fiber to the spinal cord and then on to the brain. Scratching and rubbing may interfere with these nerve endings by stimulating pain and touch receptors in the same areas, thus inhibiting the surrounding itch receptors, called pruriceptors.

In addition, Schmelz's team, together with Hermann Handwerker, also at the University of

Itch inducers (*clockwise from top left*): allergens such as pollen, feeling stressed, pests such as bedbugs and dry skin exacerbated by winter days.

Pain Has Right-of-Way

Pain traveling along nerve fibers called C-fibers causes "competitive inhibition" of separate itch-mediating C-fibers: itching is blocked (*blue arrow*) when pain neurons fire.



Erlangen-Nuremberg, discovered connections between the itch-mediating C-fibers and pain C-fibers. This finding of possible communication between signaling fibers adds a further mechanism by which pain relieves itching [*see illustration above*].

In 2001 researchers at the Barrow Neurological Institute in Phoenix identified specific nerve cells in cats that respond selectively to the signaling molecule histamine—which triggers itching—but not to heat or pain stimuli.

GEHIRN & GEIST (*top*); MATT COLLINS (*bottom*)

A Real Pain

Itching gets to be a real pain when it is chronic—that is, when it persists or recurs. According to a study by Norwegian psychiatrist Florence Dalgard, stress is the most important trigger apart from allergic reactions. Other studies have found that scabies, which is caused by mite infestation, affects about 300 million people worldwide. And more than 30 million Americans suffer from eczema, which is associated with a strong desire to scratch. Furthermore, about 42 percent of almost 19,000 dialysis patients from 12 countries included in a 2006 study reported moderate to severe itching. The situation is similar for patients with liver damage [*see glossary on page 54*].

Itching may also be triggered by the mind. Most people need only watch others scratching to start themselves. Just seeing a picture that is connected with scratching—a photograph of fleas, for example—can do the trick as well. But until recently, there was not even any clear scientific evidence of this widely shared experience.

To close this gap, our team, under the direction of medical psychologist Jörg Kupfer, conducted a psychological experiment with students. Our unsuspecting participants were asked to evaluate the educational quality of a lecture on the topic, "Itching—What Is It?" The test subjects—60 medical and psychology students—attended one of two different lectures. One group viewed images of lice, fleas, bedbugs and allergic skin reactions; the other group saw babies and calming landscapes. Unsurprisingly, the students in the first group scratched themselves significantly more frequently during the presentation than their counterparts in the second one did.

It may be that this mental trigger is associated with so-called mirror neurons. These specialized nerve cells fire both when we ourselves perform a certain action and when we observe someone else doing it [see "A Revealing Reflection," by David Dobbs; Scientific American Mind, April/May 2006]. The contagious character of yawning, for example, is attributed to mirror-neuron activity.

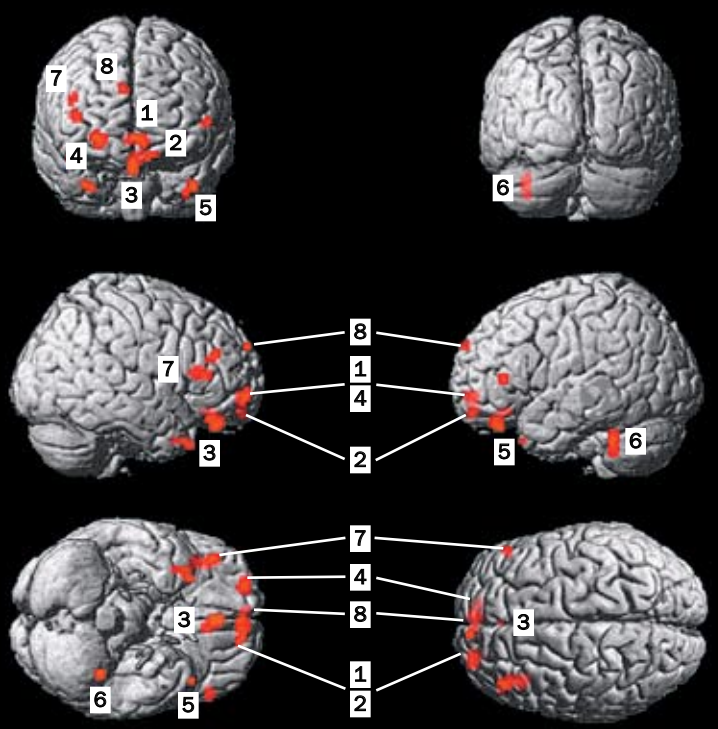
To find out which areas of the brain are par-

As the subjects itched, many brain regions fired that tend to be **associated with emotion**.

Itch in the Head

Itching triggered by histamine induces an array of characteristic brain activation in:

- Numerous convolutions (gyri) in the cerebrum that prepare movement and interpret sensory perceptions and in the left frontal cingulate gyrus, which is responsible for emotions (*1–4, 7, 8*)
- Left temporal lobe; these activities, according to one of the authors (Walter), are generated by memory retrieval and by comparisons with previous experiences (*5*)
- Left hemisphere of the cerebellum, which is responsible for coordination of movement (*6*)



1. Medial part of the superior frontal gyrus; anterior cingulate gyrus (left hemisphere)
2. Medial and orbital parts of the superior frontal gyrus; straight gyrus (left)
3. Medial and orbital parts of the superior frontal gyrus; straight gyrus
4. Orbital and dorsolateral parts of the superior frontal gyrus (right)
5. Middle temporal gyrus (left)
6. Body of the cerebellum (left)
7. Triangular part of the inferior frontal lobe (right)
8. Medial part of the superior frontal gyrus (right)

ticularly active during itching, researchers have used imaging methods to look into the heads of their test subjects after generating itchiness with histamine. Neuroscientist Francis McGlone of Unilever Research and Development in Cheshire, England, and his colleagues used functional magnetic resonance imaging (fMRI) to reveal firing in parts of the cerebellum and in regions of the frontal lobe. The researchers found that the behavioral responses result from the different frontal lobe activation for itching and pain—that is, scratching, on the one hand, and pain perception, on the other.

A team at the Bender Institute of Neuroimaging at the University of Giessen in Germany also used fMRI to study the itching triggered by histamine over a period of approximately 15 minutes, the time it generally takes for such experimentally induced itching to subside. The researchers found that several areas of the brain would activate in characteristic ways: regions, for example, in the frontal lobe, in the left temporal lobe and in the left hemisphere of the cerebellum [*see box above*]. Surprisingly, however, there was no apparent activity in the sensorimotor cortex—the areas of the cerebral cortex that process sensory stimuli and control movement. Instead many of the regions that fired are those that tend to be associated with emotion.

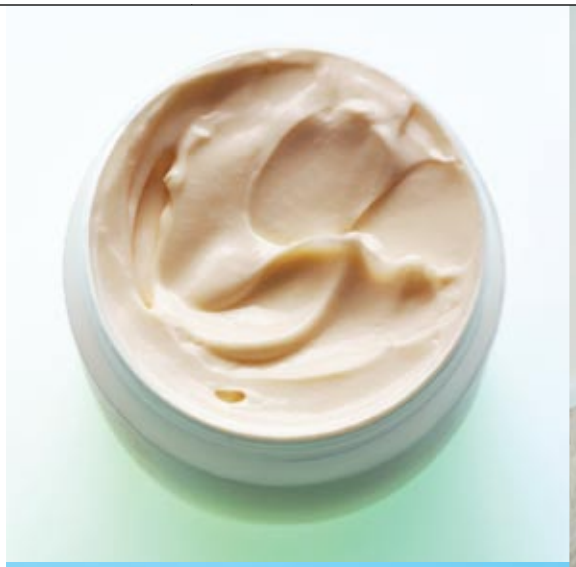
On the Trail of Neurodermatitis

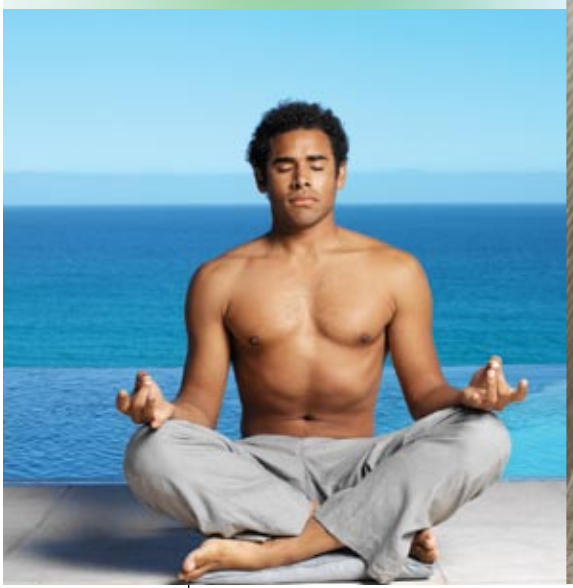
Other researchers have confirmed the importance of brain areas that process emotion. According to a recent study by Handwerker, itching

COURTESY OF BERTRAM WALTER

(The Authors)

UWE GIELER is a dermatologist and professor of psychosomatic medicine at the University of Giessen in Germany. BERTRAM WALTER is a psychologist and researcher at the Bender Institute of Neuroimaging in Giessen.





Itch soothers (*clockwise from top left*): lotions and creams, cool baths and relaxation techniques.

NEIL SNAPE *Jupiterimages (lotion)*; BLAKE LITTLE *Getty Images (bathtub)*; GETTY IMAGES *(meditation)*

is partly processed and activated in some of the same regions of the brain that pain is and, additionally, in the emotion center, the amygdala. And according to a team led by Hideki Mochizuki of the Japanese National Institute for Physiological Sciences, the cingulum, a switching center that processes emotions, and the insula, an area also associated with emotion and disgust, both fire during itching—but not during pain.

Gil Yosipovitch of Wake Forest University Baptist Medical Center has demonstrated that the brains of patients with neurodermatitis (chronic itching) react markedly differently than those of healthy persons. Only in the latter individuals does scratching inhibit activity in the cingulum. The researchers hypothesize that this control mechanism normally prevents itching from being strengthened by emotion. In neurodermatitis patients, the mechanism seems to be overridden, and itching gains the upper hand as a consequence.

Itch research has recently spread to molecular biology as well. In 2007 Zhou-Feng Chen and Yan-Gang Sun of the Washington University Pain Center in St. Louis, for example, looked at the *GRPR* gene, which contains the building instructions for a receptor that is activated by a compound called gastrin-releasing peptide (GRP). Such neuropeptides are proteins that neurons release, often with profound effects on behavior. Mice in which the *GRPR* gene has been deactivated react to substances that stimulate itching with less scratching than control animals do. When the researchers injected normal mice with a blocker for the GRP receptor, these animals were also less susceptible to itching.

The connection between itching and neuropeptides such as GRP has been a topic of research for some time and is a special focus of the work of Martin Steinhoff and his colleagues at the University of Münster in Germany. They have found

The brains of patients with **chronic itching** react markedly differently than those of healthy persons.

The mere sight of someone scratching can set off itchiness.

PM IMAGES/GETTY IMAGES

that certain neuropeptides, along with their receptor molecules and so-called endopeptidases (which degrade neuropeptides), play a key role. If the regulation of these biochemical processes gets out of whack, the result may be problems with chronic inflammation, itching and pain.

Neurodermatitis is a very common case in point. Here the endopeptidases do not work fast enough, so that the neuropeptides end up activating far too many immune cells. The consequence is a cascading inflammatory response and itching.

Soothing News

Scratching offers temporary relief but may further irritate the skin or cause it to tear. Treatments include lotions and creams (such as calamine and hydrocortisone), antihistamines, opioid antagonists (such as naltrexone, a drug used to treat narcotic and alcohol dependence), aspirin and ultraviolet-light therapy. Chronic itching is primarily treated medically. In a recent study of 385 patients, Dorothee Seipmann and Sonja Ständer of the University of Münster showed that 65 percent of sufferers benefit from such drugs. The most frequently prescribed medications are antihistamines. The epilepsy drug gabapentin is used in cases of neuropathic (caused by nerve fibers) itching, and combinations of naltrexone, pregabelin, the antidepressant paroxetine (Paxil) and the immunostatic cyclosporine are also in use.

The most promising treatment approach at the moment may include substances that affect the opioid receptors involved in itching. Opium and heroin addicts almost always suffer from itching, brought about largely by hyperactivation of the mu-opioid receptors. Pursuing this trail, researchers might explore the therapeutic approach of blocking this type of receptor. The receptors' natural antagonists are the kappa-opioid receptors, whose activation decreases itching. Initial clinical studies are already looking at substances that stimulate the kappa receptors.

A number of calming techniques, among them autogenic training (in which patients repeat a set of visualizations) and Jacobson's progressive muscle relaxation (in which patients relax muscles to relieve tension), have proved effective in supplementing medical treatment. Psychotherapy is generally not very useful in getting rid of the urge to itch.

And what can sufferers do at home to decrease persistent, bothersome itching? Cool showers or baths, particularly with bath additives that contain soothing substances suggested by a dermatologist, can help. Cold packs can also be useful in getting a localized itch under control. A cool environment, especially at night, is helpful. Air out the bedroom and wear loose-fitting pajamas—if you need to wear anything at all. Sometimes that is all it takes to reduce itching to a tolerable level. M

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GUSTOIMAGES *SPL/Photo Researchers, Inc. (this page)*; CRISTINA PEDRAZZINI *SPL/Photo Researchers, Inc. (opposite page)*

ANOREXIA MAY REPRESENT A PROFOUND PSYCHIATRIC DISORDER THAT SPAWNS AN ADDICTION TO DEPRIVATION **BY TRISHA GURA**

ADDICTED TO STARVATION

A recent tabloid captured the common wisdom about anorexia nervosa. In an interview, actor Christina Ricci blamed the pressures of success for her prior struggle with the disease. The headline flashed, "Ricci: Hollywood made me anorexic."

Christina Ricci, 2006

But did it? True, anorexia is characterized by compulsive dieting or exercise to get thin. And the pursuit of thinness in contemporary culture—particularly in Hollywood—has become a seemingly contagious obsession. Yet there is thin, and then there is emaciated. Crossing over that line means a loss of a basic survival instinct—to eat in response to hunger—that culture should not be able to touch.

What is more, cultural cues cannot easily explain why the afflicted, who are shockingly skinny, misperceive themselves as fat. Anorexics also say they feel more energetic and alert when starving: starvation boosts their metabolic rate, which is in stark contrast to the slowing of metabolism that occurs in most people during a fast.

Such mysteries cry out for a biological explanation. To find one, researchers are probing the brains of anorexics; their work is painting a new picture of anorexia as a multifaceted mental illness whose effects extend far beyond appetite. The illness is accompanied by disturbances in the brain's reward circuitry that may lead to a general inability to feel delight from life's pleasures, be they food, sex or winning the lottery. As such, the ailment shares characteristics with drug addiction—the drug in this case being deprivation itself. The study of anorexia, therefore, may yield insights into brain mechanisms for producing pleasure and how something as seemingly unpalatable as starvation or extreme asceticism might, oddly, give rise to a sense of hedonism.

An estimated 0.5 to 3.7 percent of girls and women in the U.S. suffer from anorexia, according to the National Institute of Mental Health. (One tenth as many males experience the illness.) At least two thirds of anorexics do not fully recover even after years of the current treatment, which consists largely of psychotherapy. As a result, anorexia still holds the record for the highest mortality rate (up to 20 percent) for any mental illness in young females. Cutting that death rate will require a new approach, experts say. "People have long been blaming families and media," says psychiatrist Walter Kaye of the University of California, San Diego. "But eating disorders are biological illnesses, and better treatments will come from more biologically-based approaches."

Diet as a Drug

Most people abhor dieting. But when a person with anorexia diets, he or she actually feels *better*—more alert and energetic—when starving. Anorexics do feel hunger pangs; they simply find ways to override them. Dieting becomes the ultimate accomplishment, a fix that a certain kind of dieter learns to crave.

The lack of food may function like an addictive drug for anorexics, says biologist Valerie Compan of CNRS in Montpellier, France. Almost every drug of abuse acts on the brain's natural reward circuitry—and in particular on a pleasure hub called the nucleus accumbens—to boost the levels of a signaling chemical, or neurotransmitter, called dopamine. The release of dopamine prompts good feelings and also produces the "high" in the case of many abused drugs. Some such drugs, including the highly addictive club

MARK MAINZ *Getty Images*

FAST FACTS

Deprived of Delight

1» **Researchers are painting a new picture of anorexia as a multifaceted mental illness whose effects extend far beyond appetite.**

2» **Anorexia is accompanied by disturbances in the brain's reward circuitry that may render patients unable to feel delight from life's pleasures, be they food, sex or winning the lottery. Some scientists compare anorexia to drug addiction.**

3» **Anorexia's biological risk factors appear to exert much of their insidious power at puberty, underscoring the importance of timing in prevention. Eating too little to keep up with growth or activity levels may tip the balance in favor of anorexia in teenagers who are predisposed toward developing the disorder.**

drug ecstasy, also suppress appetite—a clue that a refusal to eat might somehow arise from abnormal activity in the brain's reward system.

In October 2007 Compan and her colleagues found some evidence for that idea. When the researchers injected ecstasy into the nucleus accumbens of mice, the rodents acted like anorexics. When they were offered food, the animals did not eat much, and when food was withheld, they did not work to get it. Ecstasy suppressed the rodents' appetites, the researchers determined, by stimulating a receptor for the neurotransmitter serotonin. Activating that receptor on neurons in the nucleus accumbens led to the production of a neurotransmitter associated with addiction called CART (for cocaine- and amphetamine-regulated transcript) that ultimately depressed the desire to eat.

RECENT DATA POINT TO PERTURBATIONS IN THE BRAIN'S REWARD CIRCUITRY AS A KEY PROBLEM UNDERLYING ANOREXIA NERVOSA.

This mechanism connects activation of the brain's reward circuitry to a lack of appetite. And if the two effects happen simultaneously, an individual may come to associate a lack of food with reward. In this way, the person could become addicted to hunger itself. "Anorexia can be an addiction," Compan says, "and it appears to share the same mechanism as a drug of abuse."

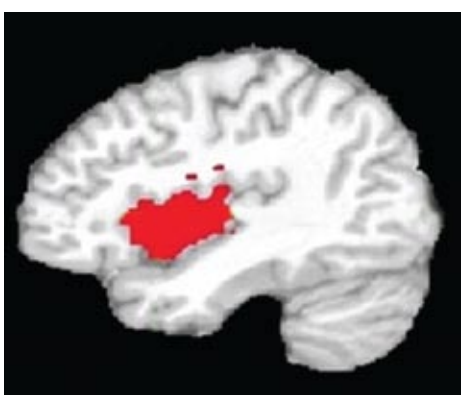
Lights Out

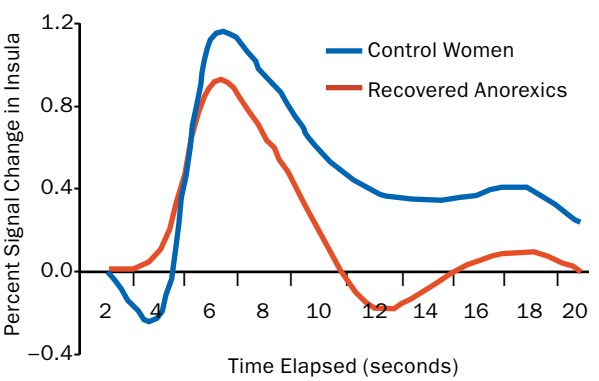
Other data, too, point to perturbations in the brain's reward circuitry as a key problem in anorexia. Some research hints that an addiction to starvation renders anorexics, like drug addicts, incapable of feeling pleasure from food and possibly other amusements as well. Kaye, along with University of Pittsburgh psychiatrist Angela Wagner and others, scanned the brains of 16 recovered anorexics and 16 women who had always eaten normally while the subjects sampled water or sugar water and reported whether they were enjoying the drink.

In May 2007 the researchers reported that all the women in the control group enjoyed the taste of the sugar water more than that of the plain water, and the pleasing sweet sensation lit up the insula, a brain structure important for recognizing taste. In contrast, in the women with a history of anorexia the insula responded much more weakly to the sweet taste, and its activation level bore no relation to how much the women enjoyed the sugar water, suggesting that these women lacked an ability to appreciate good tastes fully.

Anorexics' indifference to rewards is not limited to good-tasting food. In a study published in December 2007, Kaye's team had two groups of 13 women similar to those in the taste test play a decision-making game while lying in a functional magnetic resonance imaging scanner. Subjects had to guess if a hidden number was greater or less than five; they would win $2 for every correct guess and lose $1 for each incorrect answer.

The women in the control group responded appropriately to their wins and losses with commen-





In a control group of women who have always eaten normally, the taste of sugar water produced activity in a brain area called the insula (*shown in red*), which is important for processing taste. Drinking sugar water produced significantly less activation of the insula, on average, in the brains of recovered female anorexics (*red line on graph*) than in those of the controls (*blue line*), suggesting that anorexics cannot fully appreciate pleasant-tasting food.

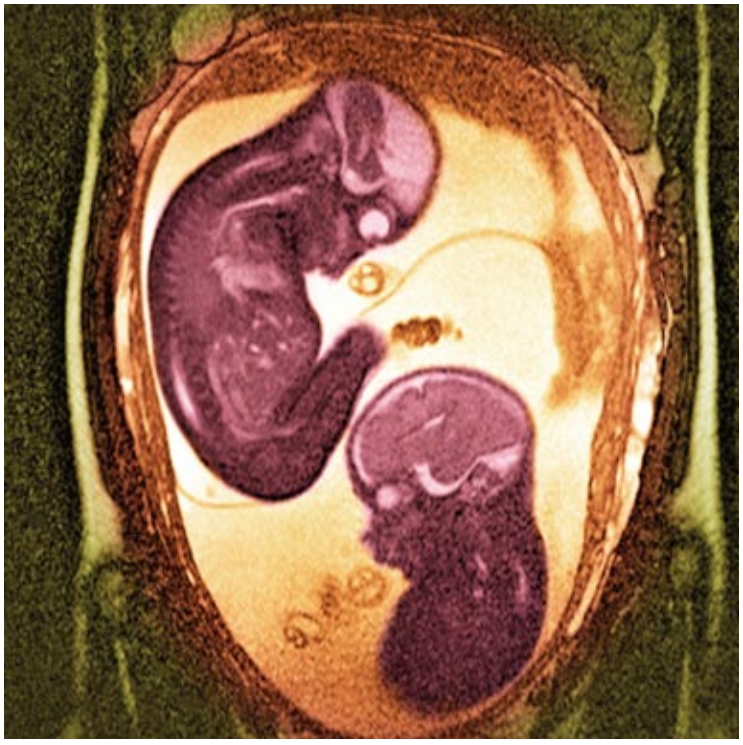
COURTESY OF TYSON OBERNDORFER; MODIFIED FROM "ALTERED REWARD PROCESSING IN WOMEN RECOVERED FROM ANOREXIA NERVOSA," BY A. WAGNER ET AL., IN *AMERICAN JOURNAL OF PSYCHIATRY*, VOL. 164, NO. 12; 2007

taries akin to "Yeah, I won!" or "Bummer, I lost." Those reactions were reflected in the participants' brains: the wins lit up a central brain region called the anterior ventral striatum, which contributes to the processing of immediate rewards, whereas the losses did not. In contrast, the women who had once had anorexia did not express joy when they won or disappointment when they lost, and their brains were similarly undiscriminating: the anterior ventral striatum of these women looked the same irrespective of the outcome of each game trial, indicating that their emotional unresponsiveness to rewards was rooted in their reward circuitry.

PUBERTY IS AN ANOREXIA TRIGGER: AT LEAST 40 PERCENT OF NEW CASES OCCUR IN GIRLS 15 TO 19 YEARS OLD.

Their brains did, however, display heightened activity in the caudate, part of the dorsal striatum, in response to a win as compared with a loss during the game. This brain region is part of a circuit that contributes to planning and evaluating long-term consequences. It may connect asceticism to reward in an anorexic's brain. The finding is consistent with anorexics' tendency to live in the future, planning for all contingencies, and to largely disregard the present. "People with anorexia have difficulty living in the here and now," Kaye explains.

Testosterone produced by a twin brother in the womb may protect his sibling against eating disorders. In contrast, exposure to prenatal estrogen from a female twin may precipitate disordered eating.



SIMON FRASER SPL/Photo Researchers, Inc.

Wired for "Perfection"

That difficulty coincides with other personality traits many anorexics share, including chronic anxiety—80 to 90 percent of anorexics report anxiety problems before the onset of disease—perfectionism, marked by a need to avoid mistakes and negative consequences (such as weight gain), and a focus on the attainment of goals. These traits define a person who worries intensely about living up to society's ultraskinny standards and perfects the art of weight loss.

Such a personality and lifestyle do not constitute a recipe for contentment. Rather an anorexic's existence revolves around rituals designed to attain an abnormal form of reward that is more about avoiding negative emotions—such as intense anxiety or the pain of perceived criticism—than about feeling good. From this standpoint, anorexia is not really about dieting but about coping with intolerable emotional distress. "Life is not rewarding for these individuals," Kaye points out.

The root of such distress may lie in altered forms of genes. Thus far the strongest candidates are those with myriad effects on the brain, consistent with the idea that anorexia stems from a multifaceted mental illness rather than from a specific anomaly in appetite regulation. They include genes for a serotonin receptor, a dopamine receptor and a protein called brain-derived neurotrophic factor that plays a general role in the growth of new nerve cells and maintenance of existing ones.

To further explore the connection between the personality of individuals with anorexia and their unique genetic makeup, Kaye, along with an international team of researchers, including psychologist Cynthia M. Bulik of the University of North Carolina at Chapel Hill, is now trying to pinpoint variations in genes that correlate with anxiety and a form of perfectionism they call "obsessionality." First reported in 2002 and still ongoing, preliminary analysis of the DNA from 1,167 individuals with anorexia has narrowed down the source to a stretch of chromosome 1 that contains at least 546 different genes.

But genes cannot be the whole story of anorexia. DNA analyses of identical twins (who share almost all of the same DNA) versus fraternal twins (who have many genetic differences) indicate that genetic variation accounts for only

How Lean Can You Go?

Many people would prefer to boast very little body fat—but what does that mean? Your body-fat percentage is the weight of your fat tissue as a proportion of your overall body weight. A high percentage of body fat means you are relatively flabby, and a low percentage means you are relatively lean. Some body fat is essential for life and reproduction [see "Essential Fat" in chart], and that bare minimum is significantly greater for women than for men because of hormonal differences related to reproduction, according to exercise physiologist Cedric Bryant of the American Council on Exercise.

Even serious athletes usually pack on more fat than this rock-bottom number. The consistent gym-goer in the "Fitness" category has slightly more body fat than the athletes, followed by individuals in the "Acceptable" range who are healthy but might wish to look leaner. Meanwhile the obese carry enough body fat to compromise their health.

Basic Body-Fat Percentages

Classification	Women (fat percentage)	Men (fat percentage)
Essential Fat	10–13	2–5
Athletes	14–20	6–13
Fitness	21–24	14–17
Acceptable	25–31	18–24
Obese	32 and higher	25 and higher

Most American adults fall into the high end of "Acceptable" or the low end of "Obese," Bryant says, whereas anorexics who exercise strenuously may sometimes dip into the "Essential Fat" range. In many cases, however, a person with anorexia does not have a very low body-fat percentage because she or he has lost so much lean body tissue that fat tissue makes up more of the body's overall mass, Bryant explains.

—Ingrid Wickelgren, staff editor

SOURCE: AMERICAN COUNCIL ON EXERCISE

50 percent of an individual's susceptibility to anorexia, according to Bulik and clinical psychologist Kelly L. Klump of Michigan State University. In addition to genes, the environment also has enormous influence over the brain.

Hormone Havoc

To anorexia researchers, environment includes puberty, a complex maturation stage that is known to be one of the most potent triggers of anorexia nervosa. According to the National Eating Disorders Association, at least 40 percent of newly identified cases of anorexia occur in girls 15 to 19 years old.

Furthermore, in a 2007 study of 772 twin girls, ages 11 to 18, Klump and her colleagues noted that disordered eating rarely showed up in any twin before the beginning of menstruation. Her observation is consistent with results published by Bulik in 2002 and with her own previous studies showing that the genetic component of disordered eating exerts its effects mainly *after* the start of puberty.

No one knows for sure what accounts for puberty's effects on gene activation, but one theory is that the surge of ovarian hormones, estrogen in particular, plays a significant role. Klump speculates that hormones trigger the expression of anorexia susceptibility genes and that the effect is most pronounced in girls with gene variants that cause anxiety, perfectionism and obsessiveness.

Hormones might play a role in anorexia long before puberty, too. In a March 2008 study in the *Archives of General Psychiatry,* Klump and her colleagues assessed the frequency of troubling eating habits such as fad dieting, bingeing and purging among 582 18- to 29-year-old twins. The young women with twin brothers ate more healthily than those who had twin sisters, the investigators found, but, more generally, disordered eating in *both* the females and males was lower in those who had a male twin. That is, females with twin sisters had the worst eating habits, followed by females with male twins and, after them, males with female twins. The best eaters were males with male twins.

What is going on? Klump believes testosterone is part of the answer. "We know that testosterone prenatally organizes the brain, making it more 'masculine,' " she says. "Thus, testosterone produced by a twin brother in the womb may actually protect his female twin against eating disorders."

(The Author)

TRISHA GURA is author of *Lying in Weight: The Hidden Epidemic of Eating Disorders in Adult Women* (HarperCollins, 2007). A former Knight Science Journalism Fellow at M.I.T. and a Resident Scholar at Brandeis University, Gura writes and blogs extensively about obesity, eating disorders and related topics (http://trishagura.com).

Exposure to prenatal estrogen may precipitate disordered eating; after all, the males in these studies had far better eating habits if their twin was male rather than female. Some researchers point out that female fetuses secrete sex hormones that might trigger the expression of anorexia susceptibility genes, such as the one for the serotonin receptor or those for related molecules. "We know that estrogen has effects on genes in the brain, and we know that estrogen is a pretty potent regulator of serotonin receptors," Klump says. Such a latent fashioning of the brain's architecture and functioning may explain, in part, the striking gender differences in anorexia. The possible influence of sex hormones also suggests that relatively large-scale distortions in brain physiology may underlie anorexia.

WARNING TO YOUNG ATHLETES: NOT EATING ENOUGH CAN LEAD TO POOR PERFORMANCE AND A DANGEROUS ADDICTION TO UNDEREATING.

Hunger Strikes

Environmental influences outside the human body might also pull genetic triggers for anorexia. One of these is likely to be undernutrition itself. That is, a lack of sufficient calories might be another "on switch" for anorexia susceptibility genes in addition to the surges of estrogen at puberty.

Therapist Shan Guisinger, who is affiliated with the University of Montana, pointed out that the growth spurts of puberty and, in many cases, intense participation in athletics can boost the caloric requirements of teens far beyond what they are getting in their diet. A 1999 study of 1,445 Division 1 NCAA athletes supports the idea that young female athletes might be at particular risk. Craig Johnson, director of the eating disorders program at the Laureate Psychiatric Clinic in Tulsa, Okla., and his colleagues found that more than one third of the females they surveyed reported attitudes and behaviors that put them at risk for anorexia, including dieting, using diet pills and wanting to have an abnormally low body-fat content. In fact, these female athletes reported a mean body-fat content of 15.4 percent, a figure that is often below that required for normal menses.

Young female athletes might be at particular risk for anorexia. Some data suggest that dieting practices common among these athletes might turn on anorexia susceptibility genes.

AGE FOTOSTOCK

But does starvation really propel a person toward anorexia, or might the anorexia-prone simply be the ones who choose to exercise and eat too little? Supporting the former hypothesis is a renowned study conducted in 1944 by Ancel Keys and his colleagues at the University of Minnesota. To observe how to best refeed prisoners of war, Keys recruited 36 young men and cut their caloric intake almost in half for 24 weeks. During that semistarvation period the subjects obsessed, fantasized and dreamed about food. When they were allowed to eat normally again, the men gorged and regained weight. Yet some started engaging in anorexiclike behaviors, including dieting and complaining about too much fat around their bellies, thighs and buttocks. The study showed that deprivation, even in normal men, could prompt the onset of anorexia in a small number who are predisposed to the condition.

In case semistarvation can spark the disorder, eating disorders experts now educate coaches and gym teachers to be on the lookout for young athletes at risk. They tell coaches to counsel their charges that not eating enough can lead to poorer performance and, worse, to a dangerous addiction to undereating.

Meanwhile psychiatrist Christopher Fairburn of the University of Oxford is tailoring a

Survival of the Thinnest

Why would a predisposition to anorexia survive in the gene pool, especially when one defining feature of anorexia is that a female stops menstruating for at least three consecutive cycles? Therapist Shan Guisinger, who is affiliated with the University of Montana, speculates that the answer may lie in the benefits of anorexia for helping early humans cope with famine.

A female whose genes made her more energetic when she was starving might well have helped her clan survive times of scarcity: she could scout and forage for food when no one else could. Traits of perfectionism and overachievement, moreover, could have helped her on difficult foraging journeys. Famine might even have activated her anorexic condition. And, Guisinger's theory goes, when food became plentiful again, the tribe would feed her enough for her to reproduce.

Although such a theory is impossible to prove, espousing it can be therapeutic. Telling a woman who suffers from a disease marked by misery and low self-esteem that she is genetically programmed to be Joan of Arc (who may have suffered from anorexia, according to Guisinger) may help her see herself as a hero rather than as a failure. She may then understand that anorexia might have once been an asset in emergencies but is an illness in a culture that emphasizes thinness at all times.

In one theory of the origins of anorexia, the afflicted are likened to French heroine Joan of Arc (*above*).

"The explanation makes sense of their experience," says Guisinger, who has used the concept in her therapy. "It explains why they feel virtuous resisting hunger, see fat on their emaciated bodies, and feel driven to exercise. Patients tell me, 'It helped me to recover.'" —*T.G.*

type of cognitive-behavior therapy (CBT) to anorexia. Originally developed to treat depression, CBT is designed to help an anorexic patient change both his or her destructive eating habits and the mental state that led to them. Kaye's group and others are exploring psychotherapy strategies that either help anorexics feel pleasure or use incentives for adopting eating behavior that is geared toward immediate rewards rather than long-term results.

Another experimental frontier involves the use of the hormone leptin, produced by fat cells, to help women with a history of anorexia resume menstruation and possibly also develop healthier attitudes about food and life. In addition, Compan and her colleagues are testing a compound in mice that blocks the activity of one type of serotonin receptor in hopes of reducing its inhibitory effects on appetite in the nucleus accumbens.

As these and other treatment ideas move forward, their origins trace back to the neurobiological, psychological and endocrine roots of disease that may have formed as early as embryonic development. "Until we better understand the biology of these conditions," Kaye says, "we can't devise better treatments." M

(Further Reading)

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- **Altered Reward Processing in Women Recovered from Anorexia Nervosa.** Angela Wagner et al. in *American Journal of Psychiatry,* Vol. 164, No. 12, pages 1–8; December 2007.
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THE ART ARCHIVE/CORBIS

Bisexual Species

Homosexual behavior is surprisingly common in the animal kingdom. It may be adaptive—helping animals to get along, maintain fecundity and protect their young

By Emily V. Driscoll

Two penguins native to Antarctica met one spring day in 1998 in a tank at the Central Park Zoo in midtown Manhattan. They perched atop stones and took turns diving in and out of the clear water below. They entwined necks, called to each other and mated. They then built a nest together to prepare for an egg. But no egg was forthcoming: Roy and Silo were both male.

Robert Gramzay, a keeper at the zoo, watched the chinstrap penguin pair roll a rock into their nest and sit on it, according to newspaper reports. Gramzay found an egg from another pair of penguins that was having difficulty hatching it and slipped it into Roy and Silo's nest. Roy and Silo took turns warming the egg with their blubbery underbellies until, after 34 days, a female chick pecked her way into the world. Roy and Silo kept the gray, fuzzy chick warm and regurgitated food into her tiny black beak.

Like most animal species, penguins tend to pair with the opposite sex, for the obvious reason. But researchers are finding that same-sex couplings are surprisingly widespread in the animal kingdom. Roy and Silo belong to one of as many as 1,500 species of wild and captive animals that have been observed engaging in homosexual activity. Researchers have seen such same-sex goings-on in both male and female, old and young, and social and solitary creatures and on branches of the evolutionary tree ranging from insects to mammals.

Recent same-sex couplings at New York's Central Park Zoo include these two young male chinstrap penguins, Squawk and Milo.

NICOLE BENGIVENO *New York Times/Redux*

Unlike most humans, however, individual animals generally cannot be classified as gay or straight: an animal that engages in a same-sex flirtation or partnership does not necessarily shun heterosexual encounters. Rather many species seem to have ingrained homosexual tendencies that are a regular part of their society. That is, there are probably no strictly gay critters, just bisexual ones. "Animals don't do sexual identity. They just do sex," says sociologist Eric Anderson of the University of Bath in England.

Nevertheless, the study of homosexual activity in diverse species may elucidate the evolutionary origins of such behavior. Researchers are now revealing, for example, that animals may engage in same-sex couplings to diffuse social tensions, to better protect their young or to maintain fecundity when opposite-sex partners are unavailable—or simply because it is fun. These observations suggest to some that bisexuality is a natural state among animals, perhaps *Homo sapiens* included, despite the sexual-orientation boundaries most people take for granted. "[In humans] the categories of gay and straight are socially constructed," Anderson says.

What is more, homosexuality among some species, including penguins, appears to be far more common in captivity than in the wild. Captivity, scientists say, may bring out gay behaviors in part because of a scarcity of opposite-sex mates. In addition, an enclosed environment boosts an animal's stress levels, leading to a

"The more homosexuality, **the more peaceful** the species," one specialist says. "Bonobos are peaceful."

Female homosexual encounters among bonobos help the apes get along: they resolve conflicts and promote bonding.

greater urge to relieve the stress. Some of the same influences may encourage what some researchers call "situational homosexuality" in humans in same-sex settings such as prisons or sports teams.

Making Peace

Modern studies of animal homosexuality date to the late 19th century with observations on insects and small animals. In 1896, for example, French entomologist Henri Gadeau de Kerville of the Society of Friends of Natural Sciences and the Museum of Rouen published a drawing of two male scarab beetles copulating. Then, during the first half of the 1900s, various investigators described homosexual behavior in baboons, garter snakes and gentoo penguins, among other species. Back then, scientists generally considered homosexual acts among animals to be abnormal. In some cases, they "treated" the animals by, say, castrating them or giving them lobotomies.

At least one early report, however, was more than descriptive, yielding insight into the possible origins of the behavior. In a 1914 lab experiment Gilbert Van Tassel Hamilton, a psychopathologist practicing in Montecito, Calif., reported that same-sex behavior in 20 Japanese macaques and two baboons occurred largely as a way of making peace with would-be foes. In the *Journal of Animal Behavior* Hamilton observed that females offered sex to the more dominant macaques of the same sex: "homosexual behavior is of relatively frequent occurrence in the female when she is threatened by another female, but it is rarely manifested in response to sexual hunger." And in males, he penned, "homosexual alliances between mature and immature males may possess a defensive value for immature males, since they insure the assistance of an adult defender in the event of an attack."

More recently, some researchers studying bonobos (close relatives of the chimpanzee) have come to similar conclusions. Bonobos are highly promiscuous, and about half their sexual activity involves same-sex partners. Female bonobos rub one another's genitals so often that some scientists have suggested that their genitalia evolved to facilitate this activity. The female bonobo's clitoris is "frontally placed, perhaps because selection favored a position maximizing stimulation during the genital-genital rubbing common among females," wrote behavioral ecologist Marlene Zuk of the University of California, Riverside, in her 2002 book *Sexual Selections: What We Can and Can't Learn about Sex from Animals*. Male bonobos have been observed to mount, fondle and even perform oral sex on one another.

Such behavior seems to ease social tensions. In *Bonobo: The Forgotten Ape* (University of Cali-

FRANS LANTING *Minden Pictures*

FAST FACTS

Fit to Be Gay

1» Same-sex couplings are surprisingly widespread in the animal kingdom. Observers have witnessed as many as 1,500 species of wild and captive animals engaging in homosexual activity.

2» Animals may engage in homosexual acts to diffuse social tensions, to better protect their young or to maintain fecundity when opposite-sex partners are unavailable—or simply because it is fun.

3» Homosexuality among some species appears to be far more common in captivity than in the wild. Captivity may bring out gay behaviors because of a lack of opposite-sex mates and a greater need for stress relief.

fornia Press, 1997), Emory University primatologist Frans B. M. de Waal and his co-author photographer Frans Lanting wrote that "when one female has hit a juvenile and the juvenile's mother has come to its defense, the problem may be resolved by intense GG-rubbing between the two adults." De Waal has observed hundreds of such incidents, suggesting that these homosexual acts may be a general peacekeeping strategy. "The more homosexuality, the more peaceful the species," asserts Petter Böckman, an academic adviser at the University of Oslo's Museum of Natural History in Norway. "Bonobos are peaceful."

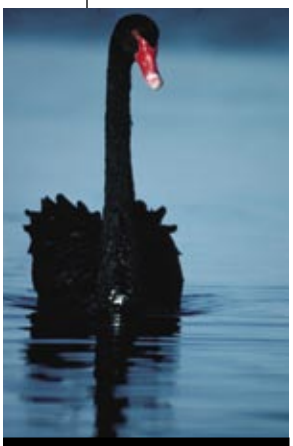
In fact, such acts are so essential to bonobo socialization that they constitute a rite of passage for young females into adulthood. Bonobos live together in groups of about 60 in a matriarchal system. Females leave the group during adolescence and gain admission to another bonobo clan through grooming and sexual encounters with other females. These behaviors promote bonding and give the new recruits benefits such as protection and access to food.

Defended Nest

In some birds, same-sex unions, particularly between males, might have evolved as a parenting strategy to increase the survival of their young. "In black swans, if two males find each other and make a nest, they'll be very successful at nest making because they are bigger and stronger than a male and female," Böckman says. In such cases, he says, "having a same-sex partner will actually pay off as a sensible life strategy."

In other instances, homosexual bonding between female parents can boost the survival of offspring when male-female pairings are not possible. In birds called oystercatchers, intense competition for male mates would leave some females single were it not for polygamous trios. In a study published in 1998 in *Nature*, zoologist Dik Heg and geneticist Rob van Treuren, both then at the University of Groningen in the Netherlands, observed that roughly 2 percent of oystercatcher breeding groups consist of two females and a male. In some of these families, Heg and van Treuren found, the females tend separate nests and fight over the male, but in others, all three birds watch over a single nest. In the latter case, the females bond by mounting each other as well as the male. The cooperative triangles produce more offspring than the competitive ones, because such nests are better tended and protected from predators.

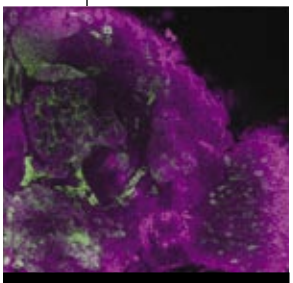
Such arrangements point to the evolutionary fitness of stable social relationships, whatever their type. Biologist Joan E. Roughgarden of Stanford University believes that evolutionary biologists tend to adhere too strongly to Darwin's theory of sexual selection and have thus largely overlooked the importance of bonding and friendship to animal societies and the survival of their young. "[Darwin] equated reproduction with finding a mate rather than paying attention to how the offspring are naturally reared," Roughgarden says.



Up to one quarter of black swan families include parents of the same sex.

Protection of progeny, social bonding and conflict avoidance may not be the only reasons animals naturally come to same-sex relationships. Many animals do it simply "because they want to," Böckman says. "People view animals as robots who behave as their genes say, but animals have feelings, and they react to those feelings." He adds that "as long as they feel the urge [for sex], they'll go for it."

A recent finding indicates that homosexual behavior may be so common because it is rooted in an animal's brain wiring—at least in the case of fruit flies. In a study appearing earlier this year in *Nature Neuroscience*, neuroscientist David E. Featherstone of the University of Illinois at Chicago and his colleagues found that they could switch on homosexual leanings in fruit flies by manipulating a gene for a protein they call "genderblind," which regulates communication between neurons that secrete and respond to the neurotransmitter glutamate.



In the fruit fly brain (*shown in cross section*), the protein genderblind (*purple*) abuts neurons that communicate using the neurotransmitter glutamate (*green*), a pattern consistent with the idea that genderblind influences a fly's sexual preference by modulating glutamate signaling.

Males that carried the mutant *genderblind* gene—which depressed levels of the protein by about two thirds—were uncharacteristically attracted to the chemical cues exuded by other males. As a result, these mutant males courted and attempted to copulate with other males. The finding suggests that wild fruit flies may be prewired for both heterosexual and homosexual behavior, the authors write, but that the genderblind protein suppresses the glutamate-

(The Author)

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PETER JOHNSON *Corbis (top)*; COURTESY OF TORKEL KLINGBERG AND FIONA McNAB; SOURCE: "PREFRONTAL CORTEX AND BASAL GANGLIA CONTROL ACCESS TO WORKING MEMORY," BY FIONA McNAB AND TORKEL KLINGBERG, IN *NATURE NEUROSCIENCE*, VOL. 11, NO. 1; JANUARY 2008 (*bottom*)

In some species, homosexual activity is almost unheard of **in the wild** but may surface in captivity.

based circuits that promote homosexual behavior. Such brain architecture may enable same-sex behavior to surface easily, supporting the notion that it might confer an evolutionary advantage in some circumstances.

The Captivity Effect

In some less social species, homosexual behavior is almost unheard of in wild animals but may surface in captivity. Wild koalas, which are mostly solitary, seem to be strictly heterosexual. But in a 2007 study veterinary scientist Clive J. C. Phillips of the University of Queensland in Brisbane, Australia, and his colleagues observed 43 instances of homosexual activity among female koalas living in a same-sex enclosure at the Lone Pine Koala Sanctuary. The captive females shrieked male mating calls and mated with one another, sometimes participating in multiple encounters of up to five koalas. "The behavior in captivity was certainly enhanced in terms of homosexual activity," Phillips says.

He believes that the females acted this way in part because of stress. Animals often experience stress in enclosed habitats and may engage in homosexual behavior to relieve that tension. A lack of male partners probably also played a role, Phillips suggests. When female koalas are in heat, their ovaries release the sex hormone estrogen, which triggers mating behavior—whether or not

Wild koalas are heterosexual, but females living together in captivity in Brisbane, Australia, shrieked male mating calls and mated with one another.

GERRY ELLIS *Minden Pictures*

males are present. This hardwired urge to copulate, even if expressed with a female partner, might be adaptive. "The homosexual behavior preserves sexual function," Phillips says, enabling an animal to maintain its reproductive fitness and interest in sexual activity. In males, this benefit is even more obvious: homosexual behavior stimulates the continued production of seminal fluid.

A lack of opposite-sex partners is also thought to help explain the prevalence of homosexuality among penguins in zoos. In addition to several gay penguin couplings in the U.S., 20 same-sex penguin partnerships were formed in 2004 in zoos in Japan. Such behavior "is very rare in penguins' natural habitats," says animal ecologist Keisuke Ueda of Rikkyo University in Tokyo. Thus, Ueda speculates that the behavior—which included both male pairings and female couplings—arose as a result of the skewed sex ratios at zoos.

Researchers have found still other reasons for homosexual behavior in domesticated cattle—which is such a common occurrence that farmers and animal breeders have developed terms for it. "Bulling" refers to male pairs mounting, and "going boaring" is its female counterpart. For cows, the behavior is not just a stress reliever. It is a way to signal sexual receptivity. The females mount

Let Them Be Gay

Sometimes zookeepers do not know how to react to their animals' homosexual behavior. In 2005 workers at Bremerhaven's Zoo on the Sea in Germany discovered that three of their five endangered Humboldt penguin couples were of the same sex. The keepers brought in four female Humboldt penguins from Sweden in hopes of tempting the males. That action angered gay and lesbian groups around the world. In a letter to Bremerhaven's mayor Jörg Schulz, a group of European gay activists protested what they called "organized and forced harassment through female seductresses."

In the end, the males were not swayed anyway. "The males have scarcely thrown the females a single glance," said zoo director Heike Kück to the German magazine *Der Spiegel.* So more males were flown in to keep the Swedish females company.

—*E.V.D.*

one another to signal their readiness to mate to the bulls—which, in captivity, may cause a breeder to know when to bring in a suitable opposite-sex partner.

Homosexual mounting is much rarer among cattle in the wild, Phillips asserts, based on his research on gaurs in Malaysia, a wild counterpart to domesticated cattle. "Cattle evolved in the forest, so a visual signal was not going to be useful for them," he says.

Stress and the greater availability of same-sex partners may similarly contribute to the practice of homosexual acts among self-described heterosexual humans in environments such as the military, jails and sports teams. In a study published this year in the journal *Sex Roles*, Anderson found that 40 percent of 49 heterosexual former high school football players attending various U.S. universities had had at least one homosexual encounter. These ranged from kissing to oral sex to threesomes that included a woman. In team sports, homosexuality is "no big deal and it increases cohesion among members of that team," Anderson claims. "It feels good, and [the athletes] bond."

In stressful same-sex environments such as prisons or a war zone, heterosexuals may engage in homosexual behavior in part to relieve tension. "Homosexuality appears mostly in social species," Böckman says. "It makes flock life easier, and jail flock life is very difficult."

Altered Spaces

In recent decades zoo officials have tried to minimize the stresses of captivity by making their enclosures more like animals' natural habitats. In the 1950s zoo animals lived behind bars in barren enclosures. But since the late 1970s zoo homes have become more hospitable, including more open space, along with plants and murals representative of an animal's natural habitat. The Association of Zoos and Aquariums (AZA) regulates everything from cage dimensions to animal bedding. The AZA also outlines enrichment activities for captive creatures: for instance, two golden brown Amur leopards at the Staten Island Zoo regularly play with a papier-mâché zebra, an animal they have never seen in the flesh.

Researchers hope such improvements might affect animal behavior, making it more like what occurs in the wild. One possible sign of more hospitable conditions might be a rate of homosexuality more in line with that of wild members of the same species. Some people, however, contest the notion that zookeepers should prevent or discourage homosexual behavior among the animals they care for [*see box on opposite page*].

In 2004 Silo (*right*) deserted his longtime male partner, Roy (*not shown*), for a female chinstrap penguin named Scrappy (*left*).

CHANG W. LEE *New York Times*/Redux

And whereas captivity may engender what appears to be an unnaturally high level of homosexual activity in some animal species, human same-sex environments might bring out normal tendencies that other settings tend to suppress. That is, some experts argue that humans, like some other animals, are naturally bisexual. "We should be calling humans bisexual because this idea of exclusive homosexuality is not accurate of people," Roughgarden says. "Homosexuality is mixed in with heterosexuality across cultures and history."

Even Silo the penguin, who had been coupled with Roy for six years, displayed this malleability of sexual orientation. One spring day in 2004 a female chinstrap penguin named Scrappy—a transplant from SeaWorld in San Diego—caught his eye, and he abruptly left Roy for her. Meanwhile Roy and Silo's "daughter," Tango, carried on in the tradition of her fathers. Her chosen mate: a female named Tazuni. M

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Your Inner Spam Filter

What makes you so smart? Might be your **lizard brain**

By Andrew W. McCollough and Edward K. Vogel

FAST FACTS

Limits of Processing Power

1» Our mental "in-box" of working memory—the brain regions and processes that keep something "in mind"—is limited to a very few items at a time. Differences in working-memory capacity are directly related to abstract-reasoning abilities.

2» Two factors are thought to limit working memory: overall storage space and total space efficiency.

3» High-capacity individuals (who tend to do better on aptitude tests) might simply be better at keeping irrelevant information "out of mind," whereas low-capacity individuals may allow unneeded data to clutter the mental in-box. A new study suggests that such filtering is key.

Anyone who has tried to find an urgent e-mail amid masses of advertisements for dubious stock opportunities and sexual-enhancement drugs understands the critical importance of being able to filter out distracting information. That e-mail you seek may be in there, but it is lost among irrelevant clutter.

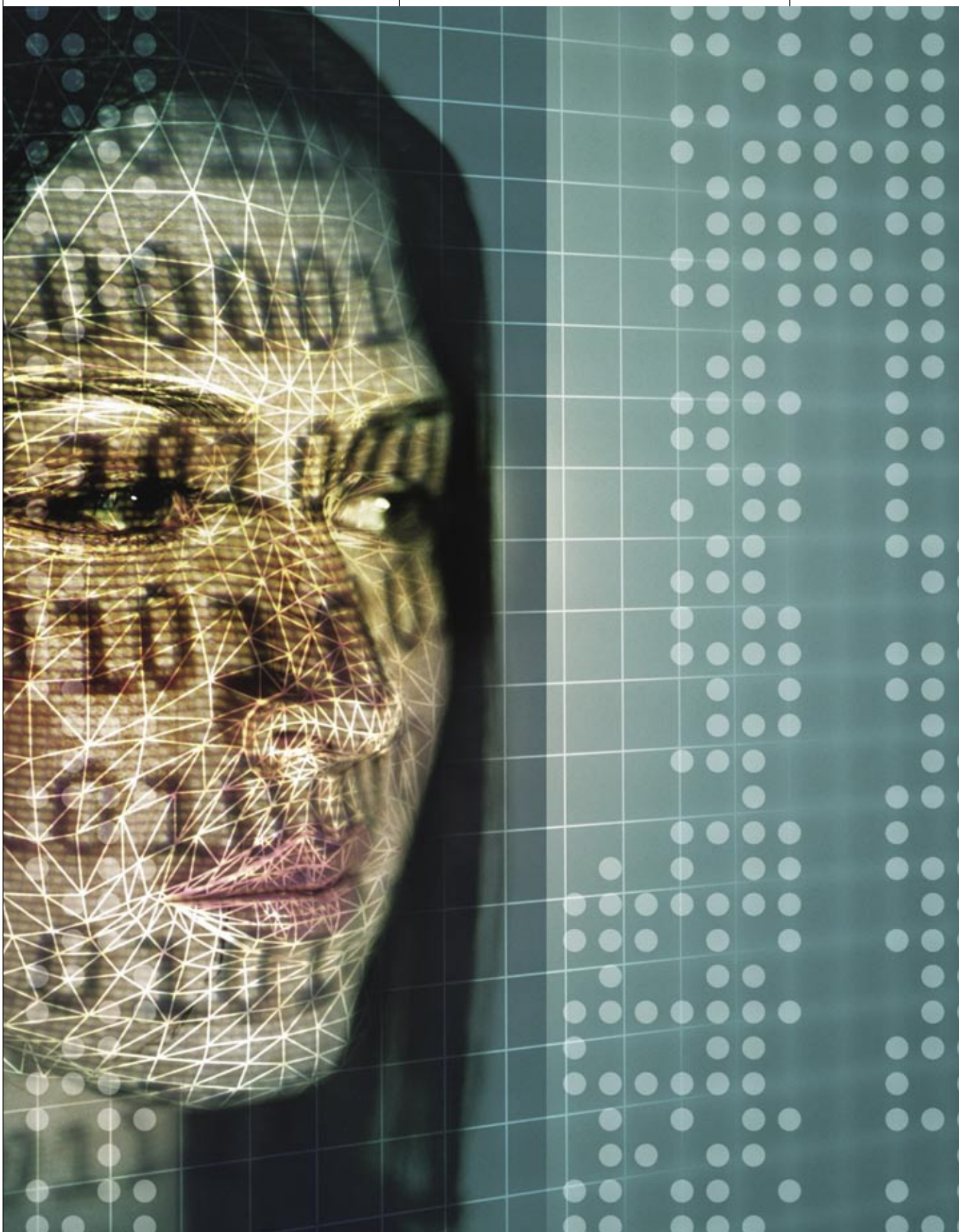
Although the capacity of our computer's e-mail in-box is limited only by disk space, our mental "in-box" of working memory—the brain regions and processes that create temporary storage—is much more constrained. In fact, several decades of research have indicated that our capacity to hold information "in mind" for immediate use is limited to a mere three or four items.

Moreover, just as people vary in height and eye color, they also vary in the capacity of this memory in-box. Interestingly, these differences in working-memory capacity are strongly predictive of a person's ability to perform abstract reasoning, mathematics and other forms of complex problem solving. This relation between memory capacity and fluid intelligence has motivated many scientists to try to understand why and how people differ in this important cognitive ability. A new study adds insights into that line of inquiry.

Hard Drive or Spam Filter?

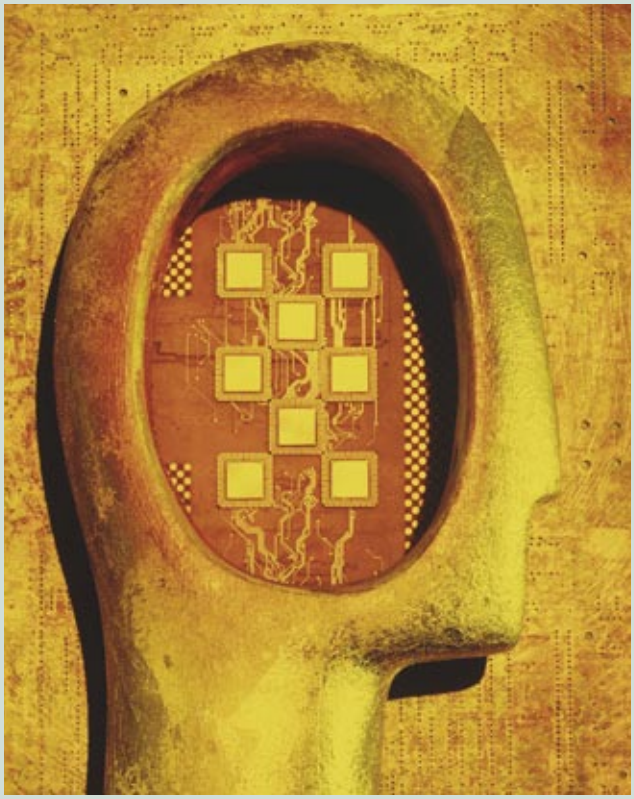
There are two primary explanations for this severe limitation in working-memory capacity. First, it could be that storage space essentially determines working memory's limits and that some people have larger "hard drives" than others do. The alternative theory is that capacity depends not on the amount of storage but on how efficiently that space is used. Thus, high-capacity individuals (who can remember more information at once and who tend to do better on aptitude tests) might simply be better at keeping irrelevant information "out of mind," whereas low-capacity individuals may allow more irrelevant information to clutter up the mental in-box. The difference may just be a matter of having better spam filters.

Some of our own recent work on differences in controlling access to working memory has provided evidence favoring this mental spam-filtering idea. In one experiment, measuring electrical signals emitted by the brain enabled us to show that high-capacity



GETTY IMAGES

The Rest of the Story: The Size of Thought



BY NELSON COWAN

Mental spam filters in our basal ganglia may strongly affect the capabilities of working memory [*see main article*]. Inefficient spam filters permit needless, excess activity in the brain regions that actually store working-memory information—including the posterior parietal areas, located along the top of the brain toward the back. In working-memory operations, these parietal areas hold information briefly, from the time it is presented until it can be used.

And there is more to the story. These parietal areas function here not so much as the permanent storage of a hard drive but rather as the temporary storage of random-access memory, or RAM, where information is held when it wis in use or might soon be used. And although evidence points to the importance of the efficiency of filtering irrelevant items from working memory, we must be careful not to overlook the possibility that differences in RAM capacity also affect working memory. If RAM size does matter, then RAM size and filtering efficiency may be imperfectly correlated. By analogy, individuals' top sprinting speeds and endurances may be imperfectly correlated, even though both qualities depend on certain common factors, such as health.

In fact, evidence suggests that the RAM-storage capacity of working memory is important. In a study published in 2005 in *Cognitive, Affective, & Behavioral Neuroscience,* neuroscien-

people were excellent at controlling what information was represented in working memory: they let in information about relevant objects but completely filtered out that about irrelevant objects. Low-capacity individuals, in contrast, had much weaker control over what information entered the mental in-box; they let in information about both relevant and irrelevant objects roughly equally. Surprisingly, these results mean that we found that low-capacity people were actually holding more total information in mind than high-capacity individuals were—but much of the information they held was irrelevant to the task.

Where Is the Filter?

So the evidence is amassing that your mental spam filter largely establishes your working-memory capacity. Yet a critical question remains unanswered: Where in the brain does this spam filter reside?

According to a study published this past January in *Nature Neuroscience,* neuroscientists Fiona McNab and Torkel Klingberg of the Stockholm Brain Institute appear to have found its location. To do so, they had participants perform a working-memory task in which they had to recall the positions of red and yellow squares on a computer screen. Sometimes they were asked to remember all the items on the screen (both red and yellow), and other times they were asked to keep track of just the red items and to forget the yellow items—an act akin to filtering spam. A symbol presented at the start of each trial told them whether they had to focus on just red squares or let all the information from the display flow into memory. The researchers recorded the subjects' brain activation using functional magnetic resonance imaging during this instruction period as a way of determining what parts of the brain became active as a person started up the mental spam filter.

McNab and Klingberg found that when participants were told they would need to filter the upcoming trial, parts of the basal ganglia (an area known to be important in movement, among other tasks)

(The Authors)

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PIERRE-YVES GOAVEC Getty Images

tists J. Jay Todd and René Marois of Vanderbilt University showed that brain activity in the posterior parietal areas—the working-memory "RAM"—correlated with working-memory performance even though the task at hand did not require much filtering.

Additional behavioral experiments have reinforced their conclusion. In a study of normal and schizophrenic adults published in 2006 in the *Journal of Abnormal Psychology,* neuroscientist James M. Gold of the Maryland Psychiatric Research Center at the University of Maryland School of Medicine and his colleagues tested subjects' memory for various items, some of which they had been told they could ignore. Compared with normal control subjects, schizophrenic patients remembered fewer items across the board. That is, they remembered fewer of the items they were told to remember and fewer of those they were told they could ignore. Yet both control subjects and people with schizophrenia did far better remembering "attended" items than items they were allowed to disregard. Filtering efficiency, in other words, was about equal in the two groups.

Meanwhile a 2006 study from my own lab published in *Memory & Cognition* showed that the storage capacity and filtering efficiency of working memory were partly related and partly distinct—something like the sprinting-to-endurance relation suggested above. Not every higher-capacity participant was able to filter out irrelevant items very efficiently, for example.

This panorama of results demonstrates that both storage capacity and filtering efficiency affect an individual's working-memory ability. New methods for analyzing the brain do not necessarily replace older ones—just as automobiles did not replace bicycles, which did not replace walking. To find the whole truth, brain-imaging methods must be used along with older behavioral methods and philosophical reasoning about the mind. Back in 1971, in an essay entitled "Art in Bits and Chunks," the late perceptual psychologist Rudolf Arnheim suggested that a psychologist's most important tool is the armchair. The statement still rings true for brain research.

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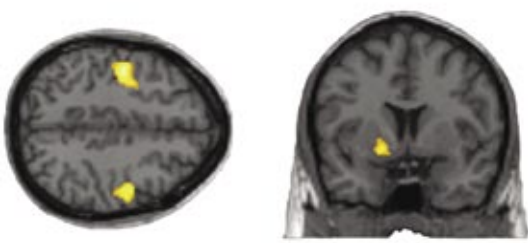
Each week in Mind Matters, www.SciAmMind.com's expert-written features, researchers of mind and brain explain and discuss their disciplines' most notable recent findings. In this installment, psychologists Andrew W. McCollough and Edward K. Vogel consider how filtering mental spam affects thinking.

and the prefrontal cortex (considered to be the brain's rationalizing, "thinking" part) became much more active than in the nonfiltering trials. And the researchers found that the jump in activity levels in these areas was largest for high-capacity individuals and smallest for low-capacity individuals. That is, when told they needed to filter, the high-capacity individuals ramped up activity in these brain regions to keep out irrelevant items. In contrast, the low-capacity individuals showed little additional activity in these areas when they were instructed to ignore the extraneous items. Thus, a leading candidate for the mental spam filter appears to be a cooperative effort between the basal ganglia and the prefrontal cortex.

In this filtering mechanism, the prefrontal cortex most likely provides details about the current task goals, and the basal ganglia lend the mental muscle to block out information that does not match these goals.

This role for the basal ganglia in helping to control the flow of information into working memory is quite similar to one of the basal ganglia's other major functions, which is selecting which motor movements to use in a given context and suppressing the movements we do not want.

Particularly intriguing is that the basal ganglia are evolutionarily ancient brain structures that have been highly conserved across species; even lizards have them. Consequently, what is thought to be our uniquely human ability to engage in abstract reasoning and problem solving appears to be dependent on brain structures that have been around far longer than humans have. The ability to filter out irrelevant spam, it seems, is critical for lizards as well as humans. M



COURTESY OF FIONA McNAB AND TORKEL KLINGBERG; SOURCE: "PREFRONTAL CORTEX AND BASAL GANGLIA CONTROL ACCESS TO WORKING MEMORY," BY FIONA McNAB AND TORKEL KLINGBERG, IN *NATURE NEUROSCIENCE*, VOL. 11, NO. 1; JANUARY 2008

When volunteers in a study were asked to perform a filtering task—they had to remember certain colored squares and ignore other squares on a computer display—areas of their basal ganglia, a region involved in movement (*right*), and prefrontal cortex, associated with making rational judgments (*left*), became more active.

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Can Animals Aid Therapy?

Is animal-assisted therapy the cat's meow or a red herring?

BY SCOTT O. LILIENFELD AND HAL ARKOWITZ

Dolphins are commonly used in animal-assisted therapies.

IN 1857 British novelist George Eliot wrote, "Animals are such agreeable friends. They ask no questions and they pass no criticism." So it is no surprise that scholars have long been intrigued by the possibility that animals possess largely untapped therapeutic powers. But are animals good for our psychological and physical health, either as pets or as "therapists"?

Most Americans are animal lovers; about 63 percent of U.S. households contain one or more pets, according to the American Pet Products Manufacturers Association. Several, but not all, studies suggest that those of us who own pets tend to be somewhat happier than those of us who do not. In addition, research by Erika Friedmann and her colleagues at the University of Maryland School of Nursing shows that pet ownership predicts one-year survival rates among victims of heart attacks.

Though interesting and potentially important, studies such as these are difficult to interpret because pet owners may differ in unmeasured ways from people who do not own pets. For example, pet owners may be better adjusted psychologically and have fewer cardiac risk factors (they may eat healthier diets and experience lower levels of hostility) than non–pet owners.

Easing Stress?

To unravel the potential influences of pets on well-being, researchers must conduct experiments that randomly assign some people, but not others, to receive a pet, either in the laboratory or in their home. Studies by psychologists Karen Allen of the University at Buffalo and James Blascovich of the University of California, Santa Barbara, and their colleagues demonstrate that the presence of a favorite pet during a stressful task—such as performing difficult mental arithmetic—largely prevents spikes in participants' blood pressure. In contrast, the presence of a friend does not. In addition, Allen's work shows that stressed-out, hypertensive stockbrokers who were randomly assigned to adopt either a pet dog or cat ended up with lower blood pressure than those who were not. These studies suggest that the presence of pets may lower our blood pressure and stress levels, although they do not tell us the reasons for this effect. They also do not inform us whether we would observe similar effects with other preferred stimuli, such as a good luck charm or a favorite doll.

Few would contest the claim that pets can give us comfort, especially in times of strain or loneliness. A far more controversial question concerns the effectiveness of animal-assisted therapy (AAT), defined as the use of an animal as either a treatment by itself or an addition to an existing treatment, such as psychotherapy. The animals used in various forms of AAT are a veritable menagerie: horses, dogs, cats, rabbits, birds, fish, guinea pigs and, perhaps best known of all, dolphins. In turn, the psychological problems for which AATs are used include schizophrenia, clinical depression, anxiety disorders, eating disorders, attention-deficit hyperactivity disorder, autism and a host of developmental disabilities.

Popularized largely by Yeshiva University psychologist Boris Levinson in the 1960s, AATs appear to be surprisingly common: a 1973 survey by Oklahoma State University psychologist Susan S. Rice and her colleagues revealed that 21 percent of therapists in the psychotherapy division of the American Psychological Association incorporated animals into their treatment in some fashion. Whether this percentage has changed in 35 years is unknown.

Leisure vs. Therapy

Do AATs work? To make some inroads into this question, we need to

COURTESY OF SCOTT O. LILIENFELD (*top*); COURTESY OF HAL ARKOWITZ (*bottom*); MUSTAFA OZERA AFP/Getty Images (*dolphin therapy*)

distinguish between two different uses of animals: recreation and psychotherapy. Some uses of animals are purely recreational: their goal is to allow their human companions to have fun. There is scant dispute that interacting with friendly animals can "work" for such purposes, because such activities often make people feel happier temporarily. To show that AATs work, however, researchers must demonstrate that animals produce enduring effects on people's psychological health, not merely short-term changes in mood, such as pleasure, relaxation or excitement.

Probably the most extensively researched AAT is dolphin-assisted therapy (DAT), which is most commonly used for children with autism or other developmental disabilities. DAT is practiced not only in the U.S.—primarily in Florida and Hawaii—but also in Mexico, Israel, Russia, Japan, China and the Bahamas, among other countries. Typically during DAT sessions children interact with a captive dolphin in the water while performing rudimentary manual tasks, such as placing rings on a peg. In many cases, the dolphin presumably serves as a "reinforcer" for appropriate child behaviors. Many DAT Web sites advance strong claims regarding this treatment's effectiveness; one asserts that "this field of medicine has shown extraordinary results of the therapy [DAT] and breakthroughs in outcomes" as compared with conventional treatments, including medication and therapy (see www.dolphinassistedtherapy.com). Do the data support these assertions?

Emory University psychologist Lori Marino and one of us (Lilienfeld) have examined the research findings regarding DAT in two reviews, one published in 1998 and the second in 2007. We found the evidence lacking for DAT's effectiveness. In many cases, researchers had shown only that children who received DAT displayed improvements on some psychological measures as compared with children who did not. Yet such results do not exclude the possibility that these changes would have occurred with the mere passage of time. In still other cases, researchers did not rule out the possibility that reported improvements were merely short-term mood effects rather than lasting changes in symptoms. Finally, no researcher adequately excluded the possibility that the observed effects could have been produced by any animal or, for that matter, by any highly pleasurable stimulus. The research literature for other AATs appears to be no more definitive.

Many Web sites advance **strong claims** regarding effectiveness. Do the data support these assertions?

Hidden Costs

Why should we care about whether AATs work? After all, if children seem to enjoy them and parents are willing to pay for them, why worry? There are at least three reasons. First, AATs can produce what economists term "opportunity costs"—the time, money and effort expended in seeking out ineffective treatments. Because of such costs, parents and children may forfeit the chance to seek out effective treatments. In the case of DAT, opportunity costs are far from trivial, because treatments frequently cost $3,000 to $5,000, not including the price of travel and lodging. Second, at least some AATs may be physically hazardous. For example, in DAT it is not legally required that dolphins be screened for infectious diseases. Moreover, there have been multiple reports of children injured by dolphins in DAT sessions. Third, some AATs result in largely unappreciated costs to the animals themselves. For example, removing dolphins from the wild for transfer to DAT facilities not only separates them from their families but also often results in the death of many dolphins within each pod.

So, to the bottom line: Are animals good for our psychological and physical health? Undoubtedly, many animals can be valued companions and provide social support; they can also make us feel better in the short term. It is possible that pets can be of particular help to people with depression or to children who have been severely neglected—for whom loneliness and lack of social support are often common problems. Still, further research will be needed to investigate this possibility. Moreover, whether animals—including dolphins—produce long-term changes in the core symptoms of other psychological conditions, such as autism, developmental disabilities or anxiety disorders, is another matter altogether. To this question, we must reserve the verdict sometimes delivered in Scottish courts: "unproven." M

SCOTT O. LILIENFELD and HAL ARKOWITZ serve on the board of advisers for *Scientific American Mind*. Lilienfeld is a psychology professor at Emory University, and Arkowitz is a psychology professor at the University of Arizona. The authors thank Lori Marino for her generous help with this column.

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Got an Original Idea? Not Likely

What fashion teaches us about the federation of ideas

BY WRAY HERBERT

Actor Meryl Streep (*left*) demonstrates intuitive social psychology.

IN THE 2006 MOVIE *The Devil Wears Prada,* Meryl Streep plays Miranda Priestly, the workaholic editor of a fashion magazine called *Runway,* and Anne Hathaway plays her deliberately unfashionable assistant, Andy. Miranda senses Andy's disdain for her world of designer skirts and belts and shoes, and at one point she icily confronts her assistant for her arrogance: "You see that droopy sweater you're wearing?" she asks. "That blue was on a dress Cameron Diaz wore on the cover of *Runway*—shredded chiffon by James Holt. The same blue quickly appeared in eight other designers' collections and eventually made its way to the secondary designers, the department store labels, and then to some lovely Gap Outlet, where you no doubt found it. That color is worth millions of dollars and many jobs."

Miranda is an intuitive social psychologist. The fact is whether you favor droopy sweaters or Manolo Blahnik shoes, few people are original thinkers when it comes to what they wear. There are a few true innovators, of course, but unless you spin and dye the fabric and design your own wardrobe, you are cribbing from someone else's mind. And what is true of sweaters is also true of less trivial ideas, which move through the ether in unpredictable ways. If you think that you coined a clever phrase or "discovered" a new talent, you almost certainly did not.

Rogue Explorer

That is because we do not really operate as free agents in the world. We are all entangled in complex patterns of collective behavior, many spontaneously organized and most entirely outside our understanding or awareness. Psychologists are very interested in these circles of ideas, how they grow and how people navigate them. Is there an ideal social arrangement for creating and sharing ideas, for mixing innovation and imitation? Are there perils

MATT MENDELSOHN (*Herbert*); BARRY WETCHER *20th Century Fox/ The Kobal Collection* (*scene from* The Devil Wears Prada)

To solve life's problems, we observe others' ideas, invent a few of our own—and **succeed or fail**.

in "borrowing" from others' minds or in being too much of a rogue explorer?

The Collective Mind

A team of psychologists at Indiana University has been exploring these questions in the laboratory, and it is gaining some insights into the collective mind. Robert L. Goldstone and his colleagues created a virtual environment, an Internet-based "world" in which groups of people—from 20 to about 200—simultaneously "forage" for ideas. The researchers use the word "forage" to make the point that ideas are really just abstract resources, food for the brain. As we solve life's various problems, we observe others' ideas in action, invent a few of our own, trade off ours against theirs—and succeed or fail. The psychologists have been studying these virtual successes and failures to see what lessons they can draw.

CATE GILLON Getty Images

Rather than navigating the world of ideas alone, people pile on the well-known bandwagon, even if that means they have to wear Crocs.

Foraging for Ideas

Here is an example of how the experiment works. Participants, interconnected via the Internet, are asked to guess numbers from 0 to 100, and they receive feedback in the form of points, depending on whether their guesses are closer or farther from the target. Think of this task as your first day on the job in a big corporation where you know none of the cultural rules; all you can do is guess and see if you guessed right. But although you are guessing and getting feedback, you are also watching all your colleagues to see what choices they make and how well they do. If they do better than you, maybe imitation makes more sense than guessing? Or maybe you will try another guess?

And so forth. Trial and error, borrowing, compromise—until you figure it out. Meanwhile all the other participants are doing the same thing, including watching you. The scientists ran this experiment several different ways, each approximating a different kind of real-life social group. For example, in "local" networks participants were connected to only a few immediate neighbors, whereas in global networks everyone was connected to everyone else in a rich web. In "small world" networks, participants were connected locally but also had a few long-distance connections so they might pick up an idea or two from, say, a distant relative.

Small vs. Global

The findings, reported in the February issue of *Current Directions in Psychological Science,* were intriguing. When the problems were easy, the global networks did best. This result makes sense because such richly connected groups can spread information rapidly, and speed is basically all that is needed to disseminate a simple notion efficiently. But as the problems became trickier, the small-world networks tended to perform better. In other words, the truism that more information is always better proved untrue when life got a little messy. And as the problems became even more complex, the small local networks proved most clever.

None of us can navigate this complicated world alone. It is too arduous and time-consuming, like designing all your own clothes instead of trusting the Gap. But there is also a hazard in connectivity. If everyone ends up knowing exactly the same thing, you have a world of like-minded people, and this homogeneous group ends up acting like a single explorer rather than a federation of ideas. People pile on the well-known bandwagon, even if it is a really bad idea. It happens in politics, in musical taste and, yes, in the world of fashion. How else can you explain the popularity of Crocs? M

» For more insights into the quirks of human nature, you can visit the "We're Only Human …" blog at www.psychologicalscience.org/onlyhuman

WRAY HERBERT is director of public affairs for the Association for Psychological Science.

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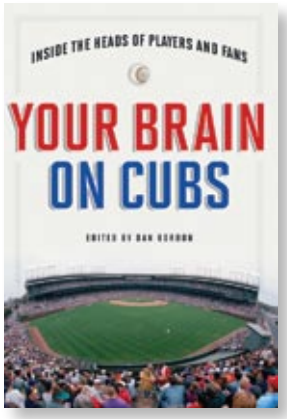
Mind Reviews

BATTER UP

Your Brain on Cubs: Inside the Heads of Players and Fans

Edited by Dan Gordon. Dana Press, 2008 ($19.95)



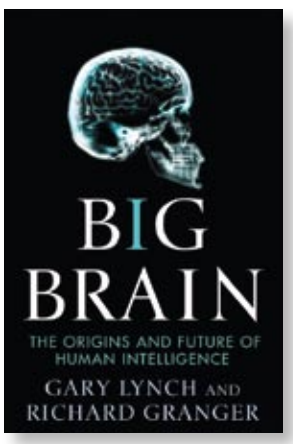
This slim volume on the neuroscience of our national pastime, with different experts penning various chapters, offers an experience much like a good day at the ballpark: perhaps slow in a couple of spots but predictably satisfying in others and ultimately marked by improbable pleasures that come to define the whole experience.

Non-Cubs fans can safely leapfrog the title. Although the book opens and closes with Cubs-specific material—fan loyalty in chapter one, fan ecstasy and agony in chapter seven—even those chapters apply to other teams, too. The five chapters in between examine hitting, which is the hardest feat in all of sportsdom, as well as universals—both in and out of baseball—such as talent and expertise, superstitions and "curses," neurological performance enhancement and handedness.

The discussions on hitting, handedness and neurological enhancement deliver the richest and most baseball-specific material. For instance, in half a second a hitter must see, evaluate, decide and swing. Yet in a technical sense, the required reaction-time-plus-swing-time actually takes *longer* than half a second. The hitting chapter does not solve this paradox but dives deliciously deep into it. Meanwhile we learn that lefties hit better than righties do because lefties process distant visual information better and their hands are more evenly gifted. In regards to neurological enhancement—using various steroids, stimulants, sedatives and hormones—bioethicist Bennett Foddy contributes one of the most original and provocative considerations I have yet read. He even includes that cheap, ubiquitous and reliable modulator of neurotransmitters and mood, the ballpark beer.

This is good science writing, deepening our appreciation of the game without cheapening the science. *Your Brain on Cubs*—sure to fire up the cognitive-pleasure centers of any baseball or brain enthusiast—gives a nice brain buzz itself.

—*David Dobbs*



SIZE MATTERS

Big Brain: The Origins and Future of Human Intelligence

by Gary Lynch and Richard Granger. Palgrave Macmillan, 2008 ($26.95)

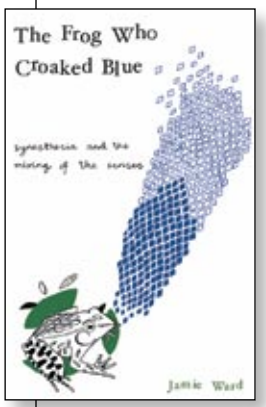
Humans have excessively huge brains. Relative to our body size, our brain is much larger than that of any of our evolutionary peers. How did it get to the top of the heap? What is it about this organ that allowed us to become the dominant species on earth? And what kind of mental abilities might brains even larger than ours confer? In *Big Brain,* neuroscientists Gary Lynch of the University of California, Irvine, and Richard Granger of Dartmouth College tackle questions such as these and give a riveting account of how the human brain evolved.

The book's central hypothesis is the astonishing idea that most of the modern human brain is designed around the sense of smell. In ancient vertebrates the olfactory system stood out from those of the other senses, in which neurons from the sensory input regions—such as skin or eyes—were connected to point-to-point maps in the brain, mirroring locations of the outside world. In contrast, axons carrying olfactory signals delivered them to random regions of the cortex. This unusual architecture served as a template as brains grew larger. Cortical circuits of this "random access" kind now operate not only olfaction but also vision, touch, hearing and the rest of the mental abilities in the mammalian brain.

The authors argue that this architecture ultimately gave rise to abstract thought, mainly because it allowed different senses to be hooked together, such as "the smell of the chocolate-chip cookie and its shape; its taste; the sound when it breaks." In big-brained creatures these association networks grew, and large brain paths evolved, connecting, for example, areas that process the sounds of words with areas that process the visual shapes of words.

If these association systems expanded beyond their extent in modern humans, they would likely enhance mental abilities even further, Lynch and Granger say. This was the case, they hypothesize, with a few hominids whose skulls were discovered in the South African Boskop region in the early 20th century. The find initially caused excitement because the skulls had large frontal bones, suggesting that they may have belonged to a separate species that had brains larger than those of humans. Lynch and Granger argue that these "Boskops" had fallen into obscurity by midcentury because they did not fit our preconceptions. The consensus among anthropologists, however, is that the skulls simply belonged to modern humans. But the picture the authors paint of a bigger-brained hominid is fascinating nonetheless.

—*Nicole Branan*



HOT-WIRED SENSES

The Frog Who Croaked Blue

by Jamie Ward. Routledge/Taylor & Francis, 2008 ($31.95)

Russian newspaper reporter Solomon Shereshevskii had gotten himself into trouble. It was the mid-1920s, and he had been assigned to cover an important speech in downtown Moscow but failed to take down a single word of it. His editor was not happy—until Shereshevskii recalled the entire speech word for word, a feat he could perform effortlessly because of the way his senses operated. Every time the reporter heard a word, it triggered certain images, flavors and smells in his mind. The speech was literally embedded in multisensory code.

Shereshevskii—whose memory later made him famous as a stage performer—had synesthesia, a condition in which one or more of the senses are inextricably linked. The variations are endless: music has color, words have flavor or numbers appear embedded in a three-dimensional map. People with synesthesia "experience the ordinary world in extraordinary ways," writes author Jamie Ward of the University of Sussex, an expert on the condition, which is thought to affect as many as one in 25 people (many of whom do not realize their perception is unusual).

The Frog Who Croaked Blue reads like a fascinating novella-length essay. Ward is clearly enthralled by the topic, and he has no trouble finding interesting issues to address. He explores synesthesia's potential causes (most people are born with it, but it can also be triggered by psychoactive drugs such as LSD), how and why the brain mixes the senses, and whether the condition might confer intellectual and even evolutionary benefits, such as a better memory. Between scientific discussions, he interweaves fascinating personal narratives from synesthetes around the world.

> "Be open to the possibility that our way of sensing the world is just one of many."

The most interesting part of the book, however, has little to do with synesthesia per se. Ward maintains that although smelling colors and hearing shapes may be exceptional, our senses are more closely intertwined than we probably realize. Certain neurons in the brain appear to be multisensory in that they can transmit auditory, visual and tactile information; when two types of stimuli are presented at the same time (when a circle appears on a computer screen at the same time that a beep sounds, for instance), these neurons respond more than twice as strongly to the combination than they do to either event alone.

Although synesthesia might seem alien to those who do not have it—Ward himself admits that he cannot fathom its more bizarre experiences—the bottom line, he says, is that we are all endowed with richly intermingling senses. "Whatever synesthesia tells us, it tells us that our own way of sensing the world is precious," he writes. —*Melinda Wenner*

Recommended Rentals

In Hollywood scientific accuracy is rarely a priority, but, as with everything, there are exceptions. If psychiatrists could give out Oscars for a day, these films would make the short list for providing authentic glimpses into the mind.

What is it like to have a mental illness? The 1993 drama ***Clean, Shaven*** (DSM III Films) tells the story of a schizophrenic named Peter Winter who searches for his adopted-away daughter after leaving a mental institution. Heralded by psychiatrists as the best ever on-screen portrayal of schizophrenia—better even than Universal's ***A Beautiful Mind*** (2001)—the film uses special effects to mimic Winter's hallucinations, showing the audience how he experiences the world. Another day-in-the-life must-see is 1945's Oscar-winning ***The Lost Weekend*** (Paramount), one of the first films to explore the dark side of substance abuse; previous movies had typically made fun of it.

On the more upbeat side, 2004's ***Napoleon Dynamite*** (Access Films) is a comedy about a geeky teenager who becomes immensely popular despite his social awkwardness. Though never mentioned outright, experts say that Napoleon probably has Asperger's syndrome, a form of high-functioning autism. Finally, few movies portray therapy accurately, but the 1980 film ***Ordinary People*** (Paramount) is a gem—some psychologists say it should be used as a teaching tool. Judd Hirsch plays a psychotherapist who helps a suicidal boy deal with the death of his brother and his dysfunctional family. —*Melinda Wenner*

GETTING PSYCHED

My Three Shrinks

Listen at www.mythreeshrinks.com

You're dining out when you notice that the rowdy crowd at the next table is having a most unusual conversation—debating the merits of a new antidepressant and chattering about the controversial diagnosis of e-mail-induced obsessive-compulsive disorder. You realize you are overhearing psychiatrists talk about some juicy stuff, and that's exactly the appeal of the podcast *My Three Shrinks*. Every couple of weeks the shrinks—Roy, a general-hospital psychiatrist, Dinah, who sees outpatients, and the doctor known only as "ClinkShrink," who spends her days with troubled inmates—arm themselves with mics, a few bottles of wine and plenty of polemic, and you get to listen in.

A typical recent episode focused on benzodiazepines, a class of depressants used to treat anxiety and insomnia. Roy kicked things off by comparing a prescription of three milligrams of Xanax (alprazolam) a day to a prescription of three beers a day. He explained that both alcohol and Xanax increase the effects of GABA, a chemical messenger in the brain that tells neurons to slow down or stop firing. Dinah and ClinkShrink agreed but argued that three milligrams is equivalent to many more beers than that.

Although the shrinks occasionally fall into shrill bickering or irrelevant tangents, their spirited conversations never fail to untangle the ethics and issues of psychiatric practice—so go ahead and eavesdrop sometime. —*Christopher Intagliata*

PARAMOUNT/THE KOBAL COLLECTION (*scene from* The Lost Weekend)

askthe**Brains**

What are ideas?

—Celine Joiris, via e-mail

Psychologist **Richard J. Haier** of the University of California, Irvine, School of Medicine replies:

WHEN AN IDEA pops into your head, it is unlikely the result of a single event—like the click of the proverbial lightbulb—in your brain. Studies have shown that no solitary brain area is an exclusive thinking center where ideas emerge. A musical inspiration may start in a different part of the brain than a mathematical concept or a notion about what to eat for dinner. Every idea, like thinking in general, probably arises from a cascade of neural events, which we should be able to discern by scientific means.

In some ways, it is the holy grail of cognitive brain research to detect an isolated thought or idea, so that by knowing only the physical data, such as which neurons fire and when, we could infer exactly what is in a person's mind. Such mind reading is theoretically possible but a daunting challenge.

Nevertheless, neuroimaging has already had some limited success. For example, by analyzing activity in the brain while a person watches a video, it is possible to get a general sense of the content of the video. Though impressive, this feat is a long way from distinguishing the signature of a specific spontaneous thought or insight from the constant cacophony of billions of neurons firing on and off, randomly and in dynamic patterns. How many neurons must fire for an idea to emerge? Where are these neurons located? Does one person require more neurons than another to form an idea? Why do some people have more or better ideas than others?

Imagine knowing the answers to even some of these questions—we might unlock the mysteries of creativity and intelligence. My colleagues and I are currently trying to identify brain areas where structure and function correlate with intelligence. In the near future, this research will evolve into experimental studies in which specific brain regions, networks and neurotransmitter systems will be manipulated by chemical, electrical or magnetic means. These experiments will aim at facilitating learning and memory, enhancing creativity and increasing intelligence. This possibility of cognitive manipulation is why there is growing interest and enthusiasm—and some concern—regarding these ideas about the nature of ideas.

How does being confident in your knowledge affect the way you apply that knowledge?

—Paul Stranahan, via e-mail

Susana Martinez-Conde, a neuroscientist at the Barrow Neurological Institute in Phoenix, explains:

SCIENTISTS DO NOT yet fully understand how confidence, knowledge and other variables interact to guide our behavior. We all make use of two types of knowledge every day: explicit knowledge (the "know what" type) and implicit knowledge (the "know how"). We are conscious of our explicit knowledge, and we can easily communicate it to others with high confidence: I know that one plus one equals two. Implicit knowledge, however, is hard to communicate to others: I know how to ride a bike, but I cannot describe the exact actions necessary because many of them arise unconsciously. Because this know-how knowledge is largely hidden from our awareness, our confidence in it may be low.

From an experimental point of view, determining how much of our behavior comes from implicit versus explicit knowledge poses a challenge. Recent brain-imaging research, however, has pinpointed explicit and implicit learning in different areas of the brain. Activity in the striatum, an area near the brain stem critical for motor control and reward, corresponds to the implicit component of performance. Explicit learning occurs in the anterior cingulate cortex, a region associated with information processing, cognition and emotions, and in the mesial prefrontal cortex, a region that may be involved in risk and reward.

When varying degrees of confidence are added to the mix, the results become more complicated. One recent study compared real memories (high accuracy and high confidence) with fake memories (low accuracy and high confidence). The researchers found that the activated brain areas were clearly different in the two high-confidence situations.

There is still much to discover about confidence, learning and knowledge and about how these variables affect behavior—I, for one, am confident that we will see a lot of future research on these topics. M

Every idea probably arises from a cascade of neural events: a musical inspiration may start in a different part of the brain than a notion about what to eat for dinner.

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

COURTESY OF RICHARD J. HAIER; COURTESY OF SUSANA MARTINEZ-CONDE

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Head Games

Match wits with the Mensa puzzlers

1 MISSING PIECES

Fill in the blanks according to the clues.

a)	**V A _ N**	**Self-centered**
b)	**V A _ N _ _ _**	**A kind of finish**
c)	**V _ _ _ _ A _ _ _ N**	**Cuisine option**
d)	**V _ _ _ A N _**	**Green**
e)	**V A _ _ _ N _**	**An ounce of prevention**
f)	**V _ _ _ _ A N**	**Well experienced**
g)	**V A _ _ _ _ _ N _**	**Mine was funny**
h)	**V A _ _ _ N _**	**Brave**
i)	**_ V _ _ _ A _ _ N _**	**Common at a buffet**
j)	**_ _ _ _ _ V A _ _ _ N**	**Going without**

2 A-E-I-O-U

Fill in the blanks below. All the missing words have the same letters except for one vowel, which changes each time.

A ____ in my eye was caused by a ____. So I said to my ____, "Observe, wife, as I ____ out justice!" As I squashed the offender, my wife stood ____.

3 TWIDDLE-TWADDLE

On the island of Twiddle-Twaddle there are two groups of people.

The Twiddles always tell the truth, unless a Twaddle is present; then the Twiddles lie.

The Twaddles always tell the truth, unless there are more Twiddles present than there are Twaddles; then the Twaddles lie.

Two islanders, Abe and Ben, are standing around talking when a third islander joins their group. Abe says, "Look! It's a Twiddle!" Ben says, "Nope! It's a Twaddle!"

Who is telling the truth? Who is lying? And to which group(s) do Abe and Ben belong?

4 RACING ROBOTS

Three racing robots are running a 57-kilometer race. The robots are all programmed the same way: every hour, on the hour, the robots assess who is winning. The robot in the lead—that is, ahead of every other robot—stops and electronically taunts the other robots until the next time check.

The contestants:

Robot Trip travels at three kilometers per hour (kph).

Robot Quad travels at 4 kph.

Robot Pent travels at 5 kph.

After the first hour, Trip has traveled three kilometers, Quad has gone four kilometers, and Pent has taken the lead at five kilometers. Pent stops to yell, "Nyah, nyah!" until the next time check.

After the second hour, Trip has reached six kilometers, Quad is up to eight kilometers, and Pent is still standing at the five-kilometer mark, taunting away. Now Quad is in the lead, so he halts and begins chanting, "Looooosers—" as the other robots press onward.

And so it goes.

Who is the big winner of the 57-km race?

5 CUT AWAY

Start with a six-letter word. At each step remove a letter, creating a word that matches the given definition.

_ _ _ _ _ _	**Not diamonds**
_ _ _ _ _	**Cooks**
_ _ _ _ _	**Toppers**
_ _ _ _	**___ been**
_ _ _	**Grades 9–12**

6 UP NEXT

What is the next number in this sequence?

1, 4, 3, 11, 15, 28, 37, 55,...

Answers

1. a) VAIN
b) VARNISH
c) VEGETARIAN
d) VERDANT
e) VACCINE
f) VETERAN
g) VALENTINE
h) VALIANT
i) OVEREATING
j) DEPRIVATION

2. Mote, mite, mate, mete, mute.

3. If Abe and Ben were of the same group, they would agree. Therefore, they must be of different groups. Because they are of different groups, if the third is a Twiddle, then they would both have to lie, and their answers would be identical. Their answers are different, so the newcomer must be a Twaddle. This means that Abe is a lying Twiddle and Ben is an honest Twaddle.

4. Trip wins.

5. Hearts, heats, hats, has, H.S.

6. 69. The differences of the differences follow a pattern of −4, 9, −4, etc.

1		4		3		11	15	...
	+3		−1		+8		+4	...
−4		+9		−4		...			

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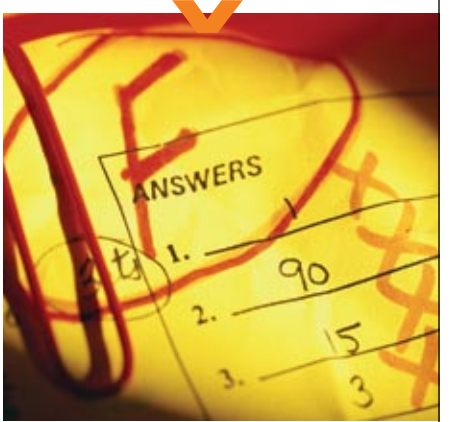

Sleep on It
During slumber, our brain is not only strengthening our memories of the day but also actively analyzing those data.

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RICK GAYLE *Corbis (head with gears)* AND GETTY IMAGES *(background)*; JUPITERIMAGES *(failing grade)*