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Kids on Meds: Trouble Ahead?
page 34

When to Trust Your Gut. *Or Not.*

The Science of *Intuition*

PLUS:

Memory Grid in Your Head

New Therapies for Stroke

Sleepless? Reset Your Body Clock

How Speech Arises in the Brain

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COVER PHOTOILLUSTRATION BY AARON GOODMAN

The Guide Inside

"Intuition, huh?" My co-worker eyed the sketches for this issue's cover story sitting on my looks-like-a-bomb-hit-it desk. Then she beamed with approval: "I depend on that for *everything*!"

Don't we all? Yet it is startling to realize just how little focused, conscious attention we apply to the everyday decisions that ultimately shape the course of our existence. Cross the street or not? Trust the stranger or no? Many of our snap judgments work out well, but sometimes our hunches lead us astray. Psychologist David G. Myers describes the science behind "The Powers and Perils of Intuition," starting on page 24.

A slower, more careful kind of decision making is involved when psychiatrists are weighing whether to prescribe antidepressants to kids or teens. The drugs, approved only for use in adults, have nonetheless been used in youngsters for around a decade. Some scientists worry that antidepressants could be altering the development of children's still growing brains; others believe the need to treat debilitating depression offsets such concerns. Beginning on page 34, Paul Raeburn's article explores the question, "Kids on Meds: Trouble Ahead?"

When people look back at their lives, they speak of "traveling down memory lane." The reference turns out to be more than a hackneyed metaphor. As we navigate the landscape of our recollections, we use a "cognitive map" of the environment created by place cells in the hippocampus, a region of the brain that is important to memory formation. Now researchers have learned how that spatial information arises. Recently discovered grid cells are key components of a mechanism that provides constant updates about location. In "The Matrix in Your Head," neuroscientist James J. Knierim describes his excitement over the finding, which ultimately could "reveal the neural mechanisms that let us remember our personal histories—a vital process that forms the very foundation of one's sense of identity." Our intuition tells us that you will want to find the story on page 42.

Mariette DiChristina
Executive Editor
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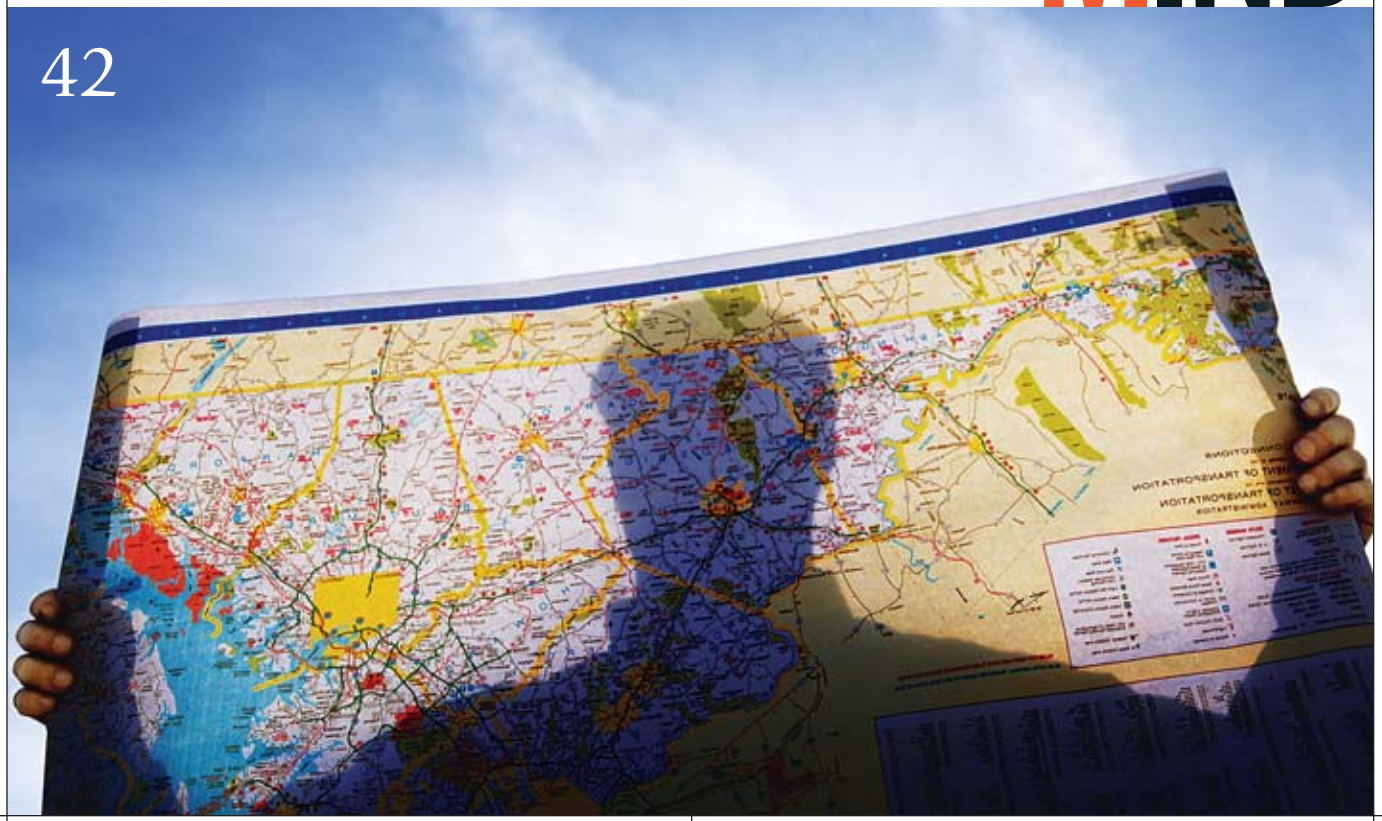

FEATURES

DEPARTMENTS

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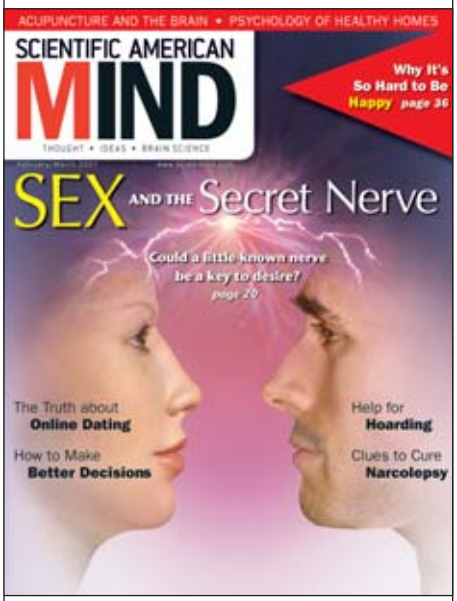


BREAKING UP IS HARD TO DO

I am a psychologist who used two online dating services and found nearly every flaw depicted in the article "The Truth about Online Dating," by Robert Epstein. I was especially put off by the assertion by one company that I was "not compatible" with certain ladies I wanted to meet and yet "compatible" with others who had one of the limiting characteristics I had listed at the company's suggestion.

But the real problem arose when I tried to terminate my membership. I called and indicated my wishes, was given a confirmation number, and then my credit card was charged for the next two months. I notified my bank, but it refused to refund the money, saying I had given the company my number so the matter was between that business and me. Obviously, this was not the sort of long-term relationship I was looking for, so I canceled the card along with the dating "service."

Larry Hourany
McKinleyville, Calif.

UNHAPPY ABOUT "HAPPY"

I wonder if Michael Wiederman, who wrote "Why It's So Hard to be Happy," could bring himself to tell a poor person that economic disadvantage is not really the cause of unhappiness but rather—on the authority of "evolutionary psychologists"—that discontentment is rooted in genetic adaptations in the distant past? These days social variables right under a researcher's nose, such as wealth and race, can respectably be ignored in favor of speculative inferences about prehistory. This article's equation of happiness with personal chemistry is a message mainly useful to the white middle class.

Anne C. Rose
via e-mail

WIEDERMAN REPLIES: *Certainly experiences and environment are important influences on happiness to the extent that they interact with the cognitive software that makes us human. So abject poverty is related to unhappiness, as is social comparison whereby we "feel poor" relative to others around us. The point made by the research on happiness and economic status is that once our basic needs are met, having "more" of anything does not result in lasting increases to happiness. I see that as a positive message for the large majority of us who will never be among the wealthiest but who might delude ourselves into thinking that we would be happier if we were.*

EYEBALLS AND ODDBALLS

"The Case of the Loud Eyeballs," by R. Douglas Fields [Perspectives], greatly interested me because I have occasionally had an experience related to the screeching sounds his eyeballs make when he is half-asleep.

I am lying in bed and have just woken up. I notice something strange: my tinnitus is gone! Wow, I think, this is wonderful. I am so happy to discover what silence is really like. But oddly, there are also no birds chirping away outside. Two seconds later: RRRRRIIIIIIINNNNNNGGGGG. My tinnitus is back, like a switch was turned on. And I hear birds chirping.

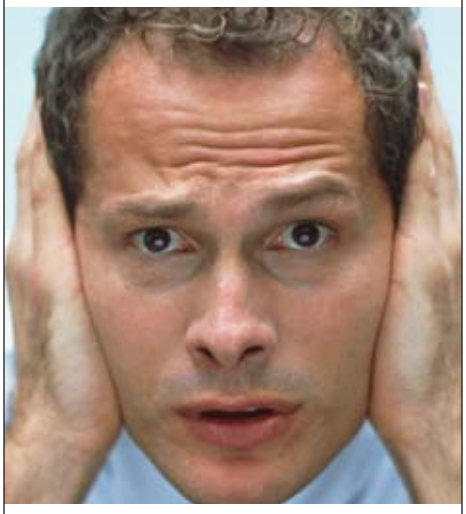
Mark Mojkowski
via e-mail

Your article made me smile because I, too, can hear my eyeballs. For me,

however, it is not a loud noise, just a swishing back and forth when I move them, usually at night before sleep, when it is quiet.

So now there are three of us. Certainly there are many more who are just not "tuned in!"

Joan Faella
Jamestown, R.I.



Readers report on their noisy eyeballs and other brain mix-ups.

FIELDS REPLIES: *Faella is right: Charles Limb of the National Institutes of Health tells me that some people hear their eyeballs not only at bedtime but all the time. In these cases, the noise is not imaginary but actually caused by the tugging of eye muscles. If disease or injury perforates the thin skull bone between the inner ear canals and the brain, the extra hole can act as a third ear tuned to internal sounds.*

After confessing about my grating eyeballs, e-mails and letters began appearing from readers around the world admitting to all manner of bizarre brain mix-ups. Colleen McCaffery of Almonte, Ontario, occasionally hears a loud cracking noise in her head as she is falling asleep, which is a benign phenomenon related to twitching known as an "auditory sleep start." And a young woman from Belgium confides that when she becomes sexually aroused, she starts sneezing! "This, of course, is a very noisy announcement of what is going on in me." Now I know why Mom taught me that a gentleman should always carry a clean handkerchief.

I sincerely thank readers for sharing these personal stories, which show us how wonderful the brain is and how little we really know about it.

DISTURBED BY DESIRE

I am the wife of a pedophile who is a registered sex offender. In "Abnormal Attraction," Peer Briken, Andreas Hill and Wolfgang Berner speak with hope about therapy for pedophiles. I see a clear stumbling block: our state's laws require all therapists to report to the police any situation in which they believe a child may be the target of sexual behavior. Do the ends justify the means here? Maybe, but the law makes therapists akin to cops with full power to arrest and prosecute. I frankly doubt a pedophile would trust a therapist and work with him or her under these conditions. I especially doubt that anyone who experiences pedophilic fantasies would seek help for these impulses before acting on them.

Name withheld
Maryland

I had to roll my eyes at the defensive and somewhat condescending posture of those who treat pedophiles. Yes, the public knows that pedophilia is a disorder. No, the public does not think that therapists make excuses for or promote child abuse. What we object to is that, ultimately, the success or failure in treating pedophiles comes down to whether or not another child is sexually assaulted by one of these patients. Subjecting unsuspecting children to the uncertain outcomes of treatment experiments is as unacceptable as imposing medical trials on random and uninformed human test subjects.

Laura Wrzeski
Lakebay, Wash.

As a journalist, I was dismayed to find several mistakes in an otherwise insightful article on pedophilia.

The authors quote a study that found that "one in seven youngsters aged 10 to 17 received an online sexual solicitation in 2005." This study is not nearly as alarming as the authors make it out to be. The statistic is misleading because the term "sexual solicitation" is defined broadly as "requests to engage in sexual activities or sexual talk or give personal sexual information that were unwanted or, whether wanted or not, made by an adult." Using this definition, an 18-year-old who asks a 17-year-old if he or she is a virgin would be considered to be making a "sexual solicitation." In fact, almost half the "sexual solicitations" in the study came not from "predators" or older adults but from other teens—in many cases the equivalent of teen flirting. The authors' implication that one in seven children are approached by pedophiles is clearly not the case.

The article also failed to report that most cases of child sexual abuse are not committed by convicted pedophiles but by trusted caregivers—relatives, clergy and family friends.

Benjamin Radford
Managing editor
Skeptical Inquirer

A COMMUNITY ISSUE

Although I was delighted that you included a story on hoarding—"Love of Garbage," by Walter A. Brown—I was disappointed at the cursory treatment that you gave to this complex behavior that affects some one million to two million Americans. Hoarding can snowball from an individual's struggle to a community health concern, which is why many cities, such as New York and Los Angeles, have organized task forces that bring together families, social service providers, health agencies, fire departments and legal assistance groups. Research is being done to better understand how to identify hoarding early and treat it effectively. I hope that you will consider publishing additional articles on this important public health topic.

Monika Eckfield
University of California,
San Francisco
School of Nursing

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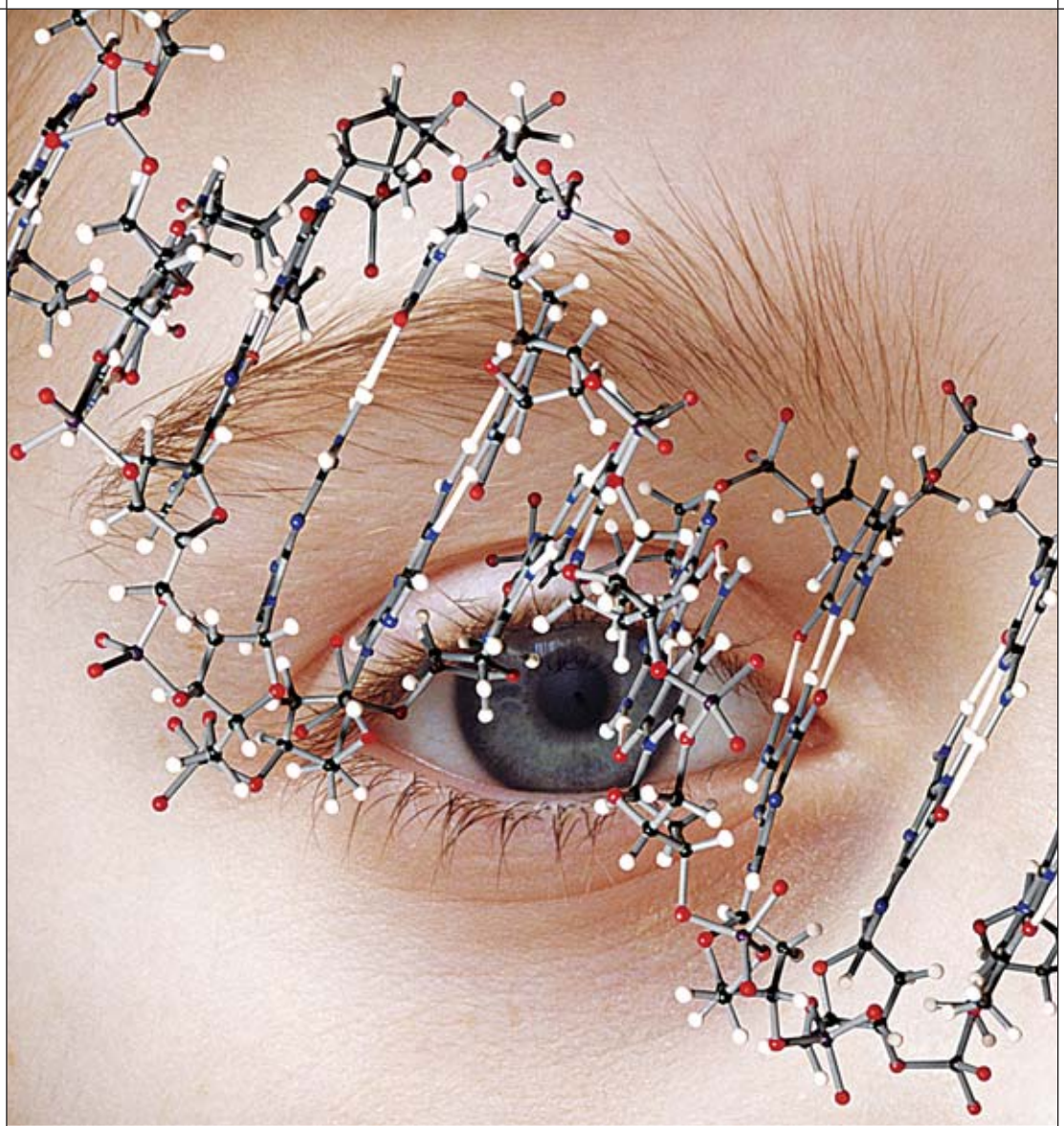
Head Lines



VICTOR DE SCHWANBERG *Photo Researchers, Inc.*

The Genetic Roots of Autism

Many studies have traced the history of families with more than one autistic member, but few scientists have attempted to crack the code of sporadic autism—which arises unexpectedly in a formerly unaffected lineage and is more common than inherited autism. Now a group at Cold Spring Harbor Laboratory believes it has found a distinct mechanism by which autism can strike sporadically.

Led by Jonathan Sebat and Michael Wigler, the team examined the entire genomes of more than 150 families with at least one autistic member. They scanned for new genetic mutations, comparing any findings with parental DNA to assure the variation was not inherited and therefore truly sporadic.

They found that sporadic autism sufferers had a higher incidence of copy number deletions—regions where segments of DNA had been spontaneously deleted—than healthy subjects or people who inherited autism.

The researchers estimate that these random DNA deletions, ranging from one to 69 genes in size, most likely contribute to mental illness in at least 15 percent of all autism patients. That proportion could rise as developing technology allows the group to find previously undetectable genetic alterations.

Now that these large-scale mutations have been identified, the Cold Spring Harbor group and other researchers can begin investigating individual genes within the target region.

Having already used this method to pinpoint cancer genes, the team is currently turning its eye to schizophrenia. Ultimately, the findings may elucidate how these afflictions arise and provide early detection tools so that treatment can begin sooner and be more effective.

—Nikhil Swaminathan

Emotional Morality

Would you take one human life to save many? The obvious answer might seem to be "yes"—but what if your choice also meant you would be sacrificing your own child? Such dilemmas suggest that moral decision making has an emotional component, and now scientists have found the brain region responsible for generating these feelings.

Researchers studied patients with damage to their ventromedial prefrontal cortex, an area in the forebrain where social emotions such as compassion, guilt and shame arise. They asked the patients to respond to a variety of hypothetical moral dilemmas evoking emotional reactions of different strengths, then compared their responses with those of people whose forebrains were intact.

The subjects with damage showed a utilitarian approach in their answers, favoring the greater good regardless of the means required to achieve such ends. For example, many of them said they would smother their own baby to save a group of other people, whereas those with intact forebrains more often said they would not do so. In less emotionally fraught scenarios, all the study participants responded similarly. For instance, nearly everyone would choose to redirect deadly fumes from a room with three strangers to a room with one.

The findings show that our natural aversion to harming others emerges from two previously documented systems in the brain—one emotional and one rational. The emotional system pinpointed in this study triggers a fast, reflexive response; it provides a shortcut to what is right in situations requiring immediate action. The rational side aids us when deliberation and calculation are advantageous. Scientists do not yet understand how the two systems interact or how one supersedes the other when they dictate contradictory courses of action.

Moreover, people with damaged forebrains can still rely on their rational side to respond to moral dilemmas. "This study doesn't mean that people who lack social emotions are dangerous," says neuroscientist Michael Koenigs, then at the University of Iowa, a member of the research team. "They tend to show little empathy and guilt, but they are not killers."

—Graciela Flores

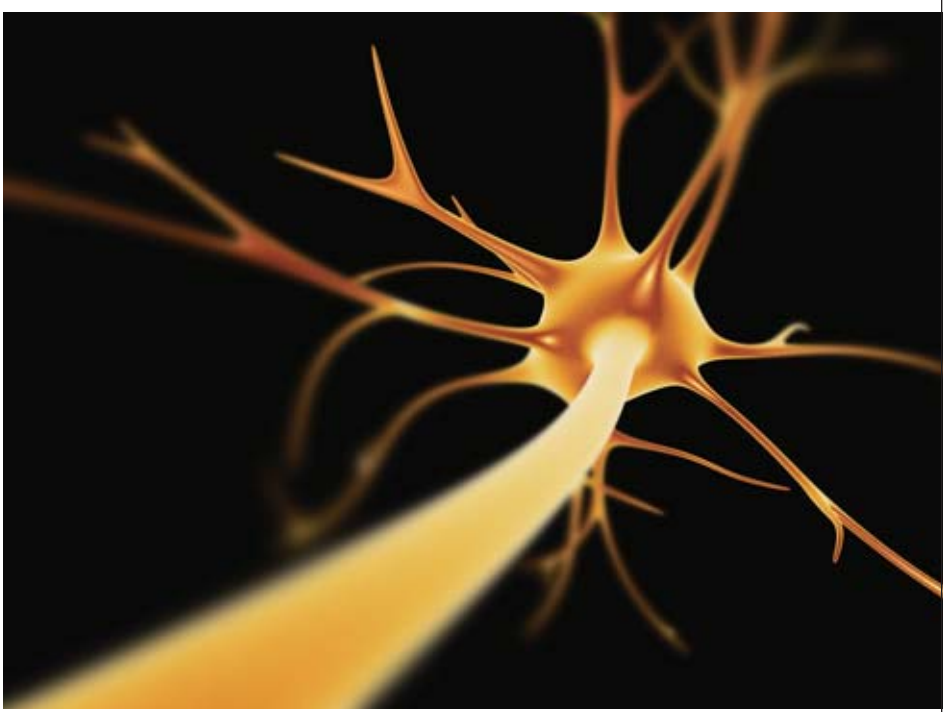
Mind Map

For years, the human brain has been compared to a computer—but it is a computer without a wiring diagram. Researchers simply do not know how the billions of neurons in the brain are connected to one another, and without this information they cannot fully understand how the brain's structure gives rise to perception and behavior. Now, for the first time, scientists have found a way to track the connections between a single neuron and other cells—a discovery that could eventually lead to a 3-D map of the brain's wiring.

A team led by Edward M. Callaway of the Salk Institute for Biological Studies in San Diego illuminated neuronal links by modifying the rabies virus. The investigators remove the gene for a protein that allows the virus to move between cells and let the crippled virus infect each nerve cell they want to study. Then, by inserting the viral gene into these neurons, they cause each brain cell to manufacture the missing protein, thereby restoring the virus's ability to move into directly connected cells. From there, the virus cannot spread any farther because its new neuronal hosts do not make the vital protein. Within a few days, the fluorescent-dyed virus creates a glowing map of a single neuron's every connection.

"Circuitry is the basis for all complex neural function," Callaway says. "Without knowing the circuit, there is no way to know how the brain works." Although every brain has different synaptic connections resulting from individual experiences, the researchers believe they will be able to identify common circuits and eventually figure out the function of specific neuronal pathways. The team hopes to work with live animals within months and to begin to construct "a precise wiring diagram of the mouse brain."

—Jonathan Beard



GETTY IMAGES (*top*); ALFRED PASIEKA *Photo Researchers, Inc.* (*bottom*)

Exercising Generates New Brain Cells . . .

Need another reason to hit the gym? New research suggests that working out builds more than just muscle. Exercise may improve memory by ramping up the creation of new brain cells.

Previous research has shown that exercise causes neuron formation in mice, so scientists at Columbia University and the Salk Institute for Biological Studies in San Diego wanted to know whether this neurogenesis also occurs in humans. Mature brains spawn new neurons in only two locations, one of which is the dentate gyrus, a region in the hippocampus linked to age-related memory decline. The researchers theorized that if exercise triggers neurogenesis in the human dentate gyrus, then exercising could improve memory and help prevent its loss in old age.

Neurogenesis is difficult to study, however, because direct evidence for newly born neurons can only be obtained postmortem. To look for neurogenesis in living people, the scientists needed to find a proxy—a marker indicating neuron formation that could be detected noninvasively. Comparing MRI scans of mice that had exercised regularly for two weeks with scans of sedentary mice, the researchers noticed that exercise increased blood flow in the dentate gyrus. Postmortem exams revealed that this change was, in fact, indicative of the birth of new brain cells.

The scientists then compared MRI scans of people who exercised regularly with those of couch potatoes. Just as in the mice, the exercisers had more blood flowing in their dentate gyrus, suggesting that neurogenesis was also occurring there.

Finally, the scientists gave the subjects a set of cognitive tests to see if exercise actually improved their memory. They found that the more physically fit the people were, the better they performed on hippocampus-mediated word-memory tasks. "Physical exercise might be a very effective way to ameliorate age-related memory decline," summarizes team member Scott Small, a neurologist at Columbia.

Small says he plans to repeat the experiments in older subjects, for whom exercise should have an even larger effect on memory.

—Melinda Wenner

. . . And Stress Kills Them Off

Stress is a killer—at least for brain cells. A new animal study shows that a single socially stressful situation can destroy newly created neurons in the hippocampus, the brain region involved in memory and emotion.

Although most of the brain stops growing by adulthood, new nerve cells are continually generated in the hippocampus, where they are essential for learning. Scientists have long known that chronic stress can inhibit this neurogenesis and lead to depression. Daniel Peterson and his colleagues at the Rosalind Franklin University of Medicine and Science wanted to find out how the brain reacted to just a single stressful episode.

The team placed a young adult rat into a cage with two older rats that quickly began to attack the newcomer. When they removed the younger animal 20 minutes later, the researchers found that its stress hormone levels were six times as high as those of other rats that had not experienced the terrifying encounter. Examining the young rat's brain, they saw that it had produced as many new neurons as its unstressed counterparts. Yet when they repeated the experiment with different rats and examined their brains after a week, only a third of newly generated cells had survived.

The finding that a single stressful event can have an impact on the survival of newborn neurons could lead to new depression treatments for humans, Peterson says. "It may become possible to prevent that loss because we have found that little window of time to intervene." *—Nicole Branan*

GETTY IMAGES (*top and bottom*)

Fuel for Thought

Day after day an overbearing colleague grates on your nerves. It's a battle to keep your irritation under wraps. Suddenly, during a particularly long encounter, you snap—you lose your temper and give your shocked coworker a piece of your mind.

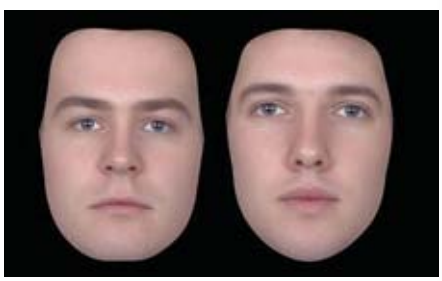
Most of us blame ourselves for such lapses in willpower, but new research suggests that willpower may not be available in an unlimited supply. Scientists have discovered that a single, brief act of self-control expends some of the body's fuel, which undermines the brain's ability to exert further self-discipline.

Researchers at Florida State University asked volunteers to perform tasks such as ignoring a distracting stimulus while watching a video clip or suppressing racial stereotypes during a five-minute social interaction. These seemingly trivial efforts depleted glucose in the bloodstream and hindered volunteers' ability to maintain mental discipline during subsequent tasks. When the study participants were given a sugar drink to boost their blood glucose levels, their performance returned to normal. Volunteers who drank an artificially sweetened drink remained impaired.

"These findings show us that willpower is more than a metaphor," notes Matthew Gailliot, a graduate student in psychology who led the research. "It's metabolically expensive to maintain self-control."

"These are remarkably provocative results," says Kathleen Vohs, a psychologist at the University of Minnesota. Her research suggests that those who exercise self-control are more likely to make impulse purchases—a finding that fits with the glucose depletion model. Vohs observes that one tantalizing implication of the results is that self-control may be toughest for people whose bodies do not utilize blood glucose properly, such as those with type 2 diabetes. Unfortunately, such people cannot benefit from the news that a sugar drink restores mental reserves. Nor should anyone take the findings as license to go on frequent sugar benders in the name of willpower. Although glucose's precise role in self-regulation is not yet clear, Vohs says, "We can be assured that it's going to be more nuanced than that." —*Siri Carpenter*

The Face of a Winner



Study participants "elected" George W. Bush's modified face (*left*) rather than John Kerry's (*right*).

Most of us think we elect our leaders based on their politics. But new research reveals that it might be the candidates' faces that count.

Anthony Little of the University of Stirling in Scotland and his colleagues modified the faces of candidates from eight different political races in the U.K., the U.S. and New Zealand. Using a computer, he combined the real faces with a picture of an "average" face made from a composite of several different people. The resulting images preserved the politicians' important facial features but rendered the contestants unrecognizable.

Then, volunteers in the lab examined each new pair of runners and decided who would be a better leader based on the faces alone. In all eight races, they chose the face of the politician who had won the actual election—George W. Bush redefeated John Kerry, and Tony Blair upset John Major once again.

Research has shown that people make a lot of judgments about others based on their faces and that most will agree about whether a face looks aggressive, intelligent or kind, for example. The tendency to judge individuals by their faces might have been useful early in human history, when our ancestors lived in small groups and chose leaders based entirely on personal characteristics, Little says. For instance, in dangerous times people tend to prefer dominant faces, as signaled by features such as a prominent chin and heavy brow.

Little says that it is unlikely that only the face counts in a political election. But the research does suggest that part of our gut feelings about candidates comes from unconscious assessments we make based solely on their faces. —*Kurt Kleiner*

BRIEFS

- **Adoptive parents** spend more time and money on their kids than biological parents do, found a study of two-parent families carried out at Indiana University Bloomington and the University of Connecticut. In addition to spending more quality time reading or conversing with their children, adoptive parents devoted a greater percentage of their total income to their kids. These results, the sociologists suggest, may mean that kids are not necessarily better off with their birth parents—contrary to widespread belief.

- **Researchers** have found the first physiological evidence that subliminal images do register subconsciously. Brain scans showed that even though volunteers were not aware of a series of quickly flashed images, their visual-processing centers activated in response to the pictures. The study, from University College London, did not address whether subliminal images could influence thought or behavior.

- **Hormones** get the blame for many teen behaviors. Now add to the list overreactions to emotional situations. In response to stress, all bodies produce the hormone THP, which reduces anxiety and calms brain activity in adults and children. In adolescents, however, THP has the opposite effect—it excites the brain and increases anxiety—reported investigators at the State University of New York Downstate Medical Center. The scientists say this discovery could lead to new treatments for teen depression and mental illness.

STEPHEN SWINTEK *Getty Images (top)*; WWW.ALITTLELAB.COM *(bottom)*

A Drug for Down Syndrome

Scientists may have finally found a drug candidate for reducing the mental retardation caused by Down syndrome. After as little as two weeks on the drug, mice with a genetic impairment similar to the syndrome performed as well as normal animals did on learning tests.

The learning and memory problems characteristic of Down syndrome may occur because its sufferers' brain cells are unable to form new synaptic connections with neighboring neurons. This inhibition could be the result of overactive $GABA_A$ receptors—tiny ion channels on neurons. The drug the researchers tested, pentylenetetrazole (PTZ), interferes with the $GABA_A$ receptors, allowing new synapses to be formed at a normal rate.

For two to four weeks, researchers gave low doses of PTZ to mice bred to have an extra copy of one of their chromosomes. As in Down syndrome, this genetic anomaly causes malformed facial bones and learning problems. Immediately after treatment with PTZ, the animals' scores on two memory tests—for recognizing objects they had seen before or remembering how they last entered a maze—were on par with normal mice. Two

months later the altered mice still did much better than they would have done otherwise.

The treatment "is allowing the normal properties of neurons to work," says Stanford University neurobiologist Craig Garner, whose group performed the experiments. "This slowly, over time, leads to an improved circuit."

Although the study results are hugely promising, there is a catch: PTZ, formerly used to treat psychiatric disorders, was taken off the market 25 years ago after being found to be ineffective and to cause dangerous seizures in some people. The dose used in the current study was much smaller than the dose that provoked seizures, however, so the researchers believe there is a good possibility that the drug can be used safely. *—JR Minkel*

A new drug may allow children with Down syndrome to learn at the rate of their healthy peers.

Mothers' Little Criminals

In late February, Rosie Costello, a mother from Vancouver, Wash., pleaded guilty to Social Security fraud and conspiring to defraud the government. Her crime? For 20 years, Costello had been forcing her two healthy children to fake mental retardation to collect disability benefits.

Parents such as Costello, who criminally exploit their children for money, may be responsible for more juvenile lawbreaking than our society currently recognizes, according to experts such as forensic psychologist Kathryn Seifert of Eastern Shore Psychological Services in Maryland, who has been studying youth delinquency for 30 years.

"Children don't just wake up one day and say 'I want to be a thief when I grow up,'" Seifert says. "It is, at least in part, learned behavior." Of the delinquent youths Seifert works with in her clinic, 62 percent have parents who are either antisocial, mentally ill or substance abusers.

Some of these kids could simply be imitating their parents' behavior, says David Brandt, a psychologist at the City University of New York. Seifert, however, maintains that some parents do purposely teach their kids criminal behavior—such as shoplifting or prostitution—for their own financial gain. "I've certainly had a number of them in my practice," she says.

According to Seifert, the first steps in stopping such abuse are raising awareness about it and identifying exploited children early on. If these kids can be helped when they are still young, they can be prevented from developing long-term problems that could lead them to abuse their own children in the same way, she notes.

—Melinda Wenner

LAUREN SHEAR *Photo Researchers, Inc. (top)*; CORBIS *(bottom)*

The nose knows: a "sniff test" may detect Alzheimer's disease early.

The Scent of Science

Most of us do not give our sense of smell a passing thought unless there are cookies in the oven or flowers in bloom. But scientists are probing this underappreciated sense to better comprehend the workings of our brains, from memory formation to Alzheimer's disease. Some of the latest findings:

- Smell and memory are intimately related—just think about how suddenly a familiar scent can whisk you into the past. Now a new study shows that smell can help the brain encode memories, too. Volunteers memorized the locations of several objects while smelling a rose scent, then some of them were exposed to the same scent while they slept. Those with perfumed sleep remembered the locations of the objects much better than their fragrance-free peers did, because the scent probably reactivated memories stored temporarily in the hippocampus.
- Neurodegenerative diseases such as Alzheimer's and Parkinson's often damage the sense of smell first, because there is more neurological machinery devoted to the other senses. A new "sniff test" could provide an early warning for these diseases. People with a normal sense of smell unconsciously stop sniffing as soon as their brain detects an odor, but those with olfactory damage take the same large sniff regardless of whether an odor is present. By measuring the amount of air taken in during sniffs, the new test can reveal a damaged sense of smell before it is otherwise noticeable.
- But why do we sniff in the first place? Olfactory neurons, once thought to respond only to the chemicals that constitute odors, have now been shown to activate when air hits the inside of the nose. The harder we sniff, the more excited these neurons become, and the better they are able to detect and decode scents.

—Karen Schrock

Predisposition for Addiction

Many people assume that an addict's substance abuse is responsible for the damage done to his or her brain. New research shows that some of that "damage" may have been there to begin with.

Chronic drug users have fewer dopamine D2 receptors than nonusers in the reward pathways of their brain, which often makes them less sensitive to natural pleasures such as food and attractive mates. Scientists believe this receptor deficit may reinforce addiction by causing users to seek from drugs what they are unable to get naturally—the "high" caused by a surge of dopamine.

Now Jeffrey Dalley and his colleagues at the University of Cambridge have shown that some people may be born with an abnormally low D2 receptor count, predisposing them to impulsive behavior and drug addiction.

The team compared the brains of six impulsive rats and six normal rats and then allowed the animals to self-administer cocaine. The impulsive rats became addicted more quickly than their nonimpulsive lab mates, and they showed a significantly lower number of D2 receptors in the ventral striatum, a brain region associated with reward anticipation and craving. The researchers found no differences in the dorsolateral striatum, an area involved in compulsive drug-seeking behavior. A decrease in D2 receptors within this brain area, according to past findings, is seen most commonly after habitual drug use.

"This last point is crucial because it suggests that progressive drug use produces progressive changes in the brain," Dalley says.

The scientists proposed a hypothesis: some drug addicts are born with a localized reduction of D2 receptors in the ventral striatum. This anomaly predisposes them to high levels of impulsivity, which may lead to their initial experimentation with drugs. Long-term drug abuse, in turn, may cause damage in the dorsolateral striatum and other parts of the brain's reward pathway, causing addicts to compulsively seek out drugs.

If the researchers are correct, D2 receptors may one day be used to identify people at high risk for drug abuse.

—Thania Benios

STEVE LEWIS *Getty Images (top)*; GETTY IMAGES *(bottom)*

Good News about Depression

A surprising discovery could lead to faster-acting and highly effective drugs to treat this devastating disorder BY WALTER BROWN

IMAGES.COM Corbis

WORRISOME SIDE EFFECTS of antidepressants—that they incite children and adults to kill themselves—have made headlines in recent years; accordingly, the Food and Drug Administration began to require warnings on these medications in 2005. Most experts, however, agree that this labeling is unwarranted, that the science in support of it is flawed and that the warning itself is detrimental to public health—reasoning that it is likely, if anything, to increase suicide by discouraging treatment of depression. Prescriptions for antidepressants have already gone down.

Although it is true that antidepressants can trigger unpleasant symptoms, including agitation, sexual dysfunction and weight gain, these side effects are not the drugs' main problem. Their biggest shortcoming is that often they do not work very well; fewer than half the patients who take them get complete relief, and that effect takes an unacceptably long time—two to three weeks—to kick in.

This is why a 2006 study led by Carlos A. Zarate, chief of the National Institute of Mental Health's Mood and Anxiety Disorders Research Unit, deserves more than a passing mention: it showed that a single infusion of ketamine, a drug already used as a painkiller and anesthetic, relieves depressive symptoms in some patients within hours and that the relief persists for several days. The finding holds out the possibility of a far more effective new class of antidepressants.

Not a Fluke

It would be easy to dismiss this report if it were a one-off observation. But this is not the first time ketamine has been shown to be a powerful antidepressant. A small study in 2000, which, like the more recent experiment, compared a single ketamine infusion with a placebo saline infusion, yielded identical results. And a study in 2002 that used a very different approach reached similar conclusions. Patients with major depression who underwent orthopedic surgery were randomly assigned to receive or not receive ketamine as part of their anesthesia regimen. Only the group that received ketamine showed postoperative relief of depression.

Ketamine binds selectively and strongly to the *N*-methyl-D-aspartate (NMDA) receptor on neurons, blocking the neurotransmitter glutamate from activating this receptor. Like ketamine's illicit chemical cousin, PCP, it is also used recreationally and has potential for abuse. It produces short-lived

This is not the first time ketamine has been shown to be a **powerful antidepressant**.

hallucinations, delusions and euphoria. Nevertheless, these psychedelic properties, though experienced by many of the depressed patients in the studies, appear to be independent of the antidepressant effect. The mind-altering effects occur within minutes and last for less than two hours, whereas the antidepressant benefits begin as the psychedelic effects start to subside and persist far longer. Robert Berman of Yale University, co-author of the 2000 report, notes that in his study the depressed patient who showed the most dramatic antidepressant response with ketamine experienced no ketamine-related psychotic symptoms. These observations suggest that it should be possible to design drugs that have ketamine's ability to alleviate depressive symptoms without any psychedelic side effects.

A New Understanding

Although the more recent report about ketamine has garnered attention, Berman's report was largely ignored. Berman suspects that the idea that a drug that blocks NMDA receptors could be an antidepressant seems more plausible now than it did seven years ago. That rise in acceptability is because the hypothesis that has dominated depression research and drug development for the past 40 years—that depression involves a deficiency of the neurotransmitter serotonin or norepinephrine—is beginning to lose its grip. Several lines of evidence point to a key role of the NMDA glutamate receptor in the action of antidepressants: NMDA receptor blockers have antidepressant effects in animal models of depression; almost all antidepressants that are given for weeks or more modify NMDA receptor function in a time frame consistent with their delayed therapeutic effects; and antidepressants alter the activity of genes that encode the protein components of NMDA receptors.

Notwithstanding the significance of the ketamine findings, Berman strikes some cautionary notes. Because of the psychedelic symptoms, patients and investigators in the 2000 and 2006 studies could often distinguish between ketamine and placebo. Depression is known to be responsive to expectation, so the obvious side effects of ketamine might well have biased the results in favor of a treatment effect for this drug.

On the other hand, Berman says that in his study he had intended to assess the cognitive effects of ketamine, not to examine its antidepressant properties. Its therapeutic pluses, he says, were a surprise. And the depressed patients in the recent study were resistant to treatment—they had not improved with at least two previous courses of antidepressant treatment. Such patients typically have a low rate of response to both further antidepressant treatment and placebo, and yet, encouragingly, 71 percent showed substantial improvement within one day of the ketamine infusion. Thus, although it is not out of the question that the profound antidepressant response to ketamine was a placebo effect, it is unlikely.

Zarate points out that the glutamate system's probable role in the action of antidepressants does not necessarily implicate it in the causes or physiological underpinnings of depression. The little available data bearing on the link between depression and the glutamate system—one study showed that depressed patients have elevated levels of glutamate in one area of the brain—are, so far, less than convincing. To figure out how ketamine may alleviate depression, Zarate and his colleagues are using brain-imaging techniques and searching for other promising antidepressant drugs that block the NMDA receptor.

But simply fiddling with the NMDA receptor or glutamate does not bring immediate depression relief. Zarate's team found that memantine, an NMDA receptor drug used to treat Alzheimer's disease, does not relieve depression. Similarly, riluzole, which inhibits glutamate release (and, therefore, may cause similar effects to those of blocking glutamate's receptor) and is used for amyotrophic lateral sclerosis (ALS), or Lou Gehrig's disease, does improve depression but with the same time delay as conventional antidepressants. Zarate and his co-workers are about to launch a study of a substance that blocks one of the subunits (NR2B) of the NMDA receptor. They hope that it will retain ketamine's antidepressant potency without triggering perceptual disturbances. M

WALTER BROWN is clinical professor of psychiatry at Brown Medical School and the Tufts University School of Medicine.

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- **Subtype-Specific Alterations of γ-Aminobutyric Acid and Glutamate in Patients with Major Depression.** Gerard Sanacora et al. in *Archives of General Psychiatry,* Vol. 61, No. 7, pages 705–713; July 2004.
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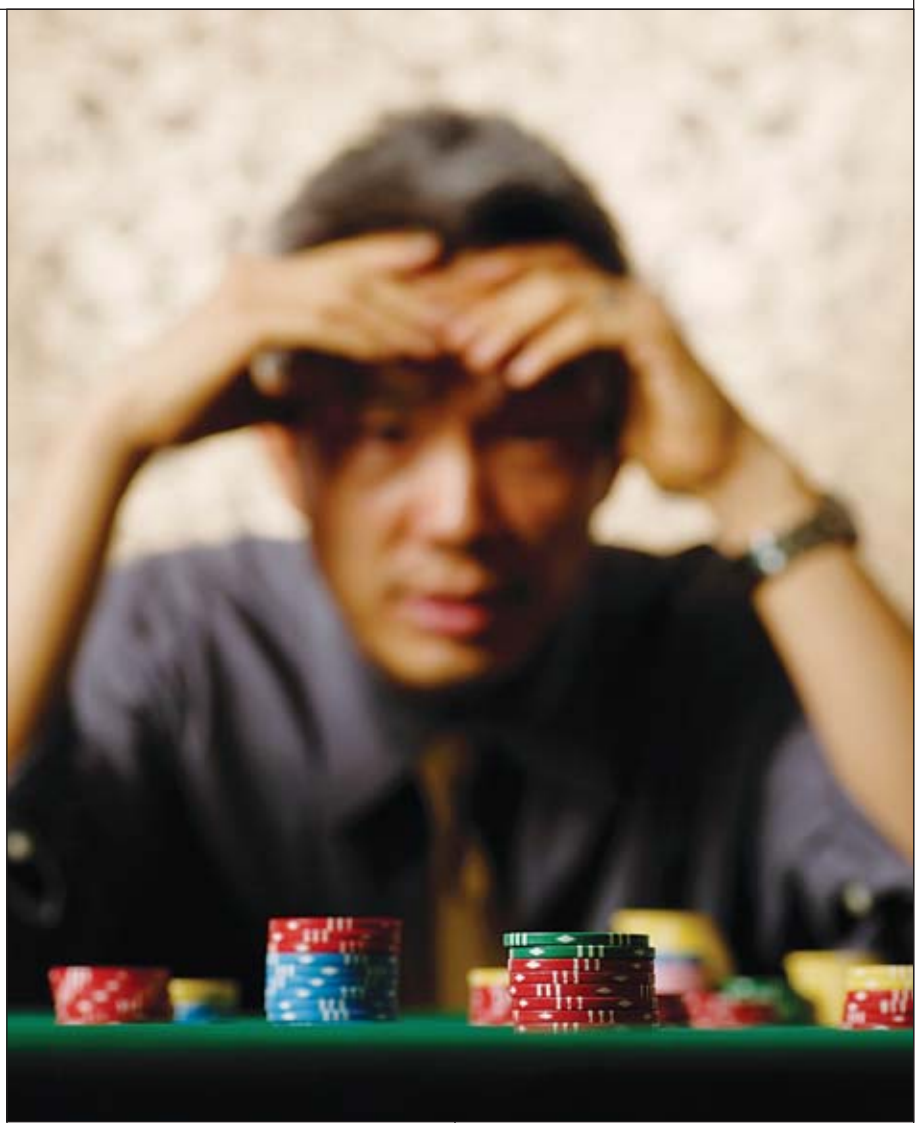
Betting on Consciousness

Gambling may offer a way to test conscious awareness without disturbing it

BY CHRISTOF KOCH AND KERSTIN PREUSCHOFF



MARCUS MOK Getty Images

MUCH OF WHAT we do goes on outside the pale of consciousness: whether we adjust our body posture or decide to marry someone, we often have no idea why or how we do the things we do. The Freudian notion that most of our mental life is unconscious is difficult to establish rigorously. Although it seems easy to answer the question "Did you (consciously) see the light turn on?" more than 100 years of research have shown otherwise. The key problem is defining consciousness such that one can measure it independently of the internal state of an individual's brain while still capturing its subjective character.

One common experimental assessment of consciousness—or awareness of sensation, perception or thought—is based on "confidence." For instance, a subject has to judge whether a cloud of dots on a computer screen moves to the left or to the right. He then reports how confident he is by assigning a number—for example, 1 to indicate pure guessing, 2 for some hesitation and 3 for complete certainty. This procedure assumes that when the subject has little awareness of the dots' direction of motion his confidence is low, whereas if he clearly "saw" the motion his confidence is high.

The Money Question

Now a report by Navindra Persaud of the University of Toronto and Peter McLeod and Alan Cowey of the University of Oxford introduces a more objective measure of consciousness: it exploits people's desire to make money. This method was adapted from economics, where it is used to probe a subject's belief about an event's likely outcome. People who know that they have information are willing to bet on it. That is, they are willing to put their money where their mouth is. Think of investing in mutual funds. The more certain you are that high technology will do well over the next year, the more money you will allocate to a technology-sector fund.

Persaud and his colleagues use this kind of wagering to reveal consciousness or lack thereof. In their experiments, subjects do not state their confidence in their awareness directly. Instead they first make a decision re-

(The Freudian notion that most of our mental life is unconscious is **difficult to establish** rigorously.)

garding whether they have perceived something and then must wager either a small or a large amount of money on their degree of confidence in this decision. If the person's decision proves correct, she wins this money; otherwise, she loses it. The optimal strategy is to bet high whenever she feels that she is not merely guessing. The experimenters apply this wagering technique to three examples of nonconscious processing.

The first experiment involves patient G.Y., who has "blindsight" from a car accident that damaged areas of his brain involved in visual processing. This condition leaves him with the nonconscious ability to locate a light or report the direction in which a colored bar on a computer screen is moving, although he denies having any visual experience of that bar; he insists that he is simply guessing. G.Y. can indicate the presence or absence of a faint, small grating correctly in 70 percent of all trials, far above chance (50 percent). Yet he fails to convert this superior performance into money when wagering; he places a high bet on only about half (48 percent) of his correct choices. When G.Y. is consciously aware of the stimulus, he wagers high—much as you or I would.

His wagering thus seems to mirror his conscious awareness of the stimulus (that is, his belief that he saw it) rather than his actual (unconscious) detection of the stimulus, suggesting that wagering may provide a means to measure awareness.

The second experiment involves an artificial grammar task in which participants learn a small number of short letter strings. They are then told that the strings obeyed a simple rule (of the kind, for example, that every "x" is followed by an "a"). But they are not told what the rule is. When shown a new string, subjects can more often than not determine correctly whether the new string follows the unknown rule. Yet only rarely can they articulate why they believe a string does or does not obey the rule. The overall rate of correct classification (81 percent) is far better than chance. Yet subjects do not convert performance into money. High wagers follow a correct choice 45 percent of the time and follow a false choice 32 percent of the time. In short, the study participants are usually right about whether the string follows the rule, but they lack enough confidence to bet on it.

Winning Hands

In the final experiment, called the Iowa gambling task, subjects pick the top card from one of four decks. Each card wins or loses the person a certain amount of money. Unbeknownst to the participants, two of the four decks have a net positive yield and two have a negative yield. They must place a low or high wager on the chosen card before it is revealed and lose or win accordingly. In the test, the subjects turn scores of cards over, one by one, each time finding out whether they win or lose. They almost always figure out which decks are winners and start to pull cards mostly from those decks—but they usually turn over at least 30 cards on those decks before they gain the confidence to bet aggressively on the results. That is, subjects only start to make money long after their own behavior should have revealed that they knew which decks were winners.

To explore this hesitation, Persaud and his colleagues used a variant of this experiment in which they queried the subjects every tenth trial regarding everything they knew about the game and the decks. When the subjects thus examined their knowledge of the game, the gap between the onsets of positive deck selection and advantageous betting disappeared, suggesting that the act of introspection alters subjects' awareness. Examining their knowledge made them more aware of what they knew. This finding indicates that if subjects learn to trust their gut instincts—and bet on knowledge they are not yet aware of—they can do better, a demonstration of the utility of the leitmotif of Western philosophy, "Know thyself."

The wagering techniques used by Persaud, McLeod and Cowey rely on people's instinct for reaping a profit. Compared with forcing subjects to become aware of their own consciousness—and in the process perturbing the very phenomenon one wishes to measure—wagering provides a more subtle way to assess awareness. This is an exciting and revealing new way to study awareness and consciousness. From such small steps comes progress in answering the age-old question of how consciousness arises from experience. M

The experimenters apply this **wagering technique** to three examples of nonconscious processing.

CHRISTOF KOCH is professor of biology and engineering at the California Institute of Technology and serves on *Scientific American Mind*'s board of advisers. KERSTIN PREUSCHOFF is a postdoctoral scholar in decision theory and neuroscience at Caltech.

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Right-Side Up

Studies of perception show the importance of being upright

BY VILAYANUR S. RAMACHANDRAN AND DIANE ROGERS-RAMACHANDRAN

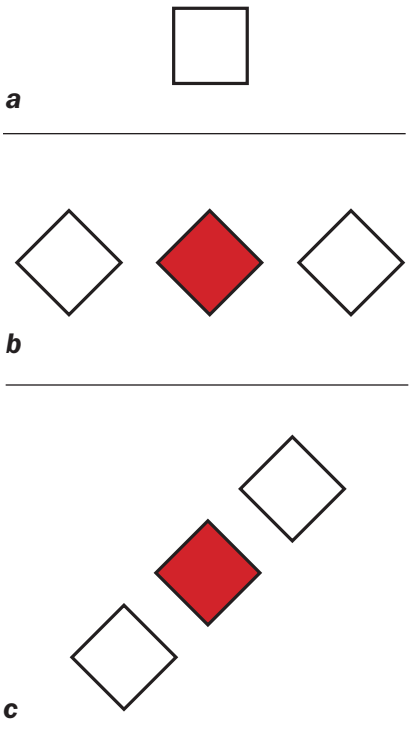
THE LENS IN YOUR EYE casts an upside-down image on your retina, but you see the world upright. Although people often believe that an upside-down image in the eyeball gets rotated somewhere in the brain to make it look right-side up, that idea is a fallacy. No such rotation occurs, because there *is* no replica of the retinal image in the brain—only a pattern of firing of nerve impulses that encodes the image in such a way that it is perceived correctly; the brain does not rotate the nerve impulses.

Even leaving aside this common pitfall, the matter of seeing things upright is vastly more complex than you might imagine, a fact that was first pointed out clearly in the 1970s by perception researcher Irvin Rock of Rutgers University.

Tilted View

Let us probe those complexities with a few simple experiments. First, tilt your head 90 degrees while looking at the objects cluttering the room you are in now. Obviously, the objects (tables, chairs, people) continue to look upright—they do not suddenly appear to be at an angle.

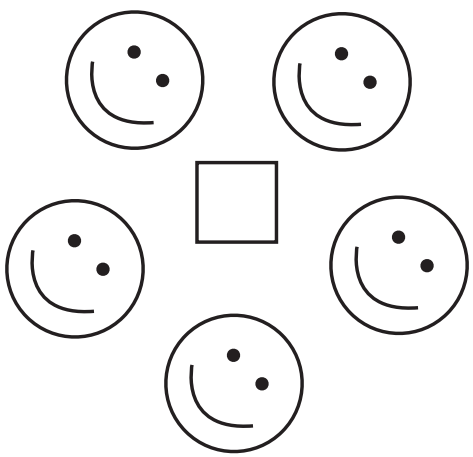
Now imagine tipping over a table by 90 degrees, so that it lies on its side. You will see that it does indeed look rotated, as it should. We know that correct perception of the upright table is not because of some "memory" of the habitual upright position of things such as a table; the effect works equally well for abstract sculptures in an art gallery. The surrounding context is not the answer either: if a luminous table were placed in a completely dark room and you rotated your head while looking at it, the table would still appear upright.



Instead your brain figures out which way is up by relying on feedback signals sent from the vestibular system in your ear (which signals the degree of head rotation) to visual areas; in other words, the brain *takes into account* head rotation when it interprets the table's orientation. The phrase "takes into account" is much more accurate than saying that your brain "rotates" the tilted image of the table. There is no image in the brain to "rotate"—and even if there were, who would be the "little person" in the brain looking at the rotated image? In the rest of the essay, we will use "reinterpret" or "correct" instead of "rotate." These terms are not entirely accurate, but they will serve as shorthand.

There are clear limits to vestibular correction. Upside-down print, for instance, is extremely hard to read. Just turn this magazine upside down to find out. Now, holding the magazine right-side up again, try bending down and looking at it through your legs—so your head is upside down. The page continues to be difficult to read, even though vestibular information is clearly signaling to you that the page and corresponding text are still upright in the world compared with your head's orientation. The letters are too perceptually complex and fine-grained to be aided by the vestibular correction, even though the overall orientation of the page is corrected to look upright.

Let us examine these phenomena more closely. Look at the square in *a*.



The brain **takes into account** head rotation when it interprets an item's orientation.

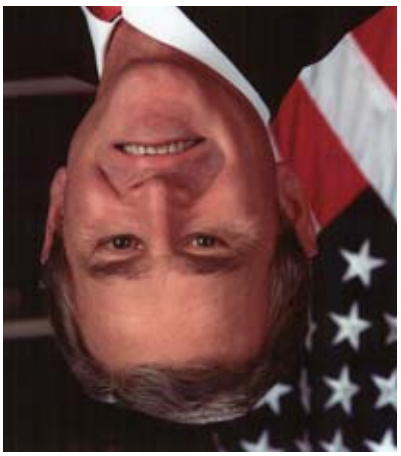
Despite the seamless **unity of perception**, the analysis of the image by the brain proceeds piecemeal.

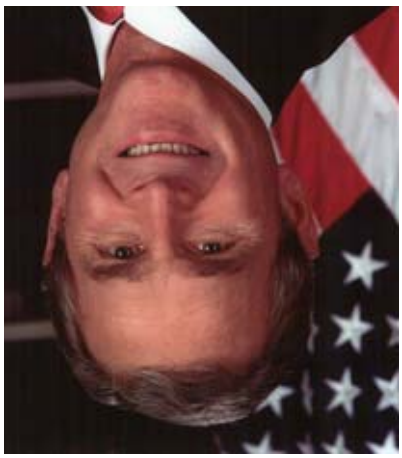
Rotate it physically 45 degrees, and you see a diamond. But if you rotate your *head* 45 degrees, the square continues to look like a square—even though it is a diamond on the retina (the tissue at the back of the eye that receives visual inputs); vestibular correction is at work again.

The Big Picture

Now consider the two central red diamonds in *b* and *c*. The diamond in *b* looks like a diamond and the one in *c* looks like a square, even though your head remains upright and there is obviously no vestibular correction. This simple demonstration shows the powerful effects of the overall axis of the "big" figure comprising the small squares (or diamonds). It would be misleading to call this effect "context" because in *d*—a square surrounded by faces tilted at 45 degrees—the square continues to look like a square (though perhaps less so than when isolated).

You can also test the effects of visual attention. The figure in *e* is a composite. In this case, the central red shape is ambiguous. If you attend to the vertical column, it resembles a diamond; if you view it as a member of the group forming the oblique line of shapes, it seems to be a square.





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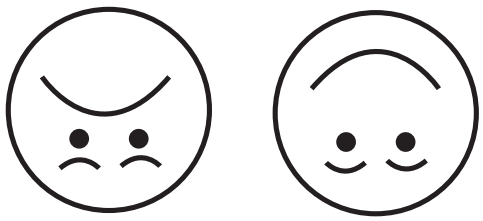

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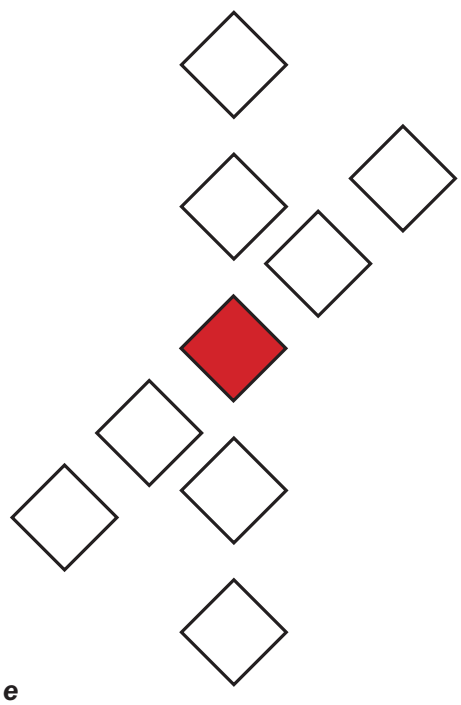


e

Even more compelling is the George W. Bush illusion, a variant of the Margaret Thatcher illusion originated by psychologist Peter Thompson of the University of York in England. If you look at the upside-down images of Bush's face on this page (*f*), you see nothing odd (other than his usual vapid expression). But turn the same images right-side up, and you see how grotesque he really looks. Why does this effect happen?

The reason is that despite the seamless unity of perception, the analysis of the image by the brain proceeds piecemeal. In this case, the perception of a face depends largely on the relative positions of the features (eyes, nose, mouth). So Bush's face is perceived as a face (albeit one that is upside down) just as an upside-down chair is readily identified as a chair. In contrast, the expression conveyed by the *features* depends exclusively on their orientation (downturned corners of the mouth, distortion of eyebrows), independent of the perceived overall orientation of the head—the "context."

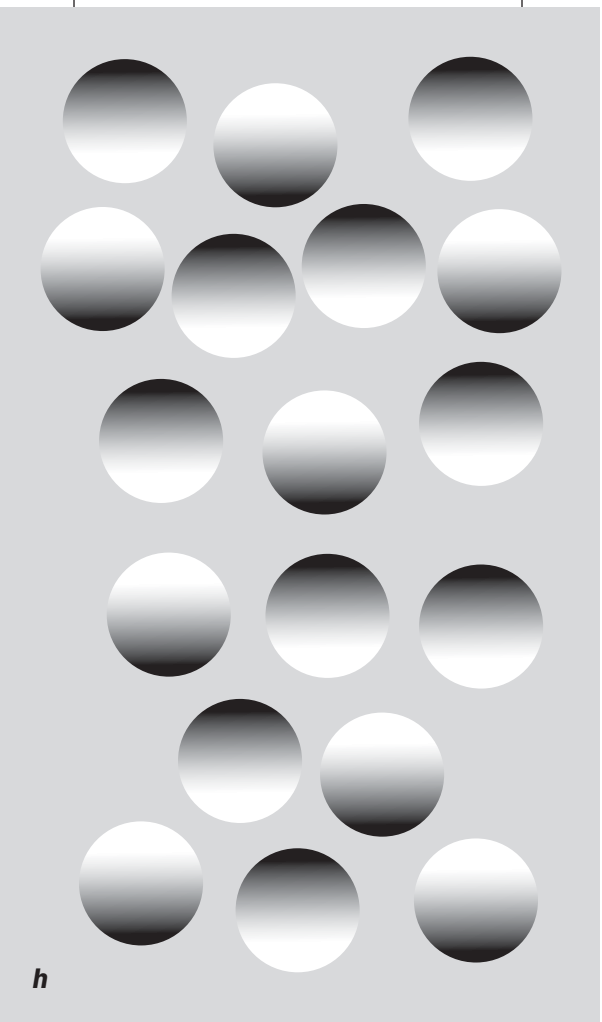
Your brain cannot perform the correction for the features; they do not get reinterpreted correctly as the overall image of a face does. The recognition of certain features (downturned mouth corners, eyebrows, and so on) is evolutionarily primitive; perhaps the computational skill required for reinterpretation simply has not evolved for this capability. For the overall recognition of the face simply as a face, on the other hand, the system might be more "tolerant" of the extra computational time required. This theory would explain why the second upside-down face appears normal rather than grotesque; the features dominate until you invert the face.

SCIENTIFIC AMERICAN MIND (*e* and *g*); TANIA LOMBROZO (*f*)

Suddenly you will see people's heads and shoulders **bobbing up and down** as they walk.

This same effect is illustrated very simply in the cartoon faces (*g*). Upside down, it is hard to see their expressions even though you still see them as faces. (You can logically deduce which is smiling and which is frowning, but that is not the result of perception.) Turn them right-side up, and the expressions are clearly recognized as if by magic.

Finally, if you bend over and look between your legs at *f*, the expressions will become strikingly clear, but the faces themselves continue to look upside down. This effect is because the vestibular correction is applied selectively to the face but does not affect perception of the features (which are now right-side up on the retina). It is the shape of the features on the retina that counts—independent of vestibular correction—and the "world-centered" coordinates that such corrections allow your brain to compute.



Depth Cues

Vestibular correction also fails to occur when we perceive shape (and depth) from clues provided by shading. In *h* you see a set of convex "eggs" scattered among cavities. The brain centers involved in computing shading make the reasonable assumption that the sun usually shines from above, so bumps would be light on top and concave areas would be light on the bottom. If you rotate the page, the eggs and cavities instantly switch places.

You can verify this effect by repeating the experiment of looking between your legs while the page is right-side up in relation to gravity. Once again, the eggs and cavities switch places. Even though the world as a whole looks normal and upright (from vestibular correction), the modules in the brain that extract shapes from assumptions about shading cannot use the vestibular correction; they are simply not hooked up to it. This phenomenon makes evolutionary sense because you do not normally walk around the world with your head upside down, so you can afford to avoid the extra computational burden of correcting for head tilt every time you interpret shaded images. The result of evolution is not to fine-tune your perceptual machinery to perfection but only to make it statistically reliable, often enough and rapidly enough, to allow you to produce offspring, even if the adoption of such heuristics or "shortcuts" makes the system occasionally error-prone. Perception is reliable but not infallible; it is a "bag of tricks."

Bobbing Heads

One last point: Next time you are lying on the grass, look at people walking around you. They look like they are upright and walking normally, of course. But now look at them while you are upside down. If you can manage yoga, you might want to try your downward dog or another inversion. Or just lie sideways with one ear on the ground. The people will still look upright as expected, but suddenly you will see them bobbing up and down as they walk. This motion instantly becomes clear because after years of viewing people with your head held straight you have learned to ignore the up-down bobbing of their heads and shoulders. Once again, vestibular feedback cannot correct for the head bobbing, even though it provides enough correction to enable seeing the people as upright. You might be bending over backwards to understand all this, but we think it is worth the effort. 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.

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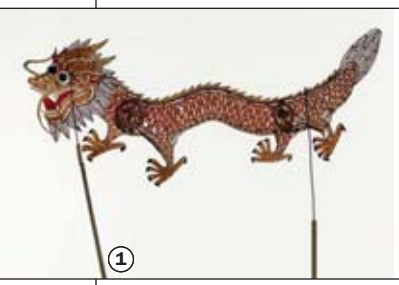
(calendar)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2


3

4

MUSEUMS/EXHIBITIONS

1 Mythic Creatures: Dragons, Unicorns & Mermaids

Why do so many different cultures include dragons in their mythology? Anthropology, archaeology and art history meet in this new exhibit designed to explore the roots of belief in fantastical creatures. Art, cultural artifacts, fossils and animal relics are displayed side by side, illustrating how, for example, narwhal tusks fueled a unicorn craze in medieval Europe. Learn how human imagination (and misinterpretation) has created stories of impossible beasts, many of which have become central myths in cultures around the world.

American Museum of Natural History
New York City
Through January 6, 2008
212-769-5100
www.amnh.org/exhibitions/mythicbeasts/

Ansel Adams & Edwin Land: Art, Science and Invention

Ansel Adams, the renowned nature photographer, became close friends with scientist and inventor Edwin Land after Land allowed him to test the first Polaroid prototypes in the late 1940s. The two brilliant minds traded ideas and inspired each other to experiment in their respective fields. This exhibit highlights the photographs that were born of their partnership—a merging of artistic and scientific genius.

Palmer Museum of Art
Pennsylvania State University
July 12–September 9
814-865-7672
www.psu.edu/dept/palmermuseum/exhibitions.html

CONFERENCES

American Psychoanalytic Association 96th Annual Meeting

Freud's work lives on. The APsaA's 2007 meeting offers scientific sessions open to anyone with an interest in psychoanalysis. More than 1,000 psychoanalysts gather to discuss the latest theories in their field, often incorporating recent neuroscience findings. This year's agenda includes a special seminar on combat stress and the mental health of soldiers.

Denver
June 20–24
www.apsa.org/

Third International Congress of Psychology and Law

Every four years since 1998, lawyers, scientists and academics from many disciplines have met to discuss the intersection of psychology and law. Sponsored by American, Australian and European associations, the 2007 conference will host several focus groups on confidentiality in mental health practice.

Adelaide, Australia
July 3–8
e-mail: psychlaw2007@sapmea.asn.au
www.sapmea.asn.au/conventions/psychlaw2007/

MOVIES/TELEVISION

2 NOVA scienceNOW: Sleep and Memory

Why do we spend a third of our lives sleeping? Evidence is building that sleep plays a crucial role in strengthening memories and facilitating learning, not just in humans but in all animals. *ScienceNOW,* NOVA's periodical news program, visits labs where rats wear hats that painlessly pick up electrical activity from their brains, investigating why we need sleep and what happens when we don't get enough. Watch the show online if you miss it on the air.

PBS
Tuesday, July 10, 8 P.M. (ET/PT)
www.pbs.org/wgbh/nova/sciencenow/

Eagle vs. Shark

In the same character-driven vein as *Little Miss Sunshine* and *Napoleon Dynamite,* this quirky New Zealand comedy follows two misfits as they awkwardly fall in love. A Sundance Film Festival favorite, the film follows the geeky duo as they take revenge on high school bullies and meet each other's eccentric families.

Miramax Films
Limited release June 1
www.eaglevsshark.net/

Harry Potter and the Order of the Phoenix

Harry and the Hogwarts gang face their darkest times yet in year five of their coming-of-age tale. Battling both the evil Lord Voldemort's supporters *and* a government bureaucracy unwilling to believe in Voldemort's return, Harry must deal with mind-controlling wizards, double-crossing professors and, on top of it all, his raging teenage hormones.

Warner Bros. Pictures
Wide release July 13
www.harrypotterorderofthephoenix.com/

3 Martian Child

John Cusack plays a recently widowed novelist who adopts a young boy in an attempt to build a family but soon finds himself in over his head. The boy's hyperactivity and behavior problems are just the beginning—the real trouble starts when Cusack finds himself believing the kid's claim that he's from Mars.

New Line Cinema
Wide release June 27
www.martianchild.com/

WEB SITE

4 SharpBrains

Everyone knows the importance of staying physically fit. But what about staying *mentally* fit? Research in the past several years has shown that mental "workouts" may improve memory, relieve stress and even help stave off Alzheimer's. This new site is an online gym for the mind, offering a blog about the science of brain fitness and links to relevant research. It also sells "exercise" software and offers personal training.

www.sharpbrains.com/

Compiled by Karen Schrock.
Send items to editors@sciammind.com

On an April morning in 2001 Christopher Bono, a clean-cut, well-mannered 16-year-old, approached Jackie Larsen in Grand Marais, Minn. His car had broken down, and he needed a ride to meet friends in Thunder Bay. As Larsen talked with him, she came to feel that something was very wrong. "I am a mother, and I have to talk to you like a mother," she said. "I can tell by your manners that you have a nice mother." Bono replied: "I don't know where my mother is." After Bono left, she called the police and suggested they trace his license plates.

On July 1, 2002, a Russian Bashkirian Airlines jet's collision-avoidance system instructed its pilot to ascend when a DHL cargo jet approached in the Swiss-controlled airspace over southern Germany. Nearly simultaneously, a Swiss air traffic controller—whose computerized air traffic system was down—offered an instant human judgment: descend. The Russian pilot overrode the software, and the plane began to angle downward.

Larsen's intuition was prescient. Police traced the car to Bono's mother, then went to her apartment, where they found her battered body in the bathtub. Bono was charged with first-degree murder. The pilot's instinct was also fateful, but tragically so. The two planes collided, killing 71 people.

Such stories make us wonder: When is intuition powerfully helpful? When is it perilous? And what underlies those differences?

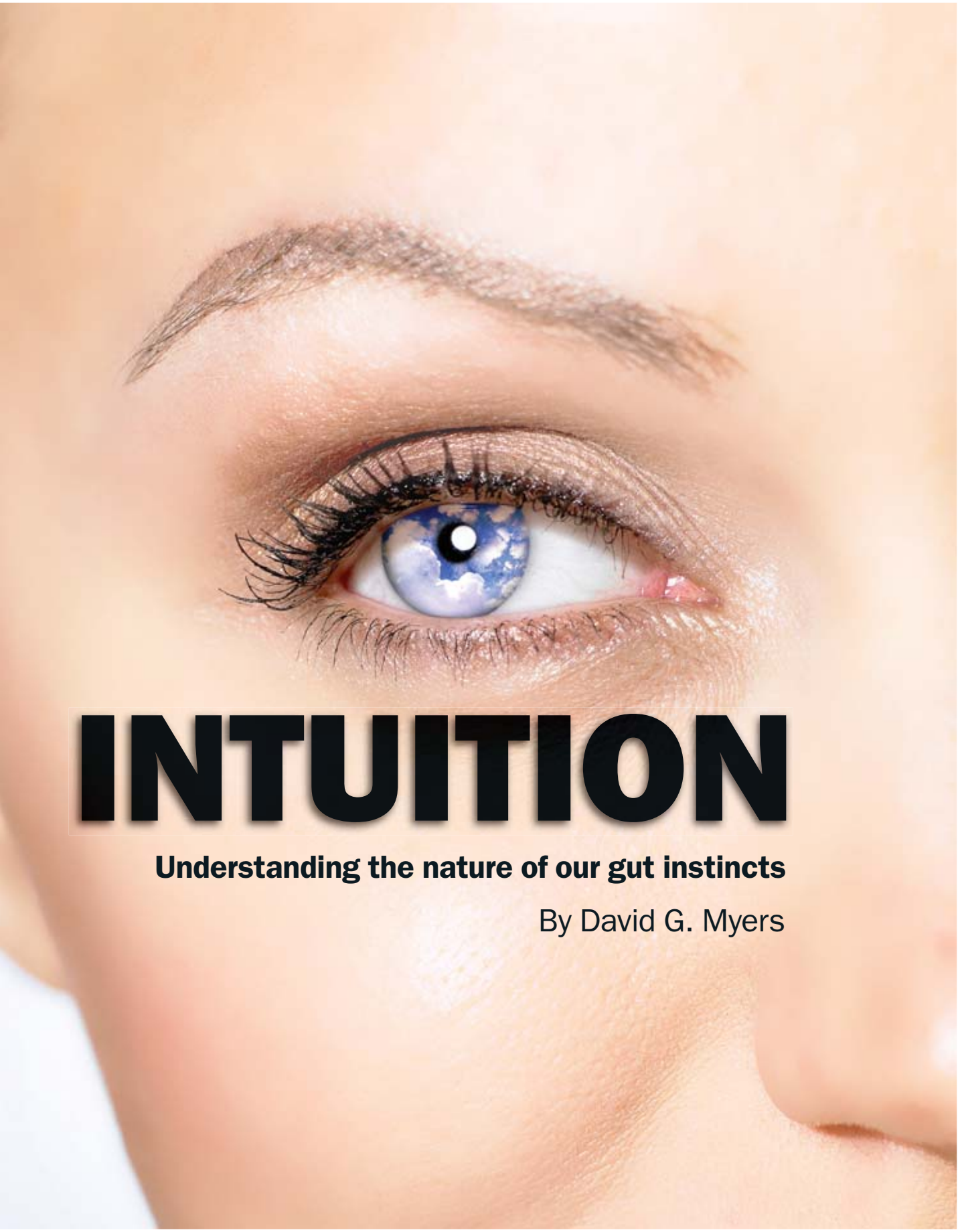
"Buried deep within each and every one of us, there is an instinctive, heart-felt awareness that provides—if we allow it to—the most reliable guide," Britain's Prince Charles has said. But bright people who rely on intuition also go astray. "I'm a gut player. I rely on my instincts," President George W. Bush explained to Bob Woodward of the *Washington Post* regarding his decision to launch the Iraq war. As popular books on "intuitive healing," "intuitive learning," "intuitive managing" and "intuitive trading" urge, should we listen more to our "intuitive voice" and exercise our "intuitive muscle"? Or should we instead recall King Solomon's wisdom: "He that trusteth in his own heart is a fool"?

These questions are both deep and practical. They go to the heart of our understanding of the human mind. And the answers could provide a valuable guide in our everyday lives when we must decide whether to follow gut instinct or use evidence-based rationality—such as when interviewing job candidates, investing money and assessing integrity.

As studies over the past decade have confirmed, our brains operate with a vast unconscious mind that even Freud never suspected. Much of our information processing occurs below the radar of our awareness—off stage, out of sight. The extent to which "automatic nonconscious processes pervade all aspects of mental and social life" is a difficult truth for people to accept, notes Yale University psychologist John Bargh. Our consciousness naturally assumes that its own intentions and choices rule our life. But consciousness overrates its control.

The Powers and Perils of

PHOTOILLUSTRATION BY AARON GOODMAN



INTUITION

Understanding the nature of our gut instincts

By David G. Myers

Gut check: Trustworthy or not?

ADRIAN WEINBRECHT *Getty Images*

In reality, we fly through life mostly on autopilot. As Galileo "removed the earth from its privileged position at the center of the universe," so Bargh sees automatic thinking research "removing consciousness from its privileged place." By studying the forces that shape our intuitions, scientists have revealed how this hidden mind feeds not only our insight and creativity but also our implicit prejudices and irrational fears.

What Is Intuition?

Consider the two-track mind revealed by modern cognitive science. In his 2002 Nobel Prize lecture, psychologist Daniel Kahneman noted that Track ("System") 1—our behind-the-scenes, intuitive mind—is fast, automatic, effortless, associative, implicit (not available to introspection) and often emotionally charged. Track 2—our familiar, conscious (explicit) mind—is deliberate, sequential and rational, and it requires effort to employ.

Two phenomena are thought to shape the processing performed by Track 1. Kahneman and his late collaborator Amos Tversky, two Magellans of the mind, proposed one influence. They theorized that humans have evolved mental shortcuts, called heuristics, which enable efficient, snap judgments. "Fast and frugal" heuristics are like perceptual cues that usually work well but can occasionally trigger illusions or misperceptions. We intuitively assume that fuzzy-looking objects are farther away than clear ones, and usually they are. But on a foggy morning that car up ahead may be closer than it looks.

A second influence on our intuitions comes from learned associations, which automatically surface as feelings that guide our judgments. Our life history provides us with a great reservoir of experiences that inform our actions. Thus, if a stranger looks like a person who previously harmed or threatened us, we may—without consciously recalling the earlier experience—react warily. In a 1985 experiment led by psychologist Pawel Lewicki of the University of Tulsa, one group of students was initially split about 50–50 in choosing which of two pictured women looked friendlier. Other students, having interacted previously with a warm, sociable experimenter who resembled one of the women, preferred that

FAST FACTS

Intuition's Double Edge

1» **Cognitive science reveals a two-track human mind, featuring a deliberate, analytical "high road" and an automatic, intuitive "low road."**

2» **Through life experience we gain intuitive expertise and we learn associations that surface as intuitive feelings.**

3» **As studies of implicit prejudice and misplaced fears illustrate, unchecked gut feelings can lead us astray.**

A

B

C

After interacting with a friendly experimenter, people intuitively preferred someone who looked like her (Person A) to one who did not. They avoided Person A, however, if the experimenter had been unfriendly.

person by a six-to-one margin [*see illustration above*]. In a follow-up, the experimenter acted *un*friendly toward half the subjects. When these subjects later had to turn in their data to one of two women, they nearly always avoided the one who resembled the unfriendly experimenter.

Intuition's Powers

Our explicit and implicit minds interact. When speaking, for example, we communicate intended meaning with instantly organized strings of words that somehow effortlessly spill out of our mouth. We just know, without knowing how we know, to articulate the word "pad" rather than "bad" or to say "a big, red barn" rather than "a red, big barn." Studies of "automatic processing," "subliminal priming," "implicit memory" and instant emotions unveil our intuitive capacities.

Blindsight. A striking example of our two-track mind comes from studies of D.F., a woman who suffered carbon monoxide–related brain damage that left her unable to recognize objects. Psychologists Melvyn Goodale of the University of Western Ontario and David Milner of Durham University in England found that, functionally, D.F. is only partly blind. Asked to slip a postcard into a vertical or horizontal mail slot, she can intuitively do so without error. Though unable to report the width of a block in front of her, she will grasp it with just the right finger-thumb distance. Thanks to her "sight unseen," she operates as if she has a "zombie within," report Goodale and Milner.

We commonly think of our vision as one system that controls our visually guided actions. Actually, vision is two systems, each with its own centers in the brain. A "visual perception track" enables us, as Goodale and Milner put it, "to create the mental furniture that allows us to think about the world"—that is, to recognize things and plan actions. A "visual action track" guides our moment-to-moment actions. On special occasions, the two can conflict. For example, we consciously perceive a protruding face in the "hollow face illusion" (in which a concave face appears convex). At the same time, our hand, guided by the subconscious, will unhesitatingly reach inside the mask when we are asked to flick off a buglike target on the face [*see illustration below*].

Reading "thin slices." In their widely publicized studies from the early 1990s, social psychologist Nalini Ambady, then at Harvard University, and psychologist Robert Rosenthal of the University of California, Riverside, have shown that we often form positive or negative impressions of people in a mere "blink" or "thin slice" of time. After subjects observed three two-second video clips of professors teaching, their teacher ratings predicted the actual end-of-the-term ratings by the professors' own students. To get a sense of someone's energy and warmth, the researchers found, a mere six seconds will often do.

Even micro slices can be revealing, as Bargh has found in a series of studies conducted from the late 1980s to the present. When he flashed an image of a face or object for just two tenths of a second, people evaluated it instantly. "We're finding that everything is evaluated as good or bad within a quarter of a second," Bargh said in 1998. Thanks to pathways that run from the eye to the brain's rapid-response emotional-control centers—bypassing the thinking part of the brain, the cortex—we often feel before we analyze.

There is presumed biological wisdom to such instant feelings. When our ancestors confronted strangers,

People consciously perceive an illusory protruding face from a reversed mask. Yet their hand "knows" what the conscious mind does not, as it reaches inside the mask for a speck on the face.

COURTESY OF PAWEL LEWICKI (*above*); THE VISUAL BRAIN IN ACTION. SECOND EDITION. A. D. MILNER AND M. A. GOODALE. OXFORD UNIVERSITY PRESS, 2006 (*below*)

Chess masters (who may have 50,000 patterns stored in memory) seem to pick the right moves intuitively.

CORBIS

those who speedily and accurately discriminated anger, sadness, fear and happiness were more likely to survive and leave descendants. And there appears to be a sliver of truth in the presumption that women may, on average, slightly exceed men at quickly reading others' emotions, reports Judith Hall of Northeastern University, based on an analysis of 125 studies. Shown a silent two-second video of an upset woman, for example, women, more accurately than men, intuit that she is discussing her divorce rather than criticizing someone. Women also have an edge in spotting lies and in discerning whether a man and a woman are genuinely romantic or are a posed, phony couple.

Intuitive expertise. If experience informs our intuition, then as we learn to associate cues with particular feelings, many judgments should become automatic. Driving a car initially requires concentration but with practice becomes second nature; one's hands and feet seem to do it intuitively, while the conscious mind is elsewhere.

Studies of learned professional expertise reveal a similarly acquired automaticity. Rather than wending their way through a decision tree, experienced car mechanics and physicians will often, after a quick look and listen, recognize the problem. After a mere glance at a chessboard, masters (who may have 50,000 patterns stored in memory) can play speedy "blitz chess" with little performance decline. Experienced Japanese chicken sexers use complex pattern recognition to separate up to 1,000 newly hatched female pullets and look-alike male cockerels an hour, with near-perfect accuracy. But all these experts are hard-pressed to explain how they do it. Intuition, said Herbert Simon, another Nobel laureate psychologist, "is nothing more and nothing less than recognition."

Experiments demonstrate that we are all capable of such "nonconscious learning." In Lewicki's research, people have learned to anticipate the computer screen quadrant in which a character will appear next, even before being able to articulate the underlying rule. In recent experiments at the University of Erfurt in Germany, Tilmann Betsch of the University of Heidelberg and his colleagues deluged people with information about the performance of various stock shares over time. Although the participants were unable to recall the return distributions afterward, their intuitive feeling about each stock "revealed a remarkable degree of sensitivity" to its performance. In experiments conducted during the 1980s and 1990s, psychologist Timothy D. Wilson of the University of Virginia learned that gut feelings have also predicted, better than rationally explained preferences, the future of people's romantic relationships and their satisfaction with art posters. Sometimes the heart has its reasons.

University of Amsterdam psychologist Ap Dijksterhuis and his colleagues confirmed the surpris-

Intuition is powerful, often wise, but sometimes perilous, and especially so when we overfeel and underthink.

ing powers of unconscious thought in recent experiments that showed people complex information about potential apartments, roommates or art posters. The researchers invited some participants to state their immediate preference after reading, say, a dozen pieces of information about each of four apartments. A second group, given several minutes to analyze the information consciously, tended to make slightly smarter decisions. But wisest of all, in study after study, was a third group, whose attention was distracted for a time—enabling the subjects' minds to process the complex information unconsciously and to achieve more organized and crystallized judgments, with more satisfying results. Faced with complex decisions involving many factors, the best advice may indeed be to take our time—to "sleep on it"—and to await the intuitive result of our unconscious processing.

Intuition's Perils

So, just by living, we acquire intuitive expertise that enables quick and effortless judgments and actions. Yet psychological science is replete with examples of smart people making predictable and sometimes costly intuitive errors. They occur when our experience has exposed us to an atypical sample or when a quick and dirty heuristic leads us astray. After watching a basketball team overwhelm weak opponents, we may—thinking the team invincible—be stunned when it is overwhelmed by a strong opponent. Or, make your own snap judgment with this quick quiz: In English words, does the letter *k* appear more often as the first or third letter? For most people, words beginning with *k* are more immediately available in memory. Thus, using the "availability heuristic," they assume that *k* occurs more frequently in the first position. Actually, *k* appears two to three times more often in the third position.

Intuitive prejudice. After actor Mel Gibson's drunken anti-Semitic tirade during a traffic arrest, after comedian Michael Richards's vile racial response to a black heckler, and after New York City police officers in two incidents killed unarmed black residents with hailstorms of bullets, each perpetrator reassured us that he was not racist. At the conscious, explicit attitude level, they may well be right. But their (and our) unconscious, implicit attitudes—which typically manifest wariness toward those unfamiliar to us or those who resemble people with whom we have negative past associations—may not agree. And so it is that people may exhibit a primitive, automatic dislike or fear of people for whom they express sincere respect and appreciation. And whereas our explicit attitudes may predict our deliberate, intentional actions, our slower-to-change implicit attitudes may erupt in our spontaneous feelings and outbursts.

Various experiments have briefly flashed words or faces that "prime" (automatically activate) stereotypes for some racial, gender or age group. Project Implicit, a collaboration among researchers at Harvard, the University of Virginia and the University of Washington, probes the results. Without the participants' awareness, their activated stereotypes often bias their behavior. When primed with a black rather than white face, people may react with more hostility to an experimenter's annoying request. And they more often think of guns: they more quickly recognize a gun or mistake tools, such as a wrench, for a gun. Even the most seemingly tolerant, egalitarian white people will take longer to identify pleasant words (such as "peace" and "paradise") as "good" when associated with black rather than white faces. Moreover, the more strongly people exhibit such implicit prejudice, the readier they are to perceive anger in black faces.

If aware of a gap between how we *should* feel and how we intuitively *do* feel, self-conscious people may try to inhibit their automatic responses. Overcoming what prejudice researcher Patricia G. Devine of the University of Wisconsin–Madison calls "the prejudice habit" is not easy. If we find ourselves reacting with knee-jerk presumptions or feelings, we should not despair, she advises; that is not unusual. It is what we do with

(The Author)

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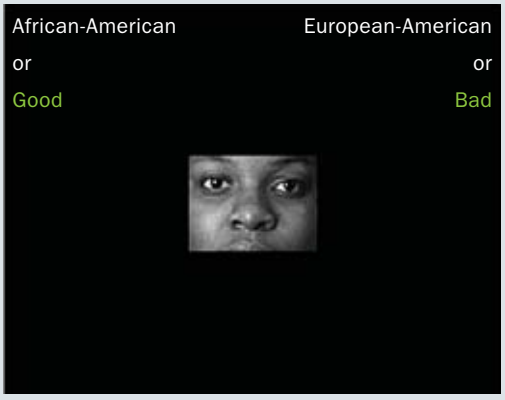
Automatic Prejudice

The Implicit Association Test, developed by psychologists Anthony G. Greenwald of the University of Washington and Mahzarin R. Banaji of Harvard University, records how speedily participants pair words and categories of people; they press a key to indicate whether the face or word is associated with a category that appears in the upper left or right. Easier pairings (faster responses) presumably reflect stronger implicit associations—intuitions—in memory.

For example, people associate a word such as "pleasant" more quickly with flowers than with insects. People's implicit prejudice scores (toward blacks, homosexuals, Muslims, the elderly, overweight people and others) correlate only modestly with their explicit prejudice scores. Some evidence indicates that brain areas associated with fear mediate automatic prejudices, and those associated with rational thought mediate controlled, conscious attitudes. *—D.M.*



© PROJECT IMPLICIT/ANTHONY G. GREENWALD, MAHZARIN R. BANAJI AND BRIAN NOSEK

that awareness that matters. Do we let those feelings hijack our behavior? Or do we compensate by monitoring and correcting our behavior?

Intuitive fears. This much is beyond doubt: we often fear the wrong things. With images of 9/11 indelibly in mind, many people experienced heightened anxiety about flying. But our fears were misaligned with the facts. The National Safety Council reports that from 2001 to 2003 Americans were, mile for mile, 37 times more likely to die in a passenger vehicle than on a commercial flight. For the majority of air travelers, the most dangerous parts of the journey are the drives to and from the airport.

In a late 2001 essay I calculated that if Americans flew 20 percent less frequently and instead drove half those unflown miles, about 800 more people would die in traffic accidents during the next year. In a follow-up article, psychologist Gerd Gigerenzer of the Max Planck Institute for Human Development in Berlin confirmed that the last three months of 2001 indeed produced an excess 353 American traffic fatalities. From their graves, the 9/11 terrorists were still killing us.

And they continued to instill fear. "We're striking terrorists abroad so we do not have to face them here at home," Bush said on a visit to Holland, Mich., my picturesque Midwestern town. "Today's terrorists can strike at any place, at any time and with virtually any weapon," echoed Homeland Security.

We hear. In a 2006 Gallup poll 45 percent of Americans said they were "very" or "somewhat" worried that they or a family member would become a terrorist victim. Nevertheless, the odds that you or I will be victimized by the next terrorist incident are infinitesimal. Even in 2001, the year more than 2,900 perished during the attacks on the World Trade Center and the Pentagon, the average American was 10 times more likely to die in a car accident and 100 times more likely to die a slow smoking-related death.

Why do we so often fear the wrong things? Why do so many smokers (whose habits shorten their lives, on average, by about five years) worry before flying (which, averaged across people, shortens life by one day)? Why do we fear violent crime more than obesity and clogged arteries? Why have most women feared breast cancer more than heart disease, which is more lethal [*see illustration on opposite page*]? Why do we fear tragic but isolated terrorist acts more than the future's omnipresent weapon of mass destruction: global climate change? In a nutshell, why do

we fret about remote possibilities while ignoring higher probabilities?

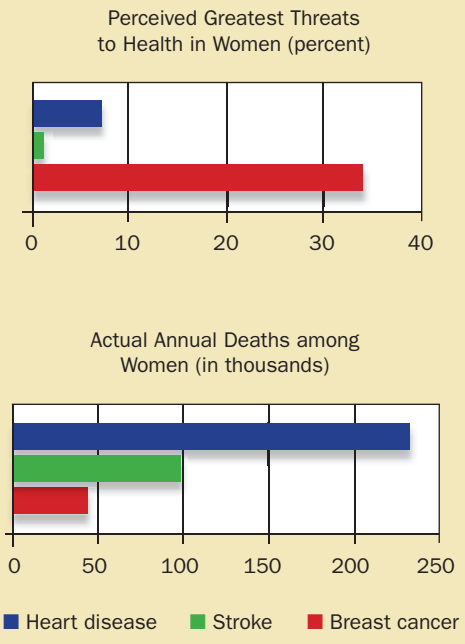
Psychological science has identified four factors that feed our risk intuitions:

- *We fear what our ancestral history has prepared us to fear.* With our old brain living in a new world, we are disposed to fear confinement and heights, snakes and spiders, and humans outside our tribe.
- *We fear what we cannot control.* Behind the wheel of our car, but not in airplane seat 17B, we feel control.
- *We fear what is immediate.* Smoking's lethality and the threats of rising seas and extreme weather are in the distant future. The airplane take-off is now.
- *We fear threats readily available in memory.* If a surface-to-air missile brings down a single American airliner, the result—thanks to the availability heuristic—will be traumatic for the airline industry. Given the difficulty in grasping the infinitesimal odds of its being (among 11 million annual airline flights) the plane that we are on, probabilities will not persuade us. Intuitive fears will hijack the rational mind.

For these reasons, we fear too little those things that claim lives undramatically (smoking quietly kills 400,000 Americans annually) and too much those things that kill in spectacular bunches. By checking our intuitive fears against the facts, with mindfulness of the realities of how humans die, we can prepare for tomorrow's biggest dangers and deprive terrorists of their biggest weapon: exaggerated fear.

In experiments presented at the 2007 American Association for the Advancement of Science meeting, cognitive psychologist Paul Slovic of the University of Oregon observed a parallel tendency to feel proportionately little concern for the many victims of genocide and greater moral concern for dramatically portrayed individual victims. In collaboration with behavioral psychologists Deborah Small of the University of Pennsylvania and George Loewenstein of Carnegie Mellon University, Slovic also found that people were more willing to contribute money to support a single starving African child than to support many such children. Moreover, donations declined sharply when the child's image was accompanied by a statistical summary of the millions of needy children like her in other African countries. "The numbers appeared to interfere with people's feelings of compassion toward the young victim," Slovic noted. Although it may be true that "the mark of a civilized human is the capacity to read a column of numbers and weep" (as Bertrand Russell allegedly said), the logical Track 2 mind is overridden by the feeling-based Track 1 mind. Mother Teresa spoke for most people: "If I look at the mass, I will never act. If I look at the one, I will."

So, intuition—fast, automatic, unreasoned thought and feeling—harvests our experience and guides our lives. Intuition is powerful, often wise, but sometimes perilous, and especially so when we overfeel and underthink. Today's cognitive science enhances our appreciation for intuition but also reminds us to check it against reality. Smart, critical thinking often begins as we listen to the creative whispers of our vast unseen mind and builds as we evaluate evidence, test conclusions and plan for the future. M



Intuitive fears do not match up with reality, as shown by a 1997 survey of 1,000 U.S. women age 25 and older.

SOURCE: L. MOSCA, W. K. JONES, K. B. KING, P. OUYANG, R. F. REDBERG AND M. N. HILL IN *ARCHIVES OF FAMILY MEDICINE*, VOL. 9, NO. 6; JUNE 2000

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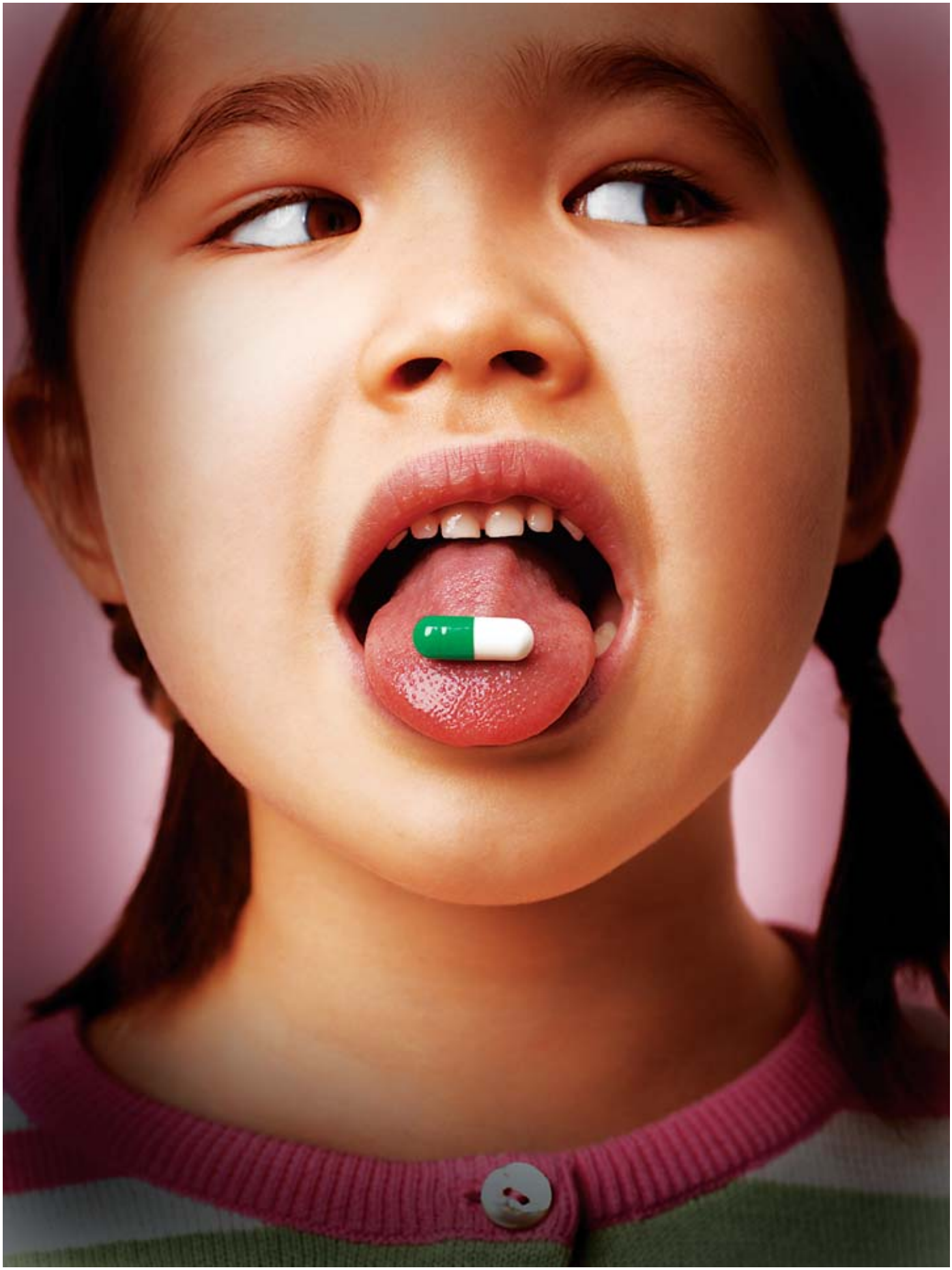


Trouble Ahead?

Antidepressants, designed for adults, may be altering the brains of kids who take them

By Paul Raeburn

On February 7, 2004, the body of Traci Johnson, a 19-year-old college student, was found hanging by a scarf from a shower rod in a drug company laboratory. Johnson had no apparent signs of depression, and the reason she killed herself was a mystery. What made her death different from other such tragedies is that she was a subject in a trial of an experimental antidepressant. The company, Eli Lilly, noted that four other patients given the drug in earlier trials had also committed suicide. Not long afterward, prompted by Johnson's death and others, the Food and Drug Administration warned doctors that antidepressants might increase the risk of suicide in children and adolescents.

GETTY IMAGES

Pallbearers carry the body of Traci Johnson, a 19-year-old who committed suicide in 2004 in an Eli Lilly research lab where she was a volunteer testing a new antidepressant.

JACQUELINE LARMA *AP Photo*

Johnson's death and the FDA's warning underscored the difficulty of treating depression in children. Was the cure worse than the disease? Nearly two decades after doctors began giving antidepressants to children, it is a question they still cannot answer definitively.

Graham Emslie, a psychiatrist at the University of Texas Southwestern Medical Center at Dallas, was one of the first psychiatrists to treat kids with antidepressants. His patients—children and teenagers—were in the grip of life-threatening depression. He wanted something more for them than the talk therapy that at the time was the only option.

Prozac and a growing number of similar successors were just then proving to be effective in treating depression in adults. But the drugs had not been tested in the supple young brains of children. Frustrated by the lack of alternatives, Emslie and others began to prescribe them anyway. They hoped the benefit would outweigh the risks—although there was no evidence to support that.

Despite the unknowns, the use of antidepressants in children and teens exploded during the 1990s. According to Julie M. Zito, a researcher at the University of Maryland who has studied antidepressant use in children, about 1.5 million kids younger than 18 are taking the medications in the U.S. (This figure comes from insurance industry and Medicaid data.)

Now, however, research suggests that suicide is only one of the potential risks. Studies have found that Prozac-like drugs might interfere with normal patterns of growth in children's still developing brains. Although the research is not conclusive, it is possible that kids on antidepressants are trading one psychiatric diagnosis for another. Children who take these drugs—in some instances starting in the preschool years—could find short-term relief and then grow up into edgy, anxious, dysfunctional adults.

Shaping the Wiring?

Amir Raz, a professor of clinical neuroscience in the psychiatry department at McGill University, is one of a handful of researchers raising concerns over the continued use of antidepressants in children and teens. "The human brain is developing exponentially when we are very young," he says. "And exposure to antidepressants may affect or influence the wiring of the brain, especially when it comes to certain elements that have to do with stress, emotion and the regulation of these."

The drugs in question, Prozac and its rela-

Drugs that affect serotonin during developmental years could alter brain function in unpredictable ways.

tives—including Celexa, Paxil, Zoloft and others—affect brain levels of the neurotransmitter serotonin, which helps to transmit signals between neurons. The drugs are known as selective serotonin reuptake inhibitors, or SSRIs, because they inhibit the removal of serotonin from the synaptic cleft (the space between neurons), leaving more of the transmitter available to exert its effects through neuronal receptors [*see box on page 40*].

Raz thinks messing with serotonin in kids is a bad idea. In addition to serving as a chemical messenger, serotonin acts as a growth factor during the first years of life. It encourages the formation of connections, or synapses, between neurons, and it is crucial for the acquisition of a normal response to anxiety-producing events in adulthood. It is also found elsewhere in the body, where it performs a variety of other functions. Drugs that alter serotonin during these critical developmental years could alter brain function in unpredictable ways, Raz says.

Not long ago, the orthodox view was that the brain grew rapidly during childhood and that by about age 12 the brain was wired up and ready to go. For better or worse, that was the brain you would rely on for the rest of your life.

"That's still very widely taught in psychology classes in college," says Jay Giedd, a psychiatrist at the National Institute of Mental Health. Giedd is one of the pioneers whose work has demolished that view. What they have found, instead, is that the teenage brain is a work in progress, undergoing continuous change and remodeling, at least until the mid-20s—and perhaps longer [see "The Teen Brain, Hard at Work," by Leslie Sabbagh; Scientific American Mind, June/July 2006].

Using the latest brain-scanning technology, Giedd and others have shown that gray matter—made up of nerve cells—undergoes a burst of overproduction just before puberty. During the teenage years, some of that gray matter is pruned away, as the brain discards neurons it does not need. Some neuronal connections are strengthened; others are weakened. A young piano student, for example, might strengthen connections in the auditory part of her brain. Some of those same connections might fall away in the math student, while he toughens up connections in a part of his brain responsible for abstract mathematical thought. It is a neurological use-it-or-lose-it proposition.

This process is not yet well understood. But if the teenage brain is still in flux—reshaping itself in response to outside stimuli—then perhaps bathing it with drugs that affect serotonin—and who knows what else—might be a very bad idea, some researchers say.

Born on Prozac

It is not just a theoretical concern. Evidence to support Raz's viewpoint comes from a study by Jay A. Gingrich, a professor of psychiatry at Columbia University's Sackler Institute for Developmental Psychobiology.

Gingrich used mice that were genetically altered so that they lacked the ability to mop up serotonin. They were—in effect—born on Prozac. He wanted to see how depression was related to serotonin and norepinephrine, another neurotransmitter. "Our simple-minded idea was these mice would look like mice treated chronically with Prozac," Gingrich says. They should have been free of anything like a mouse's version of depression or anxiety.

FAST FACTS

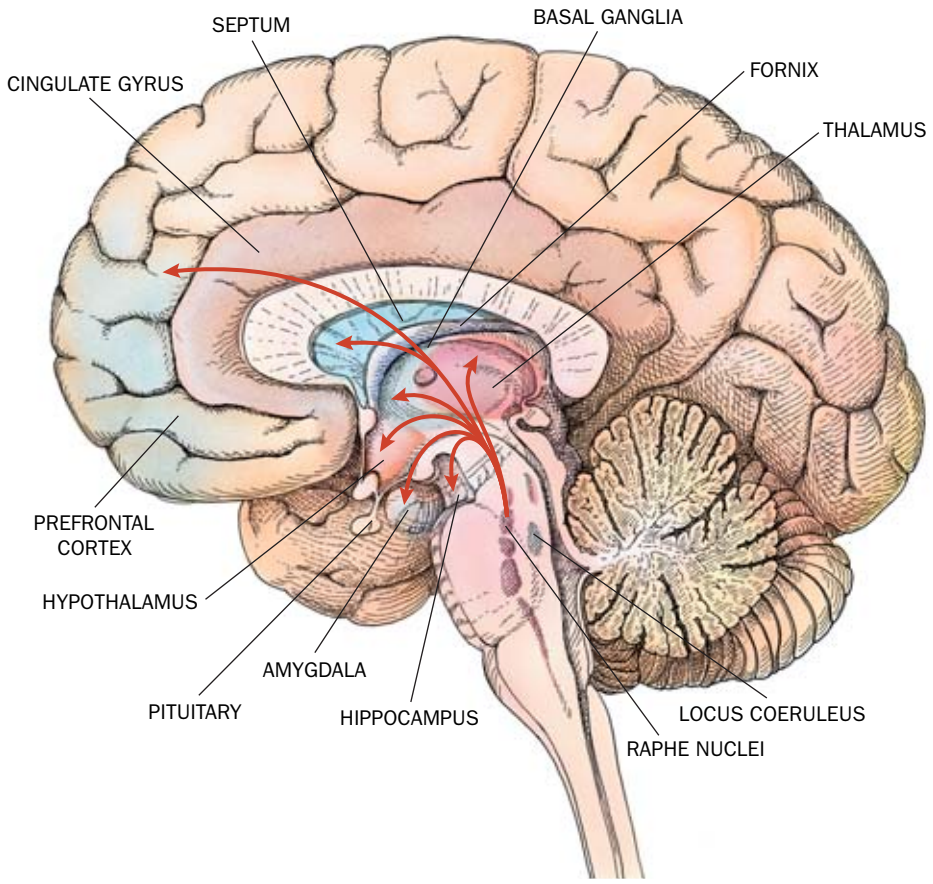
Kids and Antidepressant Drugs

1» **Antidepressant use in children 18 and younger tripled between 1987 and 1996. It doubled again by 2000, but then leveled off as concerns arose about a possible increase in the risk of suicide in kids on antidepressants.**

2» **Despite the concerns, antidepressants have been shown to be effective in the treatment of depression in children. In 2004 the Treatment for Adolescents with Depression Study (TADS) found that adolescents given both antidepressants and talk therapy showed a better response than those who were given drugs or therapy alone. All treatments led to a decrease in suicidal thinking, according to the National Institute of Mental Health, which funded the study. But the combined treatment produced the biggest decrease.**

3» **Children who are taking antidepressants should be monitored carefully for indications of suicidal thinking, nervousness, agitation, moodiness or sleeplessness that emerges or worsens during treatment.**

Where Depression Arises



Several brain areas are commonly disturbed in depression—such as those involved in mood, sleep, appetite, desire and memory. All normally receive chemical signals from neurons that secrete the neurotransmitter serotonin or norepinephrine or from neurons of both types. Reduction in the activity of circuits that use serotonin or norepinephrine apparently contributes to depression in many people. Some serotonin pathways are indicated (*arrows*).

Gingrich found quite the opposite. Because he could not chat with them about their feelings, he gave the mice stress tests. (An inability to handle stress is one hallmark of depression.) He put a small electric charge on the floor on one side of their cage. Normal mice will quickly learn to escape the tiny shock by running to the other side. These mice did not. "They have a tendency to freeze," he says. "They stay on the same side where the foot shock is being administered, or they escape much more slowly." The mice—despite having lived their entire lives as if they were on Prozac—were afflicted with what looked suspiciously like an anxiety disorder.

Gingrich concedes that the response of the mice to the stress test "sounds like a long way from depression" in humans. It is a little tough to imagine a depressed mouse—unable to get out of bed in the morning, plagued with doubts and fears, losing interest in cheese and harboring dark thoughts of self-destruction. But mice have brains that are quite similar to ours: We share some of the same serotonin-related genes. And the wiring is much the same. "You can demonstrate changes in their behavior that have some similarity with changes in a human that's depressed," he points out.

Maybe, Gingrich thought, the anxious mice suffered because of the tinkering that had been done to their genes. To find out, he repeated the experiment, this time giving Prozac to normal mice when they were very young. He let them

CAROL DONNER

grow into adults and tested their stress response. He published the results of both experiments in 2004. "They really fell apart," Gingrich says. "It was some change in the way their brains were wired. And it occurred because of the Prozac."

Finding these effects in mice is a long way from proving the same thing happens in humans. But the point of such animal studies is to search for potential problems and to raise questions. Gingrich's work certainly raises issues about the safety of antidepressants in children.

Gingrich is not the only one to raise such matters. Tim Oberlander, a pediatrician at the University of British Columbia in Canada, reported in February 2005 that infants exposed to SSRIs before birth are less sensitive to pain than their counterparts who were not exposed. It is unclear how that finding ties into Gingrich's work, except that it, too, raises suspicions about the effects of SSRIs on the developing brain.

In January 2003 the FDA reported that children who took Prozac for 19 weeks had grown, on average, almost half an inch less—and gained two fewer pounds—than kids who received a dummy pill. "We don't know if this is a temporary effect or will become more accentuated over time," said Thomas Laughren, who heads the FDA's psychiatric drug evaluation, in the journal *Science*. "That's one of the problems with the use of drugs in kids: we don't know the long-term risks."

Diagnosis Is Key

Even in the face of this evidence, however, many psychiatrists believe that antidepressants do far more good than harm in children and teens. Like Emslie in Texas, Harold Koplewicz, a professor of psychiatry at New York University and one of the city's top child psychiatrists, has been using SSRIs aggressively in children and teenagers for more than a decade. "I am probably the first person to give these meds to kids clinically," he says. As recently as a few years ago, most psychiatrists thought they should try talk therapy with kids before giving them medication. But that has changed, he declares.

He has seen what happens to teenagers who are not treated. "After they've had one episode of depression, they're 60 percent more likely to have another. If they have two, they're 90 percent more likely to have a third. And subsequent episodes are more difficult to treat.... Every good clinician will tell you the risk of not taking the medication is greater" than the possible risks of taking SSRIs.

Evidence is emerging to support Koplewicz's position. In an effort to learn exactly how antidepressants work in young patients, David Rosenberg, chief of child and adolescent psychiatry at Wayne State University, is using brain scanners to look at depressed children and adolescents. "We are seeing striking changes in the chemistry of the brain," Rosenberg says. But not the changes that medication critics might expect. His research focuses on the chemical messenger glutamate. "Glutamate is kind of like the brain's light switch," he notes. "If serotonin is the lighting in the room, glutamate would be the switch that turns serotonin on and off."

> Many psychiatrists still believe that antidepressants do far more good than harm in children.

Rosenberg has found that a reduced level of glutamate in certain parts of the brain is linked to depression. And the effect of antidepressants is clear: after treatment, glutamate becomes normal, and the symptoms of depression diminish. "When prescribed appropriately, antidepressants do far more good than not," he says.

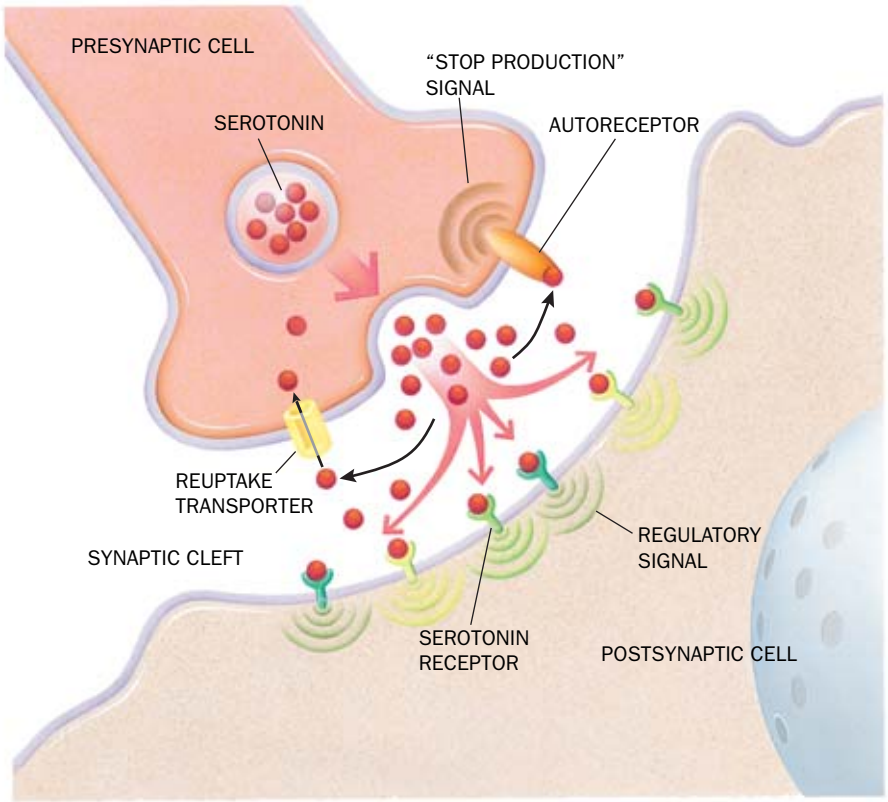
What is more, Rosenberg's brain scans have shown that *not* using antidepressants in depressed patients might have a lasting influence on the brain as well. He has found that untreated depression eats away at important parts of the brain. "In adults, the longer you have the illness, the less gray matter you have in the amygdala, the hippocampus and the temporal lobe areas," he says. All those brain regions are associated with thinking and learning. Preliminary results suggest the same is probably true with children and teenagers.

Rosenberg is careful to say that the benefits outweigh the potential for harm only when antidepressants are prescribed appropriately. "Antidepressants can be dangerous if the diagnosis is

(The Author)

PAUL RAEBURN is the author of *Acquainted with the Night,* a memoir of raising children with depression and bipolar disorder. He is also the host of *Innovations in Medicine* and *The Washington Health Report* on ReachMD, XM satellite radio channel 233.

Chemical Signals



Serotonin (*red spheres*) secreted by a nerve cell called the presynaptic cell binds to receptors (*shades of green*) on the postsynaptic cell and directs that cell to fire or stop firing. The postsynaptic cell's response is influenced by the amount of serotonin in the synaptic cleft and by the types of receptors present. Serotonin levels in synapses are reduced by two kinds of presynaptic molecules: autoreceptors (*orange*), which direct the cells to inhibit serotonin production, and reuptake transporters (*yellow*), which absorb the neurotransmitter. Several antidepressants, including Prozac, increase synaptic serotonin by inhibiting reuptake.

not accurate," Rosenberg says. "If you don't have a true clinical depression and you're getting antidepressants, probably at best it won't help and at worst it can do a lot of harm."

That is a particular problem with children, many of whom are misdiagnosed. Depression in teenagers "is a difficult diagnosis, because it seems like adolescence on steroids," Koplewicz says. Adults with depression usually recognize that they have a problem, and they want to fix it. Children and teenagers rarely ask to see a psychiatrist. They have to be cajoled, wheedled or somehow lured into the psychiatrist's office. And getting there is only part of the problem. With the exception of experts such as Koplewicz, psychiatrists—even child specialists—are not very good at diagnosing depression. Family doctors and pediatricians—who prescribe most of the antidepressants—are worse. Often the diagnosis is made by trial and error. Doctors try one drug. If it does not work, they prescribe another, until they find something that does.

The patients of clinicians like Koplewicz and Emslie, who were among the first to receive anti-

TOMO NARASHIMA

If the kids grow into adults without major problems, then perhaps the worrying has been for naught.

depressants as children, are the best resource of all for scientists who want to study the long-term impacts of antidepressants on kids. If children who started taking SSRIs as toddlers can grow into young adults without major psychological problems, then perhaps all the worrying has been for naught. Emslie has continued to follow some of the patients to whom he first gave antidepressants 15 years ago. The patients have not been examined rigorously, but based on cursory examination, they seem fine. "In terms of anything that's grossly apparent, we haven't seen any evidence of problems in development," he says.

Emslie has not done a formal study of these adult children of Prozac. If the drugs cause subtle but important changes in brain development, he could easily miss them. To be sure that they are healthy, he would need to compare them with controls—similar young adults who had not taken Prozac as children. It is also possible that these patients would be doing much worse now if they had not taken Prozac when they were younger. But again, in the absence of a formal study, it is impossible to know. And it is a difficult issue to try to study: it would be unethical to withhold potentially useful drugs from children who need them or to give them to children who do not.

Emslie believes that the use of antidepressants in still developing young brains might actually prevent the development of hardwiring for depression. "In the really early age people, you might influence the way neurotransmitters develop," he says. And in children, "you might not have the same side effects you see in adults."

Another encouraging piece of news appeared in April, when University of Pittsburgh researchers reviewed 27 studies of antidepressants in children and adolescents and concluded that the benefits far outweigh the risks. The researchers called on the FDA to reconsider its warning on antidepressant use in children and teens.

It could be years before these questions are resolved. In the meantime, Emslie and others will continue to prescribe SSRIs in children—because they are concerned about the alternative. Untreated depression in children is a scourge that afflicts not only them but also their parents, their brothers and sisters, their teachers and their friends. It turns childhood into a dark, interior battle for survival. Psychiatrists are not the only ones arguing for the continued use of antidepressants; many of their patients and the parents of their patients seek the medicines, too. "It seems," Emslie says, "that the impact of depression, the best we can judge it, is greater than the impact of the treatment." Koplewicz agrees. "At this time," he says, "the best treatment for teenagers is Prozac-like drugs." M

WARNING

SUICIDALITY IN CHILDREN AND ADOLESCENTS

ANTIDEPRESSANTS INCREASED THE RISK OF SUICIDAL THINKING AND BEHAVIOR (SUICIDALITY) IN SHORT-TERM STUDIES IN CHILDREN AND ADOLESCENTS WITH MAJOR DEPRESSIVE DISORDER (MDD) AND OTHER PSYCHIATRIC DISORDERS. ANYONE CONSIDERING THE USE OF [INSERT ESTABLISHED NAME] OR ANY OTHER ANTIDEPRESSANT IN A CHILD OR ADOLESCENT MUST BALANCE THIS RISK WITH THE CLINICAL NEED. PATIENTS WHO ARE STARTED ON THERAPY SHOULD BE OBSERVED CLOSELY FOR CLINICAL WORSENING, SUICIDALITY, OR UNUSUAL CHANGES IN BEHAVIOR. FAMILIES AND CAREGIVERS SHOULD BE ADVISED OF THE NEED FOR CLOSE OBSERVATION AND COMMUNICATION WITH

Concerns over antidepressant use led the FDA to issue a warning label for these medications.

LEONARD LESSIN, FBPA *Photo Researchers, Inc.*

(Further Reading)

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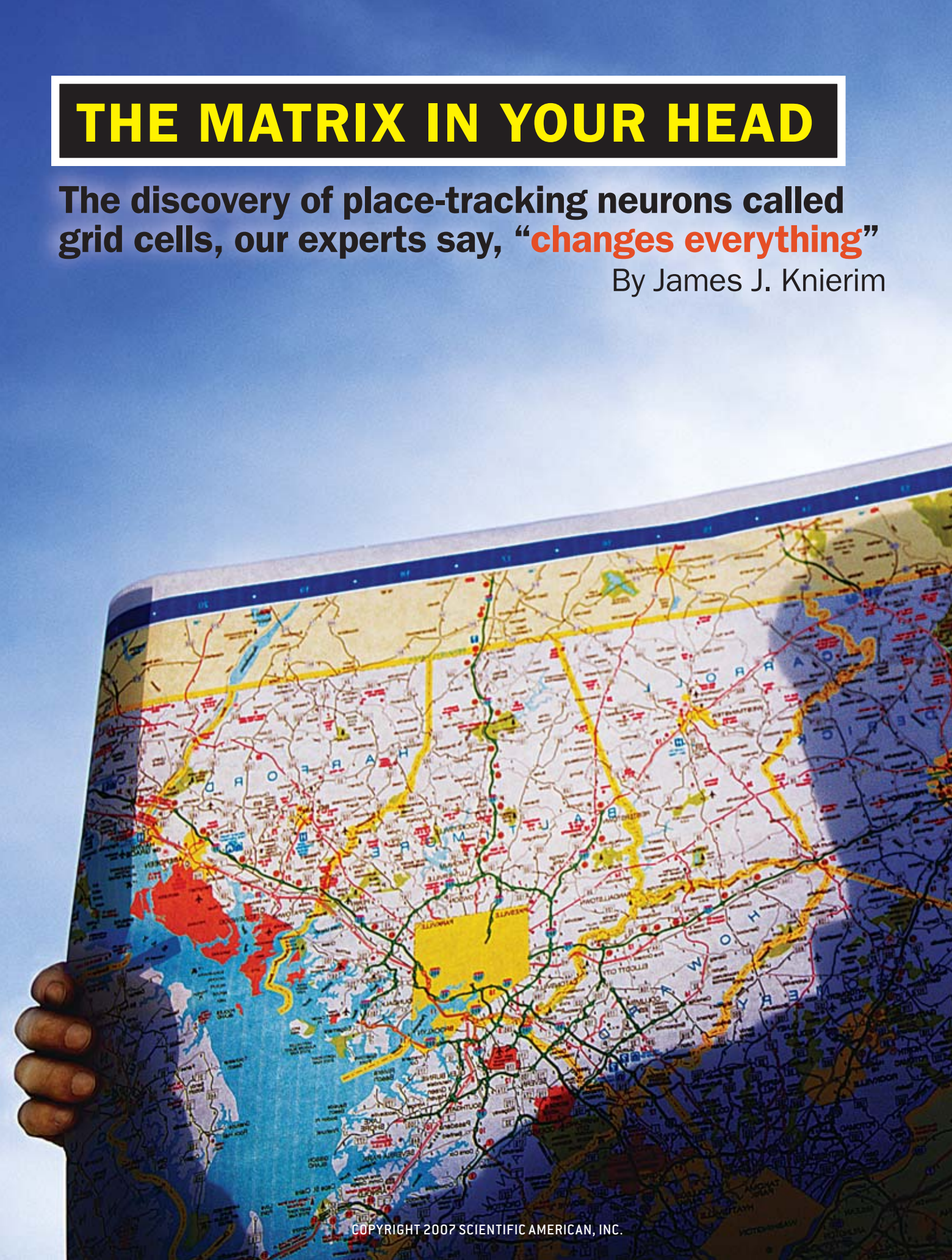
THE MATRIX IN YOUR HEAD

The discovery of place-tracking neurons called grid cells, our experts say, "changes everything"

By James J. Knierim



In the 2001 suspense thriller *Memento*, the lead character, Lenny, suffers a brain injury that makes him unable to remember events for longer than a minute or so. This type of amnesia, known as anterograde amnesia, is well known to neurologists and neuropsychologists. Like Lenny, sufferers remember events from their life histories that occurred before their injuries, but they cannot form lasting memories of anything that occurs afterward. As far as they recall, their personal histories ended shortly before the onset of their disorders.

The cause of Lenny's problem was probably damage to his hippocampus, a pair of small, deep-brain structures crucial to memory—and also important to some of today's most exciting and consequential neuroscience research. Decades of research have made clear that the hippocampus and surrounding cortex do more than just place our life events in time. The hippocampus, along with a newly discovered set of cells known as grid cells in the nearby cortex, traces our movement through space as well. And by doing so, it supplies a rich array of information that provides a context in which to place our life's events. The picture that is emerging is of historic importance and more than a little beauty.

Exactly how does the brain create and store autobiographical memories? Although that question has fascinated scientists, philosophers and writers for centuries, it was only 50 years ago that scientists identified a brain area clearly necessary for this task—the hippocampus. The structure's role was made clear in 1953, when William Scoville, a Hartford, Conn., surgeon seeking to relieve the epileptic seizures that were threatening to kill a patient known as H.M., removed most of H.M.'s hippocampus and discovered he had rendered him unable to form new, conscious memories. Since then, the case of H.M., along with extensive animal research, has firmly established that the hippocampus acts as a kind of encoding mechanism for memory, recording the timeline of our lives.

In the 1970s another discovery inspired the theory that the hippocampus also encodes our movement through space. In 1971 John O'Keefe and Jonathan Dostrovsky, both then at University College London, found that neurons in the hippocampus displayed place-specific firing. That is, given "place cells," as O'Keefe dubbed these hippocampal neurons, would briskly fire action potentials (the electrical impulses neurons use to communicate) whenever a rat occupied a specific location but would remain silent when the rat was elsewhere. Thus, each place cell fired for only one location, much as would a burglar alarm tied to a tile in a hallway. Similar findings have been reported subsequently in other species, including humans.

These remarkable findings led O'Keefe and Lynn Nadel, now at the University of Arizona, to propose that the hippocampus was the neural locus of a "cognitive map" of the environment. They argued that hippocampal place cells organize the various aspects of experience within the framework of the locations and contexts in which events occur and that this contextual framework encodes relations among an event's different aspects in a way that allows later retrieval from memory.

FAST FACTS

Finding Our Place

1» Rats (and presumably humans) have thousands of specialized brain cells, called grid cells, that track an animal's location in the environment.

2» Each grid cell projects a virtual latticework of triangles across its environment and fires whenever the rat is on any triangle's corner.

3» Every time the rat moves, it announces its location on multiple grids; collectively, the grid cells thus track the rat's location and path.

4» Grid cells populate cortical areas next to the hippocampus, long recognized as a center of memory. Many researchers believe the grid cells' spatial data enable the hippocampus to create the context needed to form and store autobiographical memories.

GREG PEASE Getty Images (preceding pages)

This view has been hotly debated for years. Yet a consensus is emerging that the hippocampus does somehow provide a spatial context that is vital to episodic memory. When you remember a past event, you remember not only the people, objects and other discrete components of the event but also the spatiotemporal context in which the event occurred, allowing you to distinguish this event from similar episodes with similar components.

But *How?*

Despite intensive study, however, the precise mechanisms by which the hippocampus creates this contextual representation of memory have eluded scientists. A primary impediment was that we knew little about the brain areas that feed the hippocampus its information. Early work suggested that the entorhinal cortex, an area of cortex next to and just in front of the hippocampus [*see box on next page*], might encode spatial information in a manner similar to that of the hippocampus, though with less precision.

This view has now been turned upside down with the amazing discovery of a system of grid cells in the medial entorhinal cortex, described in a series of recent papers by the Norwegian University of Science and Technology's Edvard Moser and May-Britt Moser and their colleagues. Unlike a place cell, which typically fires when a rat occupies a single, particular location, each grid cell will fire when the rat is in any one of many locations that are arranged in a stunningly uniform hexagonal grid—as if the cell were linked to a number of alarm tiles spaced at specific, regular distances. The locations that activate a given grid cell are arranged in a precise, repeating grid pattern composed of equilateral triangles that tessellate the floor of the environment [*see box on next page*].

Imagine arranging dozens of round dinner plates to cover a floor in their optimal packing density, such that every plate is surrounded by other, equidistant plates; this arrangement mimics the triggering pattern tied to any given grid cell. As the rat moves around the floor, a grid cell in its brain fires each time the rat steps near the center of a plate. Other grid cells, meanwhile, are associated with their own hexagonal gridworks, which overlap each other. Grids of neighboring cells are of similar dimensions but are slightly offset from one another.

These grid cells, conclude the Mosers and their co-workers, are likely to be key components of a brain mechanism that constantly updates the rat's sense of its location, even in the absence of external sensory input. And they almost certainly constitute the basic spatial input that the hippocampus uses to create the highly specific, context-dependent spatial firing of its place cells.

This discovery is one of the most remarkable findings in the history of single-unit recordings of brain activity. Reading the paper announcing

Each week in Mind Matters, www.sciammind.com's expert-written "blog seminar," researchers of mind and brain explain and discuss their disciplines' most notable recent findings. In the premiere installment, reproduced here, spatial cognition scientists James J. Knierim and A. David Redish ponder the discovery of grid cells—specialized neurons that encode in complex fashion an animal's location.

Mind Matters examines a new finding every week. Join the discussion at www.sciammind.com

When you remember a past event, you also remember the spatiotemporal context in which it occurred.

(The Author)

JAMES J. KNIERIM is associate professor of neurobiology and anatomy at the University of Texas Medical School at Houston, where he studies the role of the hippocampus and related brain structures in spatial learning and memory.

It is one of the most remarkable findings in the history of single-unit recordings of brain activity.

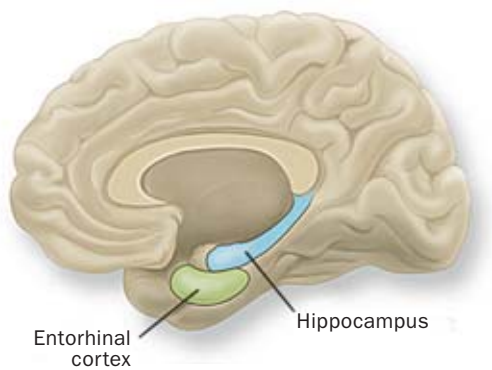
this discovery in my office for the first time, I realized immediately that I was reading a work of historic importance in neuroscience. No one had ever reported a neural response property that was so geometrically regular, so crystalline, so perfect. How could this even be possible? Yet the data were convincing. "This changes everything," I muttered.

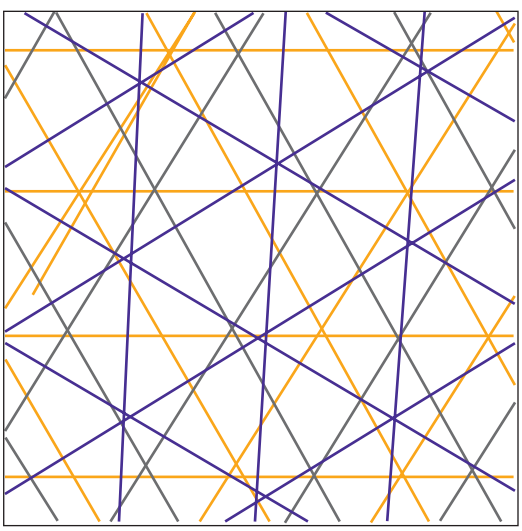
My excitement rose partly from the sheer beauty of the grid-cell response pattern. But it rose, too, from a belief that this was a major step in our quest to understand how the hippocampus might form the basis of episodic memory. Grid cells give us a firm handle on what kind of information is encoded in one of the major inputs into the hippocampus. From this foundation we can start to create more realistic models of what computations occur in the hippocampus to transform these grid representations into the more complex properties that have been discovered about place cells over the past three decades. For example, different subsets of place cells are active in different environments, whereas all grid cells appear to be active in all environments. How is the general spatial map encoded by grid cells turned into the environment-specific (or context-specific) maps encoded by place cells?

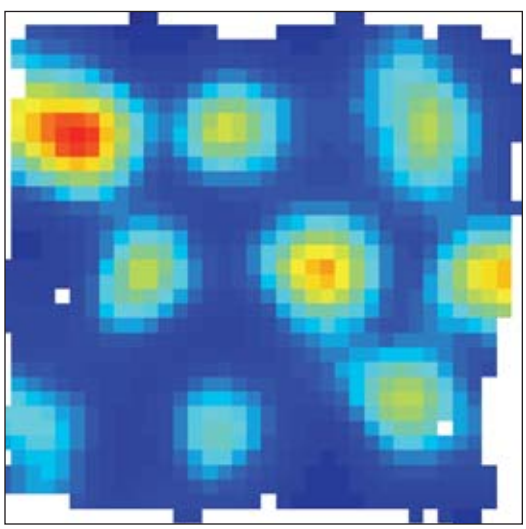
Moreover, the discovery of grid cells affirms emphatically that the hippocampus and medial temporal lobe are outstanding model systems for

The Brain's Tracking System

The "cognitive map" of the environment arises in the hippocampus—long known to be important for memory—and in grid cells in the entorhinal cortex. An individual grid cell projects across the environment a latticework of perfectly equilateral triangles (*bottom left*), the corners of which are sensitive to the rat's presence. Because the grids projected by the brain's thousands of grid cells overlap, the grid cell system fires whenever the rat moves (*bottom right*). The animal's location is thus constantly updated.







KATHERINE SUTLIFF, FROM "IN THE PLACE SPACE," BY D. K. BILKEY, IN *SCIENCE*, VOL. 305; AUGUST 27, 2004, REPRINTED WITH PERMISSION FROM AAAS (*brain*); FROM "NEUROSCIENCE: NEURONS AND NAVIGATION," BY GYORGY BUZSAKI, IN *NATURE*, VOL. 436; AUGUST 11, 2005 (*triangular grids*); MAY-BRITT MOSER *Norwegian University of Science and Technology* (*grid cell activity*)

A Window into Cognition

By A. David Redish

Over the past 30 years, the place cell has become one of the most studied examples of a cellular correlate—that is, a neuron demonstrably connected to a particular behavior, sensation or mental activity—not driven by an immediate sensory or motor cue. As James J. Knierim notes in the main article, each hippocampal place cell fires action potentials only when the rat is in a specific location within an environment (the "place field" of the cell). Thus, if you know where each place cell's place field is, you can track an animal's path by observing the activity of its place cells. Systems neuroscientists call this process "reconstruction." When the animal is asleep, the population of place cells "replays" the animal's experience; using the reconstruction process, it is possible to follow the sequence being replayed and thus to know, in a sense, what the animal is thinking. Place cells provide a way to directly observe cognition, even in the rat.

The term "cognitive map" traces its origin back to Edward C. Tolman. In a classic 1948 paper, the University of California, Berkeley, psychologist proposed that somewhere in the brain existed a representation of the environment—constructed by the animal—which could be used to make plans and navigate the world. The key was that the map had to be "cognitive"—that is, constructed internally from a combination of cues and memory.

The 1971 discovery of hippocampal place cells by University College London neuroscientists John O'Keefe and Jonathan Dostrovsky seemed to put the cognitive map in the hippocampus. (A hippocampal place cell fires only when a rat occupies a specific location in a given environment.) But the cognitive map, asserted O'Keefe and his colleague Lynn Nadel, now at the University of Arizona, in their 1978 book *The Hippocampus as a Cognitive Map,* was still a cognitive construct. Place cells, properly understood, reflected not any specific environmental cue but rather the animal's perception of its place in the environment.

The question of what made a place cell fire when the rat was in its place field remained unanswered. Computational models suggested that place cells encoded some association between external and internal representations of space. But no one really knew what information

Each grid cell fires when a rat is in any one of many locations that are arranged on a stunningly uniform hexagonal grid in the brain.

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the hippocampus was actually being fed to do these computations.

As Knierim observes, the discovery of grid cells seems to answer exactly that question—which is why cognitive scientists find grid cells intensely exciting. As soon as the paper was published, researchers started examining their earlier work on the entorhinal cortex to try to find the grid cells hidden in their data. Theorists immediately began to build computational models of how the grid is formed and how it might drive hippocampal activity.

Grid cells, like place cells, can provide a way for us to observe and trace cognition. And because the entorhinal grid cells project directly to the hippocampal place cells, we now have an access point to examine broader mechanisms of cognitive processing. Papers by the Norwegian Unversity of Science and Technology's Edvard Moser and May-Britt Moser and other researchers have done exactly that.

One of the most interesting things about the grid cell discovery is that no one predicted it. Theories and models had envisioned that the entorhinal cortex would play an important role in the cognitive map and that entorhinal cells would show more stable intercellular relations across environments than place cells do. But no one imagined that the entorhinal cells would cover the environment with tessellating triangular grids—and anyone who had suggested such a thing would have been laughed out of town.

A. DAVID REDISH is associate professor of neuroscience at the University of Minnesota and author of Beyond the Cognitive Map *(MIT Press, 1999).*

understanding the way in which the brain constructs cognitive representations of the world "out there" that are not explicitly tied to any sensory stimulation. There is no pattern of visual landmarks, auditory cues, somatosensory input or other sensations that could possibly cause a grid cell to fire in such a crystalline fashion across any environment. This firing pattern—which is similar regardless of whether the rat is in a familiar, lit room or in a strange location that is pitch-dark—must be a pure cognitive construct. Although grid cell firing patterns are updated and calibrated by sensory input from the vestibular, visual and other sensory systems, they do not depend on external sensory cues.

Some have argued that hippocampal place cells are similarly independent. But the known influence of external landmarks on place cells, and their tendency to fire in single locations, led others to argue that place cells are driven primarily by unique combinations of sensory landmarks that exist at particular locations. This argument cannot explain the firing patterns of grid cells.

The Road Ahead

So what does account for grid cell dynamics? One possibility is that these cells allow an animal to constantly update its physical location on its internal cognitive map by keeping track of its own movements. That information is in turn conveyed to the hippocampus, which combines this spatial representation with other data about an event to create specific, context-rich memories of unique experiences—the ability that *Memento*'s Lenny had lost.

The discovery of grid cells has generated a palpable sense of excitement. We can anticipate that further research into grid cells (along with the other major input to the hippocampus, the lateral entorhinal cortex) will reveal the neural mechanisms that let us remember our personal histories—a vital process that forms the very foundation of one's sense of identity. M

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We Get Comments...

Like most blogs, Mind Matters invites reader comments and questions. Unlike most blogs, reader comments and questions often get answered by leading researchers—the authors of the posts that provide reviews of recent papers, as well as some who visit the blog—and *Scientific American Mind* editors. The sampling below, from the installment on grid cells, includes posts from readers, James J. Knierim, who wrote the installment's lead piece, and Mind Matters editor David Dobbs.

Do Grid Cells Map Dreams?

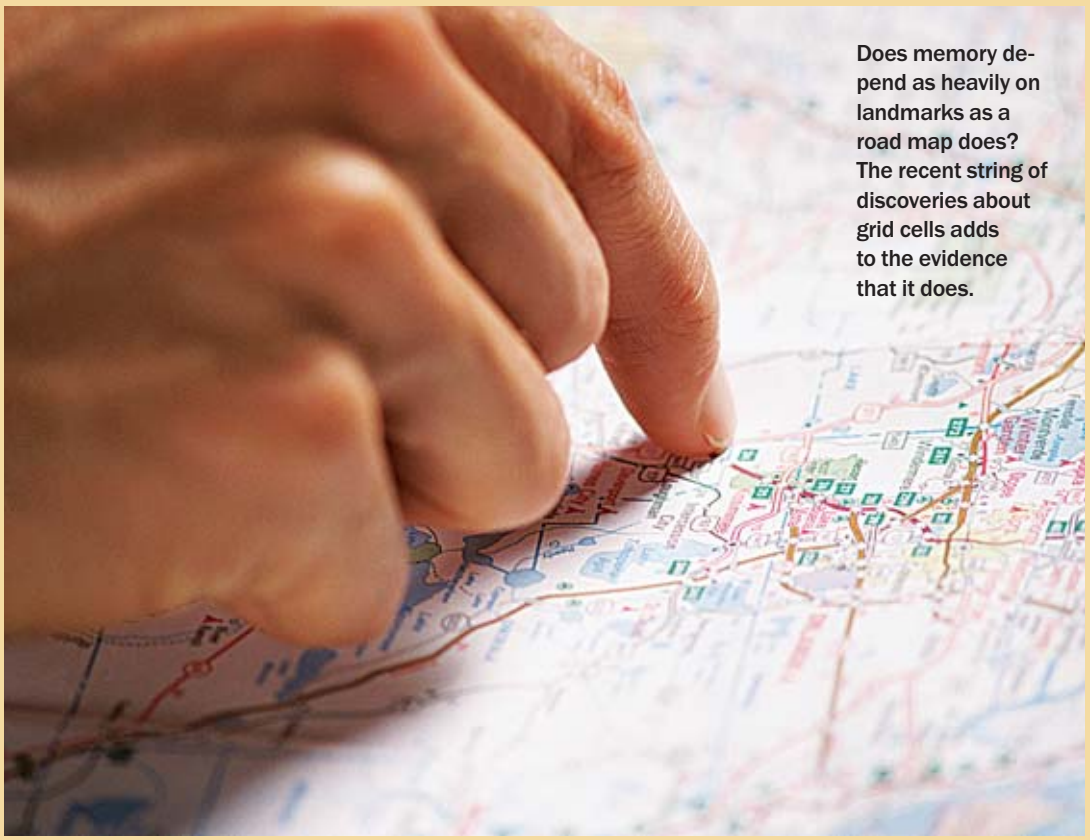
What are your thoughts on the stored memory of dreams/daydreams in relation to grid cell activity? Is dream space plotted in the same way as reality, and perhaps are those people who seem to never recall their dreams simply not accessing those portions of the spatial map while asleep? ***—Ian***

KNIERIM REPLIES:

Good question, Ian. When a rat sleeps, the hippocampal place cells sometimes fire in the same order in which they fired during a short behavioral sequence when the rat was awake. This process is thought to be related to the formation of long-term memories, as the hippocampus "replays" the rat's recent experience to the neocortex for long-term storage. Grid cells are presumably also involved in this process, because they are a gateway between the hippocampus and the neocortex.

Mythical Mapping

I can't help but be impressed by a seeming relation between the apparent functions of these entorhinal and hippocampal structures and humankind's practice of projecting important mythical events onto features of physical landscapes. American Indians actually visit specific landscape features to recall specific events of their past. History, for us, is a matter of documentation, but before writing it was a



Does memory depend as heavily on landmarks as a road map does? The recent string of discoveries about grid cells adds to the evidence that it does.

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matter of memory—group memory. Tying this history to places might serve a societal function similar to that played by grid cells for individual memories. ***—Bill Crane***

KNIERIM REPLIES:
There may well be a relation between these cultural practices and how our brain is actually wired to remember events. Something about places, either real or imagined, helps us to remember events.

A well-known example is a mnemonic trick used by performers to memorize long lists of random items. As the audience calls out each item, the performer imagines the item as being placed in a particular location in a familiar room. When it is time to recall the list in order (forward or reverse), the performer mentally steps through the sequence of locations and is able to recall the items previously imagined there.

DOBBS ADDS:
The memory-aid method Jim describes (tying items to familiar locations) is called the method of loci, and it was used routinely by the Greeks and Romans to remember long speeches. I have a friend who can remember random strings of numbers or words. He associates the words or numbers to familiar spots along the 18 holes of his favorite golf course. A learned and lively book called *The Art of Memory,* by Frances A. Yates (University of Chicago Press, 1966), describes this method.

As to aboriginal wanderings: Bruce Chatwin's superb book *The Songlines* (Viking, 1987) concerns routes to which Australian aborigines tied narrative songs relating essential myths or stories. Lovely book.

There's a nice neurospatial-anthropology thesis waiting to be written here ....

The Wow Factor

The computational power of the brain is astounding. A tiny color topographic plotter/position tracker in the brain is a great new understanding.
—Jim Arneson

profile

Seeing the Person in the Patient

By Siri Schubert

On a Sunday morning in 1963 Theodore Millon woke up in a Pennsylvania hospital. He was in bed at a psychiatric ward shared by 30 patients. One of them thought he was Jesus Christ, another believed he was the pope, and a third claimed he was a corporate CEO who had been hospitalized by mistake. Millon began to fret. "I am wearing a hospital gown like all the other patients," he thought. "Am I really a professor of psychology? Or did I just imagine that?"

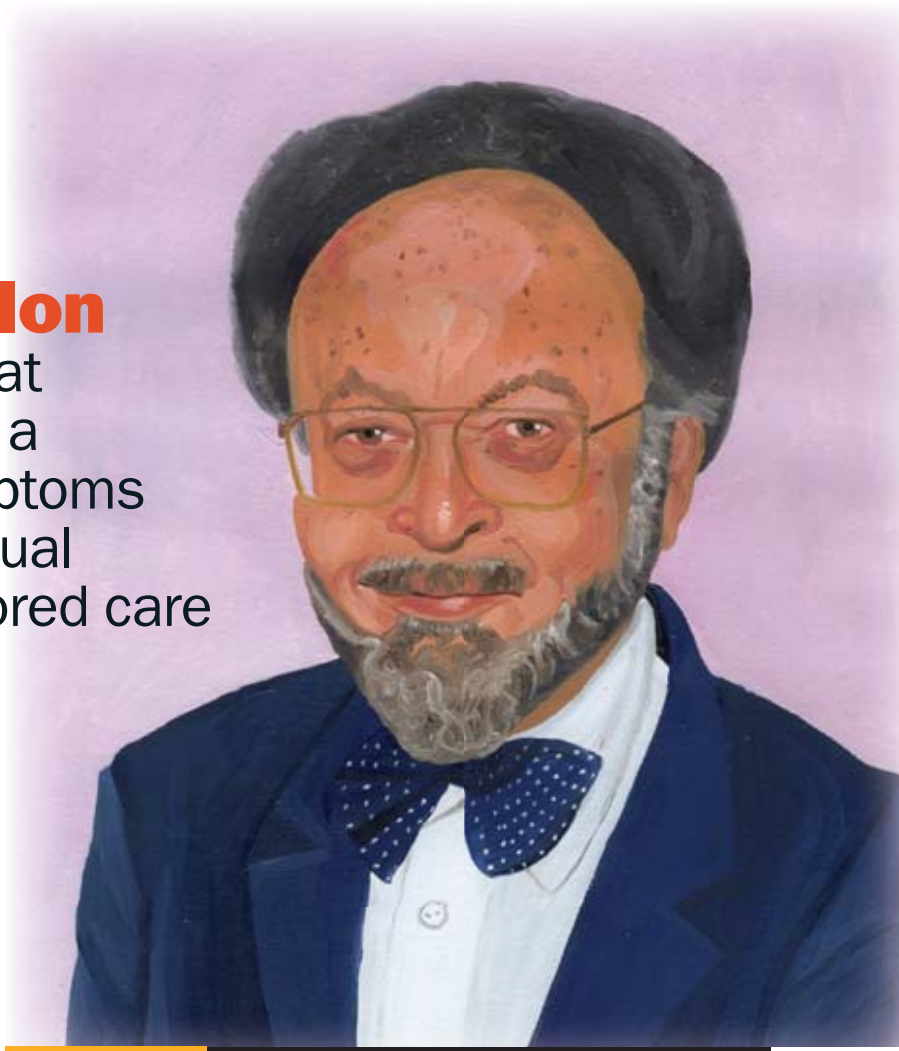
Apprehensive, he went to the nurses' station and called the head of the hospital. His anxiety finally eased when the director confirmed that he was, in fact, a clinical psychology professor at Lehigh University and chair of the board of trustees at Allentown State Hospital who was voluntarily spending the weekend in the psychiatric ward. "That experience shocked me, and I never spent another night there," Millon remembers, although he would still occasionally walk incognito among the patients.

Experiencing the world from the patients' vantage point gave Millon a uniquely powerful window into their needs and had a lasting impact on him. "It became clear to me how primitive our understanding of psychological disorders and our methods of treating them still were," he recalls. It especially bothered him that doctors typically saw the mentally ill only as collections of symptoms. "I wanted to understand the patient behind the illness," says Millon, who now heads the Institute for Advanced Studies in Personology and Psychopathology in Florida and is an emeritus professor at Harvard Medical School.

These perspectives informed Millon's first major book, *Modern Psychopathology* (Saunders, 1969), which became a standard text for American psychologists and psychiatrists. His so-called biosocial-learning theory of personality and the Millon Clinical Inventories constructed around it are still influential in clinical research and practice.

Millon's "personalized psychotherapy" promoted goals and methods tailored to the individual, and his work is one of the major reasons why research into personality and personality disorders has gained so much importance in psychology over the past 25 years. His latest book, *Resolving Difficult Clinical Syndromes: A Personalized Psychotherapy Approach* (John Wiley & Sons, 2007)—co-authored with psychiatrist Seth Grossman of the Institute for Advanced Studies in Personology and Psychopathology—

Theodore Millon promoted the view that a patient is not just a collection of symptoms but a unique individual who needs tailored care



offers a revised and comprehensive manual for the treatment of such disorders.

Millon had his first exposure to mental pathology at home. He describes his mother, Molly Gorkowitz Millon, who was quite gifted musically, as emotionally labile. Today she probably would be diagnosed as having bipolar disorder, or manic depression. As a child, he wanted to learn why she was that way. "I never completely succeeded," he says. But the desire to understand people became compelling.

Many years passed, however, before he found his professional path. The son of immigrants from Poland and Lithuania, young Millon loved the theater and wanted to make that his career. But his father, Abraham, who ran a textile factory in Brooklyn, N.Y., forbade him. And when his mathematically gifted son said he instead wanted to pursue math or music, Abraham nixed those ideas as well. Millon's father believed that those were not decent professions for "a nice Jewish boy," who should study something useful, such as business. Millon bowed to his father's wishes and became an accounting major at the City College of New York, where he would also meet his future wife, Renee.

VANESSA DELL

FAST FACTS

Theodore Millon

1» Born in 1928 in Brooklyn, N.Y. Received his Ph.D. from the University of Connecticut in 1954, with a dissertation on "the authoritarian personality."

2» Professor at the University of Miami from 1977 to 2001 and at Harvard Medical School from 1982 to 1995. In 1986 co-founded the *Journal of Personality Disorders* with psychiatrist Allen J. Frances of Duke University.

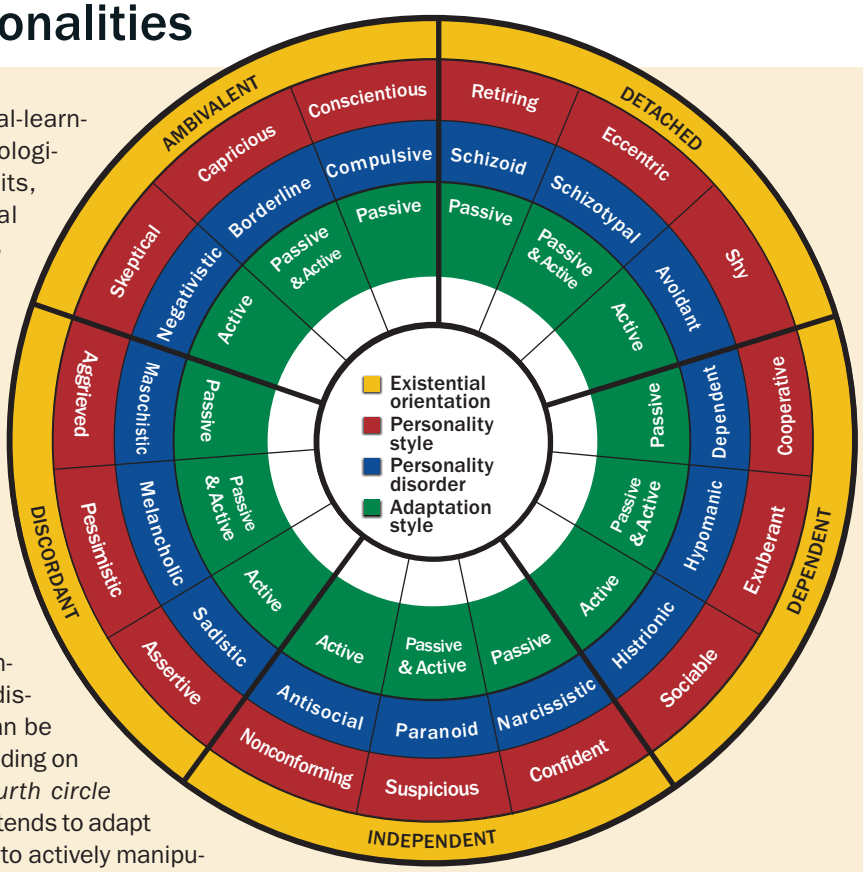
3» In 2003 received award from the American Psychological Association (APA) for Distinguished Professional Contributions to Applied Research. Today the APA annually honors a promising personality researcher with its Theodore Millon Mid-Career Award in Personality Psychology.

The World of Personalities

Theodore Millon's 1969 biosocial-learning theory took into account biological factors such as inherited traits, which influence neuropsychological development in early childhood, as well as environmental factors, which affect the personality's further development by means of learning processes. Since then, his model has expanded to include the role of evolutionary theory, emphasizing how various survival strategies contribute to individual personality types.

Millon distinguishes among five so-called existential orientations of personality (*outermost circle*). Every person is either "independent," "dependent," "detached," "ambivalent" or "discordant." Each one of these types can be expressed in one of three ways, depending on an individual's adaptation style (*fourth circle in*)—the degree to which an individual tends to adapt passively to his or her environment or to actively manipulate his or her surroundings. Each of these categories can differ further: as a personality style (*second circle in*) or as a personality disorder (*third circle in*).

For instance, in its "normal" expression, the independent personality—found in a strongly self-motivated person—appears as "nonconforming," "suspicious" or "confident." Its "abnormal" expression, in contrast, can take the form of an "antisocial," "paranoid" or "narcissistic" disorder. Whether a person develops a normal style or a disorder depends on how he or she reacts to challenges of the environment. If his or her behavior deviates markedly from cultural norms, and if the individual or others suffer as a result, a disorder occurs. —S.S.



Personality types as described in Millon's biosocial-learning theory vary depending on an individual's character traits and the way in which he or she approaches personal relationships and the environment.

Millon was unable to get interested in accounting so he switched majors (briefly to economics, then to philosophy and physics). He fared well in an introductory psychology course and attended a series of psychology lectures—a key event that awakened his interest in personality research. The professor conducting the lectures, psychologist Gardner Murphy, had just published *Personality* (Harper and Brothers, 1947). "That became my bible," Millon says.

Murphy's theory about personality development immediately appealed to Millon. The theory presented dispositions and the environment—meaning biological and social factors—as contributing to development in combination, instead of regarding them as competing explanatory models. It was in this tradition that Millon himself later created his biosocial-learning theory, which explains how both inherited predispositions and social learning shape personality [*see box above*].

The significance of a person's environment—whether it is family or culture—for personality runs through Millon's career. In the 1970s he worked in the psychiatric ward of a VA hospital in Chicago with colleagues from Romania and Thailand and patients who were mostly African-American. During that time, he was also a member of the committee that prepared the *Diagnostic and Statistical Manual of Mental Disorders-*

(The Author)

SIRI SCHUBERT is a freelance journalist and lives in San Francisco.

Similar symptoms can be caused by different problems, depending on the individual.

III (*DSM*)—which is the standard American reference work for diagnosing mental illnesses. It presented, for the first time, explicitly formulated diagnostic criteria for personality disorders.

These experiences prepared Millon for his role as a mediator when he served from 1988 to 1992 as president of the International Society for the Study of Personality Disorders—and gave him insights into how cultures can clash.

At the society's conferences around the globe, a speaker from the U.S. might, for example, discuss a patient's extreme perfectionism as a sign of an obsessive personality. Japanese researchers would not understand the presentation. "In Japan, no one would talk about such things as pathological behavior, because perfectionism is part of societal expectations," Millon explains. What people perceive as normal or not normal strongly depends on their cultural background.

According to Millon, borderline personality disorder, for example, is typical of modern Western societies. Victims are unsure about who they are, what they want to be and what makes their life meaningful. This type of unstable personality reflects its surrounding societal conditions: vague role models and changing ideals, lifestyles and conditions mark the cultural environment. If a person in this culture also grows up amid chaotic family circumstances, it could have detrimental effects on his or her personality.

For similar reasons, Millon promotes personalized psychotherapy and accuses therapists who ascribe to traditional schools of taking too narrow a view of their patients. "They distance themselves from human reality in the process," he warns. Millon believes that therapists must consider their patients' entire life and every aspect of their personality. His strategy is guided by the patient's individual characteristics and combines various treatment methods, so that a therapist can deal with several problems simultaneously. For example, a shy person should first overcome his or her anxieties, which would ease mastery of the subsequent steps, such as gaining self-confidence and learning competence.

Personality at the Root

Even when a therapist is dealing with a client's depression or another chronic mental illness, rather than a less severe personality disorder, Millon recommends tailoring treatment to the patient's character. Similar symptoms can be caused by different problems, depending on the individual. After a divorce, for example, a person with a dependent personality may develop depression because he feels helpless without his partner. A narcissist, in contrast, seeks to maintain a self-image as a perfect person and may be depressed after a divorce because she feels so damaged that her self-image has collapsed. In addition, patients' inclinations to follow their doctors' advice depend on their personality. A patient with a dependent personality or an obsessive one would probably follow prescriptions to the letter, whereas a mistrustful person would not.

Millon is critical of excessive use of psychopharmacology. "Almost any person suffering from depression can probably profit from antidepressants," he says. "But there is the danger that they will not help in the long run." Therapy should help patients to change root problems in their life and uncover new possibilities.

Millon compares today's psychiatric practices with the state of medicine when physicians concentrated on treating the effects of disease, such as smallpox lesions and the inflamed lungs of tuberculosis victims, rather than their causes—viruses and bacteria.

"We are beginning, now, to understand that a dependent personality gets depressed for different reasons than someone with a narcissistic personality," Millon says. For both therapists and physicians, he recommends studying a patient's personality before beginning treatment of the underlying illness—a step Millon took himself as a young man, when he traded his white coat for a hospital gown. M

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A growing body of research shows that groups can systematically enhance their performance

The Science of Team Success

By Steve W. J. Kozlowski and Daniel R. Ilgen

The right stuff: The dramatic rescue of *Apollo 13*'s astronauts would have been impossible without the coordinated efforts of NASA engineers. Research is revealing why some groups work so well together.

"Houston, we've had a problem," were the famous words that announced a crisis onboard *Apollo 13*. Halfway through *Apollo*'s mission to the moon, one of the spacecraft's oxygen tanks exploded, putting the lives of the crew in grave jeopardy. A group of engineers from NASA was hastily assembled. Their mission: invent a way for the crew to survive and to pilot their damaged vessel back to Earth. The engineers were successful, transforming a potential disaster into a legend of effective teamwork.

NASA

As experienced members leave and new people join a group, crucial bits of collective knowledge can be lost.

DAVID TROOD Getty Images

Human history is largely the story of people working together in groups to explore, achieve and conquer—and in our modern world the role of teams is only growing, spurred by globalization and the enabling factor of communications technology. Teams do not always play the role of hero, however. They have also been implicated in many political and military catastrophes, including the U.S. government's sluggish response to Hurricane Katrina, the failure to prevent the tragedy of 9/11 and the explosion of NASA's space shuttle *Columbia*.

Given the centrality of work teams, it is more than a bit remarkable how much our society's perspective is focused on the individual. We school our children as individuals. We hire, train and reward employees as individuals. Yet we have great faith that individuals thrown into a team that has been put together with little thought devoted to its composition, training, development and leadership will be effective and successful. Science strongly suggests otherwise.

We recently reviewed the past 50 years of research literature on teams and identified factors that characterize the best collaborations. It turns out that what team members *think*, *feel* and *do* provide strong predictors of team success—and these factors also suggest ways to design, train and lead teams to help them work even better.

Unfortunately, although society places a great value on teamwork, the way organizations make use of teams often runs against known evidence for what works—and even against common sense. For example, it seems obvious that teams need sufficient resources to enable members to accomplish their goals. Still, in this era of down-

FAST FACTS

Building Better Teams

1» **An effective work group should be designed well from the start, bringing together people who can contribute to the right mix of knowledge, skills, tools and other resources necessary to succeed.**

2» **Face-to-face meetings, social interaction among members and a leader who establishes a good relationship with every worker help a team make the best use of its expertise and create a cohesive mission.**

3» **Generic teamwork skills such as setting goals, adapting to change, resolving conflict and providing feedback allow teams to learn from each challenge and continually improve their performance.**

Organizations reward individuals based on individual performance rather than team performance.

sizing and cutbacks, one has to question the wisdom of many managers who believe that more can *always* be accomplished with less.

Consider, too, that organizations typically reward people with salaries, bonuses and promotions based on individual performance rather than team performance. These rewards can often inhibit team members' willingness to work together and help one another, even when the success of the team depends on it. Such success requires a delicate balance between meeting the goals of the team as well as those of the individuals who populate it. Research on goal setting, cooperation, competition, conflict and negotiation contributes to a better understanding of how people remain in teams and work together.

Indeed, a crucial question that should be asked before putting a team together is whether you need one at all. Some businesses recognize the importance of teams and promptly restructure every task so that it becomes a group responsibility, even when the assignment is something that could be done easily by an individual working independently. The result is a team that is more likely to impede performance than enhance it. Another question is, What type of team structure is required? The task of some teams is such that their employees can function independently for long stretches and occasionally confer and pool their results, as with a team of salespeople working in different geographic regions. Others, such as surgical teams, require a high and constant degree of coordination.

The job assigned to a team also determines the primary focus of activities, and how well the individual members complete their related duties determines the team's efficiency. That is why team studies have turned to an approach known as organizational psychology, which focuses on the task as central to understanding the dynamics of teamwork and team performance. (In contrast, a traditional social psychology perspective

SCHLEGELMILCH *Corbis*

An effective group brings together people with the necessary knowledge, skills and tools to do the job.

focuses more on interactions among peers, and the work merely serves as the context for those exchanges.) As mentioned before, the task sets minimum requirements for the resource pool—the constellation of knowledge, skills, abilities and other characteristics (such as personality, values)—that is available across team members.

The Collective Mind

One of the most important things a team brings to a task is what its members *think,* the relevant information they carry in their heads. This knowledge can include a mastery of the tools they use and an understanding of the task at hand, its goals, performance requirements and problems. Some knowledge may be shared by all workers, whereas particular members might have specialized skills or know-how. The ability to access and use this distributed expertise efficiently is one characteristic of successful teams.

Successful teams must deal with parasitic members—those who do not contribute anything to the group.

A 1995 experiment by psychologist Diane Wei Liang, then at the University of Minnesota, psychologist Richard L. Moreland of the University of Pittsburgh and Linda Argote, professor of organizational behavior and theory at Carnegie Mellon University, nicely demonstrated how team members benefit from their collective knowledge when they learn together. These researchers trained college students to assemble transistor radios either alone or in groups of three. A week later the subjects were tested with their original group or, for people who received solo training, in newly formed groups. Members of groups that had trained together remembered more details, built better-quality radios and showed greater trust in fellow members' expertise. People in newly formed groups were less likely to have the right mix of skills to complete the task efficiently and knew less about one another's strengths.

With a different group of collaborators, Argote studied the effect of individual turnover on another chore, making origami birds. Again, groups of three trained together and were given six time periods to make as many paper products as possible. The groups with turnover produced significantly fewer folded creations than groups whose members stayed constant, suggesting aspects of group knowledge were being lost when people were replaced.

In an interesting twist, organizational behav-

RANDY FARIS *Corbis*

ior expert Kyle Lewis of the McCombs School of Business at the University of Texas at Austin found that the development of a team's ability to access distributed knowledge required face-to-face interaction. In groups that communicated exclusively by phone or e-mail, this skill did not emerge—an observation of increasing importance, given the rise of teams that operate remotely and coordinate sometimes only through computer interactions. It should prompt concerted efforts to understand the reasons for such barriers and explore whether webcams, videoconferencing or other technologies that allow people to interact will help overcome this problem. For now, the best solution may be to guarantee some face time for team members throughout their project.

Beyond an understanding of the nuts and bolts of any given project, another cognitive influence on team effectiveness is the emergence of an overall objective, mission or strategic imperative of the group—something psychologists call the team climate. The powerful effect of climate on the real-world impact of teams is well established. For example, one of our groups (Kozlowski's) showed that high-tech businesses whose engineers agreed on the objective to stay technologically up-to-date showed improved performance and had more employees pursuing continuing education and displaying positive job attitudes. Several studies across many industries have shown that when a team has absorbed a mission statement that values customer service, this attribute predicts customer satisfaction. Likewise, when a team agrees that the objective is safety, the result is more safety-conscious behavior by team members and a reduction in the rate of accidents.

Ties That Bind

Climate emerges in groups with strong ties among their members. For example, team members who have a good relationship with their leader tend to share climate perceptions with their boss and co-workers. Teams that have frequent informal social interactions also show greater consensus on climate than those that do not.

Part of the glue that binds people to their bosses or to one another is emotional. Although less is understood about how emotional state affects team performance than about cognitive influences, it is clear that how teams feel can drag down productivity or boost it up—or otherwise complicate it. For example, a shared positive attitude can reduce the number of absences in teams and lower the likelihood that people will leave the group.

But there are hints that good moods do not always lead to good outcomes. Social psychologist Joseph P. Forgas of the University of New South Wales in Australia, for example, asked teams to hold a discussion after they watched happy or sad videos and found that greater divisions arose in the groups that were given a prior "feel good" stimulus.

It also appears that team members tend to change their moods in concert. Social psychologist Peter Totterdell of the University of Sheffield in England and his colleagues had nurses record their moods each day at work over a period of three weeks. They found that the mood of different teams shifted together over time. Totterdell has measured a similar convergence in the affect of teams of accountants and cricket players.

The fact that emotions move in this lockstep way has led to a concept of emotional contagion, the idea that emotions within teams are transferred from one person to others close by. In a well-controlled laboratory study, professor of management Sigal Barsade of the Wharton School of the University of Pennsylvania investigated the effect of emotional contagion on team process and performance. The research involved using a drama student posing as a research subject whom Barsade trained to participate with a happy, optimistic attitude or an unpleasant, pessimistic one. She found that this one person's behavior did lead to group-level changes in emotion, both for positive and negative affect. Although the scientific study of how mood influences performance of the individual and the team as a whole is still in its infancy, this area promises to yield important insights.

One person's behavior leads to group-level changes in emotion, both negatively and positively.

(The Authors)

STEVE W. J. KOZLOWSKI and DANIEL R. ILGEN study the dynamics of teams at Michigan State University.

If teamwork skills were ubiquitous, there would be **enormous benefits** to students and society.

Works Well with Others

Finally, whatever the task, the way people perform, or *do,* the work as a team makes a profound difference. The important elements here appear to be general teamwork skills that are not specific to any particular task. Some of the research in this area centers on bad behaviors that degrade team performance and spirit—dealing with "free riders," for example, who rely on other team members to do their job and thus contribute less than their fair share. This type of disruptive behavior can be limited by requiring that contributions be visible and members accountable.

There are also many positive ways in which the best teams act that give them an advantage: individuals are aware of one another's performance, provide backup coverage for members, set goals, coordinate their actions, communicate effectively, make decisions, resolve conflicts, and adapt to changing circumstances and new ideas. A key point is that this learning process can be a dynamic one that helps to shape and improve the team over time—and team leaders can play a major role. Prior to action, for example, the leader can help set team learning goals commensurate with current team capabilities. During action, the leader monitors team performance (and intervenes as necessary). As the team disengages from action, the leader diagnoses performance deficiencies and guides process feedback. This cycle repeats, and the complexity of learning goals increases incrementally as team skills accumulate and develop. This kind of feedback loop has been shown to reliably improve team thinking and performance.

Work from Kozlowski's group, however, has found a trade-off in the type of feedback provided and the resulting performance. Feedback directed to individuals yields higher individual performance at the expense of team performance; team feedback yields better team performance at the expense of individual performance. If both types of feedback are provided, both levels of performance cannot be maximized. The findings indicate that team designers need to be mindful of

On-the-job training: every task a team undertakes is a chance to learn new skills and to learn how to work together more effectively.

ASHLEY COOPER *Corbis*

precisely what they want to be salient to team members and should design supporting goal and feedback systems accordingly. Such systems may need to be adaptive, shifting the balance depending on current needs.

One reason that achieving the right level of feedback is so important is that teams learn best while doing. In some cases, notably in the military and in aviation, this on-the-job training can be supplemented with sophisticated and realistic simulations of combat missions or of takeoffs and landings. This virtual training approach is starting to find applications elsewhere, such as in medicine, although in most cases the best place to develop team skills is on the job itself. General teamwork proficiency turns out to be one area where classroom training appears to make a strong difference, perhaps because these are generic skills not related to a specific job. Accordingly, semester-long college-level programs that significantly improve students' knowledge of generic teamwork competencies have been developed. Nevertheless, encouraging work by one of our teams (Ilgen's) has demonstrated that knowledge of these team competencies can improve significantly with only 30 minutes of individual training.

Leaders play a crucial role in developing group skills by setting goals, monitoring performance and giving feedback.

ERIN RYAN *zefa/Corbis*

Missed Opportunities

Although these skills can be taught, they rarely are—and few formal experiences to impart generic team-process and leadership experiences are available. If such courses are provided at all, they tend to be very late in the educational process—in college courses or in professional programs such as business school, for example—and these courses are usually geared toward imparting factual knowledge rather than building skills. We sampled a number of well-known M.B.A. programs and found that fewer than half listed a course devoted primarily to leadership or teams.

Furthermore, although it is not uncommon for educators from elementary school through college to include assignments organized around group projects in which students may display teamwork and leadership behaviors, attention is usually on the group's output—a report, for example—with little or no attention placed on guiding the nature and effectiveness of the team process.

If teamwork were taught along with reading, writing and mathematics, and if these skills were ubiquitous, there would be enormous benefits to students and society alike. For now, though, it is often only after a great triumph or tragedy that the importance of teamwork is drawn into the spotlight. Ironically, these occasions focus largely on singling out individuals for reward or to assign blame, as the case may be. Despite literally thousands of studies that show much can be done to design teams properly and to ensure they do their jobs well and get better as time goes on, the question rarely turns to how the successes can be replicated or problems avoided the next time around. We think it is just a matter of applying the science. M

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Rhythm and BLUES

Have you ever taken a long-haul flight? If so, you know that the timepiece in your head sometimes ignores the one on your wrist. If you leave Boston in the evening and, seven hours later, arrive in Paris at breakfast time, your body screams, "Why am I getting up? It's the middle of the night!" Croissants or no, your internal clock persists in its own rhythm, and it can take several days to synchronize your sleeping patterns with your new surroundings.

In fact, this powerful clock is very small. It lies within the suprachiasmatic nucleus (SCN)—an area of the brain no larger than a grain of rice—which sits in the hypothalamus directly above the optic chiasma (where the right and left optic nerves meet). The SCN takes cues from light receptors in the retina to send its own signals to the pineal gland, which releases various hormones in response. In this way, the SCN orchestrates our circadian rhythms, pacing all sorts of daily physiological fluctuations, including body temperature, blood pressure, heart rate, hormone levels and sleep-waking times.

Chronobiologists have long sought to understand just what makes the SCN tick. Recently they have found that circadian rhythm disturbances are characteristic of an array of neuropsychiatric conditions, including Alzheimer's disease and schizophrenia. Certain hallmark symptoms of these disorders may stem directly from faulty internal timekeeping. As a result, some researchers speculate that light therapy and the sleep hormone melatonin could benefit individual dementia and psychiatric patients, just as those treatments often help weary, jet-lagged travelers.

Running Late

"Interrupted sleep or abnormal sleep times are a common symptom of many psychological disorders," explains Russell G. Foster, a University of Oxford chronobiologist. Depression offers a case in point: 40 to 65 percent of depressed persons suffer severe sleep disorders. Age can also upset the balance between sleep and emotional well-being. "If you ask older people about their sleep habits, it becomes clear that many have a harder time sleeping through [the night] than they did when they were younger," says Eus van Someren, a researcher at the Netherlands Institute for Neuroscience in Amsterdam.

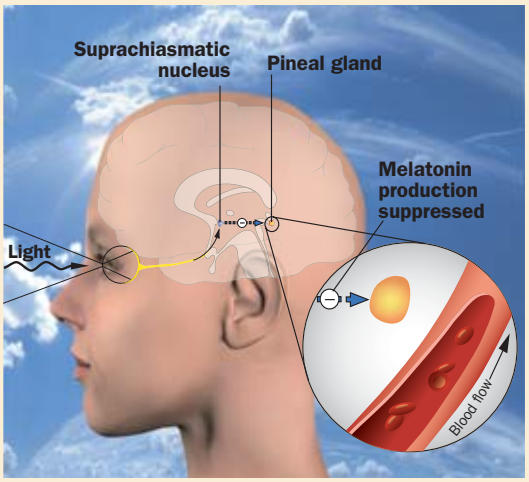
To explore the matter, van Someren and his colleagues studied the nerve cells in the SCN that produce vasopressin, a hormone that controls salt and water balances in the body. In the brain, this same hormone regulates functions that underlie some of our circadian rhythms—namely, temperature, wakefulness and activity levels. Van Someren discovered that as the body grows older, the number of cells that produce vasopressin decreases. As a result, older people generally find it increasingly difficult to keep their internal clock in step with the day-night cycle.

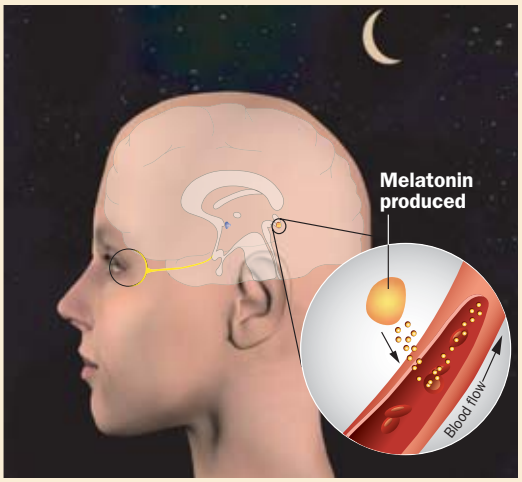
The problem is particularly dramatic in people suffering from Alzheimer's, which appears to slow circadian rhythms: the body clock always runs late. David Harper and his colleagues at McLean Hospital in Belmont, Mass., have found that body temperature in Alzheimer's patients often drops to its lowest point between 9 A.M. and noon, not between 4 and 5 A.M. as is normally the case. In addition, Alzheimer's victims have a postponed activity pattern, a circadian rhythm disturbance that

Abnormal sleeping patterns characterize an array of neuropsychiatric diseases, but resetting the body's clock may alleviate some symptoms By Ulrich Kraft

Both Alzheimer's disease and schizophrenia can grossly warp time, as kept by the body's internal clock. The abnormal sleep and activity patterns that result may exacerbate and even cause certain hallmark symptoms.

Melatonin Switch





The passing of daylight hours is detected by the eye's retina and transmitted to the suprachiasmatic nucleus (SCN). This bundle of neurons, about the size of a grain of rice, lies in the hypothalamus, near the point where the two optic nerves cross, and operates as our master clock. It controls daily body rhythms, such as the activity of organs and the sleep-waking cycle. During daytime, the SCN fires powerfully and—through intermediate chemical steps—suppresses the secretion of melatonin, the sleep hormone, by the pineal gland (*left*). At night the SCN firing drops, and melatonin flows into the bloodstream, making us drowsy (*right*).

distinguishes them from other dementia patients. (Those suffering from frontotemporal degeneration, for example, have body clocks that tend to run fast.)

Because of this body-clock delay, Alzheimer's patients are apt to rove about precisely when family members and other caregivers want to sleep—a mismatch that leads to high rates of hospitalization for the night wanderers. "The majority of Alzheimer's patients don't get put into care facilities because of failing memories," van Someren says. "The reason why they can no longer be cared for at home has more to do with their disturbed sleep-waking rhythm, the fact that they haunt the house at night." Sadly, institutionalization often leads to a rapid decline.

Let There Be Light

Van Someren and his research team decided to test whether Alzheimer's patients could shift their sleeping patterns in response to light therapy. Indeed, light has the most pronounced regulatory effect on the biological clock [see "Lighten Up," by Ulrich Kraft; Scientific American Mind, October/November 2005]. In rats, as in people, the number of SCN neurons that produce vasopressin decreases with age, leading to sleep disorders. But if elderly rats are exposed to bright light during the day, vasopressin production increases and their sleeping patterns start to become more normal. "Apparently the cells aren't actually destroyed," van Someren says, "they just become dormant."

His team found that care facilities for the elderly are often, literally, gloomy: the afternoon light in one center in the U.S. measured a mere 27 lux (one lux equals one lumen per square meter). By comparison, a family living room is normally around 50 lux, and dull winter daylight reaches 5,000 lux. The researchers installed powerful lamps at 12 institutions in the Netherlands, six of which received full-spectrum artificial lights—emitting the frequencies needed to adjust the body's clock—and six of which received normal artificial light. "This allowed us to conduct a controlled placebo study not much different from those conducted with other medications," van Someren explains.

Some participants took melatonin in the eve-

(The Author)

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GEHIRN & GEIST/SIGANIM

None of us should ignore our internal clock; our health is more dependent on it than we think.

ning, in addition to receiving light by day. When stimulated by the SCN, the pineal gland releases melatonin, primarily at night, signaling back to the SCN the start of the sleep phase [*see box on opposite page*]. Many experts trace insomnia in the elderly to decreasing melatonin production. "With the onset of dementia, melatonin synthesis decreases even more. This further weakens another important input to the SCN," van Someren adds.

The scientists observed 189 Alzheimer's patients for up to three and a half years. As predicted, melatonin and light therapy reset some patients' circadian rhythms. The longer these subjects received treatment, the better they slept. In addition, moods improved, particularly in those prone to depression. But another finding surprised the scientists: the mere installation of full-spectrum lamps slowed mental deterioration at least as well as cholinesterase inhibitors—the most prevalent type of drug used to treat Alzheimer's—have been reported to do. Light combined with melatonin worked even better.

"If the issue is putting the brakes on cognitive deterioration," van Someren asserts, "our method is superior to cholinesterase inhibitors." Light therapy and melatonin have not consistently helped Alzheimer's patients in other studies. Harper notes that treatment needs to be tailored to individual time zones; not all circadian delays are shifted to the same degree. Still, the Dutch studies are promising. A circadian rhythm that has been knocked out of phase is not merely a consequence of neurodegenerative disease but itself contributes causally to the most important symptom—mental deterioration.

Schizophrenic Time

Like Alzheimer's patients, people who have schizophrenia frequently become active at night and sleep by day. Many psychologists believe that because of the disease's symptoms—hearing voices, optical hallucinations, loss of a sense of reality—schizophrenic patients cannot find work. Consequently, they need not get up in the morning, and so they do not. Foster sees things differently. He believes that the circadian rhythms of schizophrenic patients are shifted such that they must sleep into the afternoon.

To test this hypothesis, Foster and his team outfitted 14 schizophrenic patients with wristwatchlike devices to record physical activity. In addition, they regularly measured the subjects' blood melatonin levels. They quickly determined that melatonin production—and with it, sleep—came late, rarely before 2 or 3 A.M. In some subjects, both melatonin production and sleep lagged so far behind that the rhythm actually collapsed. "We'd never seen anything like it," Foster relates. "Their internal clocks were apparently completely decoupled from their surroundings and simply fluctuated uncontrollably over time."

Such decoupling occurs in certain forms of blindness. If people cannot perceive light, they lack the winding key that sets their body clock. But how sighted people could have such an uncoupled biological clock remains a mystery. Foster hypothesizes that there may be genetic defects at work. More to the point, Foster wonders whether the circadian system might offer an entirely new therapeutic approach to alleviating schizophrenic symptoms, including depression, cognitive problems, memory loss and psychotic episodes. "A disturbed sleep-waking rhythm can trigger precisely the same problems," he explains. "It may be that the symptoms are not actually a symptom of schizophrenia but a secondary consequence of abnormal sleep."

Foster and his colleagues are attempting to readjust the internal clocks of people suffering from schizophrenia using the same methods as van Someren—more bright light during the day and melatonin at night. The first lamps have been installed, and the study will begin soon. Already Foster is sure of one thing: "None of us should ignore our internal clock but rather accept that our well-being and health are more dependent on it than most of us think." M

(Further Reading)

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ROGER WRIGHT Getty Images

Studies of genes in people and songbirds are providing clues about how and when the remarkable human talent for speech arose

PROGRAMMED FOR SPEECH

By Sebastian Haesler

Does speech—that uniquely human trait—come from our genes, or is it learned? Luminaries such as linguist Noam Chomsky of the Massachusetts Institute of Technology have championed the role of evolutionary inheritance over that of culture. But for many years, proponents of this position could only look to languages themselves for evidence. They observed that many tongues share grammatical structures and other attributes, bolstering the argument that speech is innate. The suspicion that a "speech gene" might exist, however, remained unresolved. Then, in 1990, something extraordinary happened.

It could not have been a coincidence that a particularly large number of children from one family showed up at an English speech therapy school. The children mumbled almost unintelligibly and stumbled over grammar—they could not, for instance, describe events in a correct chronological order.

In studies led by Jane A. Hurst at Oxford Radcliffe Hospital in England, researchers found that the affected members of the family, dubbed the KEs, had a physically normal speech apparatus—lips, jaw, tongue and vocal chords. Their other fine-motor skills were normal, as were their hearing and IQ. For three generations about half the family members had suffered from the same speech defect. Clearly, the disorder had a genetic component and was specific enough in its effects to offer the hope that it was directly connected to that elusive speech gene.

When the gene responsible for the impediment was pinpointed just a few years later, it finally provided evidence that the ability to speak is indeed written in our DNA. But how exactly do genes regulate a complicated mental process such as speech? Studies of the gene in people and in our animal cousins—especially songbirds, whose vocal learning resembles that of people—could help explain why speech evolved in humans but not in any other species. They might also lead to therapies for speech impediments like the one plaguing the KE family.

> Some songbirds learn their songs in a way that is strikingly similar to how children learn speech.

Language in Our Genes

Geneticists led by Simon E. Fisher of the University of Oxford identified in the KE family a segment on chromosome 7 in which there must have been a mutation. But determining which of the dozens of genes in that segment was at fault promised to be a lengthy process of trial and error. The researchers got a lucky break when they found a boy from an unrelated family who had a similar speech problem. The boy had a visible defect on chromosome 7 in the same segment as the one that looked suspicious in the KE family. The chromosome was broken at a gene known as *FOXP2*, so the researchers started looking specifically at that gene. In 2001 they successfully identified *FOXP2* mutations in KE family members with the speech defect, and the same defect was later confirmed in other people with similar speech impediments.

Ever since the first published reports about *FOXP2*, molecular geneticists and linguists have been engaged in a vociferous debate about how, precisely, the gene affects speech. Although the gene appears to be crucial for normal development, its specific role remains to be clarified. *FOXP2* codes for a protein that affects hundreds or perhaps even thousands of other genes, and scientists have barely begun to understand its complex influence. Mutations in the *FOXP2* gene appear to hinder the development of brain regions responsible for motor control as well as regions involved in language processing. Furthermore, the *FOXP2* gene exists in a variety of species—from reptiles to mammals—so it must serve other functions besides facilitating speech.

Many researchers, including my team at the Max Planck Institute for Molecular Genetics in Berlin, are especially interested in *FOXP2* in birds, because some songbirds learn their songs in a way that is strikingly similar to how children learn speech. By studying the role of *FOXP2* in birdsong, we are revealing how it might affect the development of language in people.

Genes ensure that the brain develops normally in a number of ways. Specialized nerve cells need to be formed, they need to produce the correct connections to neighboring cells, and they need to be able to emit signals or conduct messages to other neurons. In addition, nerve cells in the brain must develop the capacity to process information so that they can "learn" things. Gene products, namely, proteins into which the

FAST FACTS

Innate Speech

1» **The discovery of the *FOXP2* "speech gene" created a sensation in the 1990s. Mutations in the gene lead to specific linguistic and speech disorders.**

2» ***FOXP2* is also part of the genetic makeup of monkeys, songbirds and even crocodiles. Apparently it is not solely responsible for human capacities but is only one factor among many.**

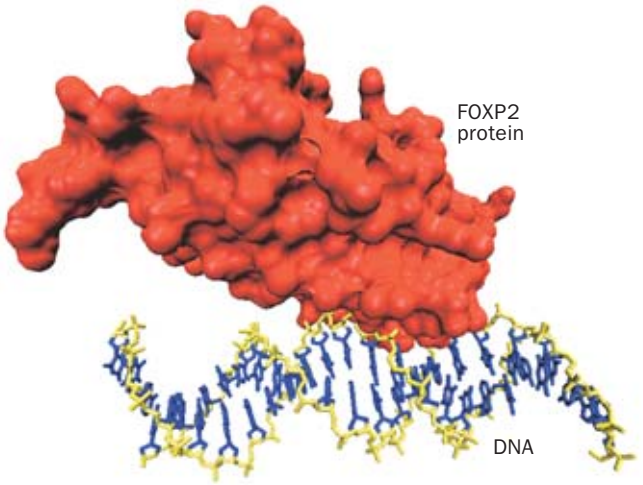
3» **There are striking similarities between human beings and song-learning birds such as zebra finches. Both acquire their "language" through imitation. Current work has shown that birds need the FOXP2 protein for this purpose.**

Naming the Speech Gene

Where do scientists get the name *FOXP2* for the gene involved in human speech? "FOX" is an abbreviation for "forkhead box," a characteristic DNA segment present in many genes. Mutations in this gene give the head of fruit fly embryos a fork shape—hence the name "forkhead."

The *FOX* gene family is so large and branched that scientists further classify it into subdivisions A through Q. Accordingly, *FOXP2* means forkhead box gene family, subgroup P, member number 2. Moreover, *FOXP2* has siblings: *FOXP1, FOXP3* and *FOXP4.*

—*S.H.*



The forkhead box of the *FOXP2* gene codes for the part of the protein that binds to other segments of DNA, acting as an on-off switch for thousands of target genes.

genetic code is translated, are involved in all these processes.

FOXP2 codes for a transcription factor, a protein that binds to other segments of DNA, thereby affecting whether or not different genes are read and translated into their respective gene products. ("FOX" stands for "forkhead box" [*see box above*], which refers to the specific DNA sequence that codes for the part of the protein that latches onto other DNA molecules.)

As a transcription factor, the FOXP2 protein serves as an on-off switch for numerous target genes. Because all genetic material exists in duplicate (except in the case of the male Y chromosome), a *FOXP2* mutation on one chromosome causes the body to produce only half as much of the transcription factor as it should. The resulting shortage somehow causes the speech defect found in the KE family.

Complex Interactions

To find out how the disturbed regulation of *FOXP2* genes leads to speech disorders, we must first identify the regions of the brain in which *FOXP2* is normally active. We can draw conclusions about the function of a particular gene based on when and where it is expressed, meaning when and where the cell produces a protein in accordance with the DNA blueprint.

The FOXP2 protein is produced very early on in the embryo's developing brain, particularly in those regions that later become the cerebellum, the thalamus and the basal ganglia. Consistent with this pattern of expression, a structural analysis of the brains of patients with the telltale speech defect revealed that the volumes of their cerebellum and basal ganglia differed from those of people with unimpaired speech. In addition, when these patients spoke, parts of their basal ganglia were less active relative to those of normal subjects.

Both the basal ganglia and cerebellum control body movements. They are activated whenever complex motor skills are learned, such as those involved in playing a piano. Presumably these regions are also responsible for motor function during the formation of sounds. It seems plausible that the KE family's difficulty in articulating words is rooted in the malformation of these areas of the brain.

The effects of a faulty *FOXP2* gene do not stop there, however. Brain changes also appear in two well-known cortical speech centers: the Wernicke speech area and Broca's region. Neurolinguists have long suspected that Wernicke's area controls the understanding of speech, whereas Broca's region is involved in the pro-

(The Author)

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SEBASTIAN HAESLER AND HOLGER KLEIN

The similarity between avian song and human speech may extend all the way to the molecular level.

duction of speech. We know now, however, that this strict division is a little too cut-and-dried because a number of other areas of the brain are involved in both understanding and producing speech. The human brain probably processes spoken information in many areas of the brain simultaneously.

The idea that the brain uses parallel processing to understand and control speech is consistent with another observation: in the KEs, parts of the brain that are normally not involved in speech are active. This activity could be a direct consequence of the *FOXP2* defect—a proper amount of the transcription factor would have made those areas behave normally—or it could be a sign that the brain is attempting to compensate for one of the other flaws caused by the mutation.

Differentiating between the direct and indirect effects of *FOXP2* is no simple matter. For example, because the gene is active during the embryonic stage, its dysfunction could disturb brain development. The brain could be "wired" incorrectly, or certain specialized nerve cells could fail to form. On the opposite end of the spectrum of possibility, the brain might develop normally but run into problems with information processing later on—for example, during the phase when children learn to speak. The real effects of the *FOXP2* mutation probably lie somewhere in between these two extremes.

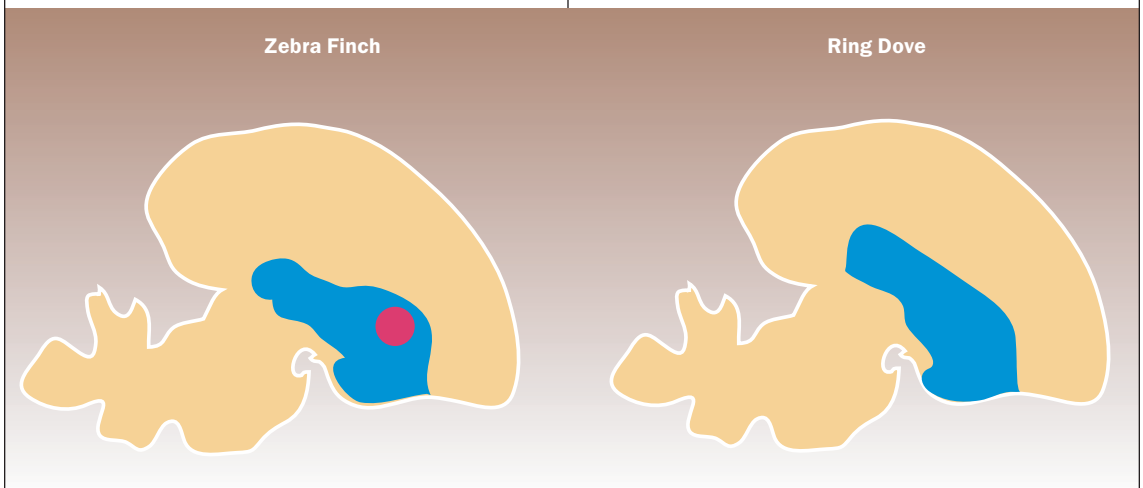
Bird Babble

To probe further *FOXP2*'s effects on cognitive development, researchers are turning to animals for clues. The *FOXP2* gene has been identified in primates, whales, birds and even crocodiles; it is highly likely that all vertebrates have it. The sequence of the gene in these animals is almost identical to that in humans. For example, only three of the 715 amino acids in the mouse *FOXP2* gene product differ from those in the human version. The timing and location of the gene's expression in the brains of other species are also very similar. So what is the *FOXP2* gene doing in the brains of these animals, none of which is capable of speech?

Although most animals have vocalizations that seem to be innate, a few species—among them songbirds, parrots, hummingbirds, some marine mammals and bats—do learn vocal patterns by imitating their parents. To some extent, this process is similar to that of a human infant making his or her first efforts at learning speech. At first, baby sparrows can imitate only minute elements of their future song, for instance. This type of vocalization is referred to as subsong, and it is similar to infant babbling. When the young animal hears an example of what is correct, it adapts its vocal output.

Through intensive practice, young songbirds increasingly come to sound like their role models, mastering the repertoire by the onset of sexual maturity. As is the case with humans, songbirds are dependent on what they hear to develop normal vocalization. If songbirds are subjected to loud noises, if they become deaf or if the feedback from their "teacher" is interrupted, they never learn to sing properly.

The similarities between learned avian song



GEHIRN & GEIST/SIGANIM

Birds that must learn how to sing, such as the zebra finch, produce the FOXP2 protein (*red*) in area X (*blue*) in their brain. Birds that know their songs at birth, like the ring dove, do not make the protein.

and human speech run even deeper. Both humans and songbirds have developed neuronal structures that specialize in the perception and production of sounds. Compared with humans, whose brains use parallel processing to comprehend speech, songbirds have a rather more modularly constructed brain in which various centers assume specific roles. In the avian brain, auditory stimuli reach the high vocal center, which controls the muscular movements of the vocal organ via the motor center; damage to this region prevents singing.

Another important data path in bird brains extends from the high vocal center via area X—a song-learning center in the basal ganglia—to the thalamus and from there back to the cortex. This so-called corticobasal ganglia loop also exists in the brains of mammals, including humans, where it is vital for learning. In young birds, lesions in area X lead to abnormal twittering, whereas such lesions seem to have no effect in the adults of most songbird species—until they try to learn a new song. Apparently the corticobasal network is important for learning songs but not necessarily for singing them. In humans also, FOXP2 proteins are produced in large quantities in the basal ganglia, which is where the structural and functional anomalies occur in patients with *FOXP2*-related speech defects.

Genetic Songwriter

In the brains of zebra finches, area X contains more *FOXP2* during the song-learning phase than during infancy or adulthood. Likewise in the canary, which changes its melody once a year after breeding season, *FOXP2* is expressed particularly strongly in area X during this learning phase [*see illustration on opposite page*].

Accordingly, *FOXP2* may well be involved in song plasticity—the ability to learn new songs. To explore this possibility, our team genetically reduced the amount of *FOXP2* in area X in zebra finches to artificially induce a situation similar to a *FOXP2* mutation in humans. The crucial question is, What happens to a melody if less *FOXP2* is expressed in area X while it is being learned?

Our initial results show that the zebra finches have difficulty learning their songs when they have less than the normal amount of the FOXP2 transcription factor. We concluded that this protein is necessary for zebra finches to learn a song, but it is less important for motor functions overall. Thus, a *FOXP2* mutation does not simply cause the brain to develop abnormally. The defect continues to play a role once the brain has become fully developed—an important clue about what happens in humans who have the speech problems displayed by the KE family.

Careful analogy of the zebra finch's impaired song learning with the problems seen in the KE family leads us to believe that affected family members may have difficulty imitating the sounds made by their parents. They are unable to harmonize their own speech with that of others. Should this suspicion be borne out, it would mean that the similarity between avian song learning and human speech acquisition extends all the way to the molecular level.

The logical implication is that the evolution of language is not a unique feature of the human lineage. Many species share the structure and molecular makeup of the brain that was already in place as our ancestors began to speak. Only as existing genes and neuronal systems continued to develop was the path cleared for the uniquely human capacity for speech. M

JIM BRANDENBURG *Minden Pictures*

Songbirds such as this warbling western meadowlark could help provide clues about how genes regulate human speech.

(Further Reading)

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Getting Advice GOOD

How to recognize a **real expert**, **good advice** and the **limits of such counsel**

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By Yvonne Raley

Seeking expert medical advice? The Internet seems to invite us to dispense altogether with consulting a doctor in person. When I Googled "expert advice" and "medicine," I got 1,650,000 hits. "Expert advice" and "psychology" garnered 950,000. (Your results may differ.) Sites such as Kasamba (www.kasamba.com) and AllExperts (http://allexperts.com) offer expert counsel on just about *any* subject.

It's one thing to be on guard with commercials and quite another to evaluate Web sites.

DON KLUMPP Getty Images

Living in technologically advanced times, we are likely to need expert advice. But that very need can make us vulnerable to questionable claims of authority.

We cannot avoid relying on expert opinion. We simply do not have the factual knowledge required to answer all of our questions. Certain fields are so technical, moreover, that *only* a true expert's opinion will do—and especially for medical decisions, a doctor's advice is crucial. But our very need for such advice is also why claims of expertise so easily lend themselves to abuse, much to the detriment of the person looking for help. Professionals in the advertising industry are well aware of the persuasive powers of such appeals to authority. Consequently, they spend billions of dollars on advertising and employ ostensibly trustworthy—or not so trustworthy—experts who try to lure us into buying products or services. It's one thing to be on our guard when watching commercials, however, and quite another to evaluate the credibility of Web sites, self-help books and the like.

How do we know whom to trust? What makes someone an authority? And what are the limits of expert advice? Following are some guidelines.

Know Who Knows

Relevant expertise. The first question to ask of any claim of competence is this: Is the claimant actually knowledgeable in the relevant field? Behind too many such claims lies a fallacy called *argumentum ad verecundiam,* Latin for "argument to shame" or "argument to respect." More commonly, this misleading position is called an "inappropriate," or "irrelevant," appeal to authority. The fallacy occurs when the authority making a claim or cited to justify a claim is not a specialist in the proper field, such as when a podiatrist advocates a cholesterol-lowering drug.

Neutrality. Advice is most reliable when it helps the person seeking guidance without providing undue financial gain or other advantage for the expert. We should be wary of an expert who has a vested interest, such as a physician who is affiliated with a company that sells the drug he or she is recommending. Of course, it is unrealistic to expect complete neutrality: a doc-

tor may have participated in researching the drug being recommended, and this experience may have convinced him or her of the medicine's efficacy. Therefore, we must research and evaluate an expert's credentials with care.

Verifying Bona Fides

Degree. Most of the medical Web sites I have visited do not tell you anything about the doctors who provide the advice or the area of medicine in which they specialize. That warrants a background check. It is crucial to look into the institutions where proclaimed experts have received their degrees. The paths of accreditation have been muddled by several hundred "diploma mills"—nonaccredited institutions where a diploma can be purchased or earned with very little work. Diploma mills operate largely online, making it sometimes difficult to determine whether they actually have a physical (and thereby traceable) presence somewhere or which classes (if any) must be passed to obtain the degree. Many diploma mills have names that resemble those of major research institutions, and because an Internet domain name can be purchased for less than $100, it is all too easy to be misled. The U.S. Department of Education provides a list of all accredited institutions.

Affiliations. Most doctors have an affiliation with a hospital, a medical group, a university or some other research group. Such associations are preferable over connections to pharmaceutical companies or industry-funded research institutes (which may indicate a bias). Also, certain relationships, such as those with major research universities, are more prestigious than others are.

Publications. To earn status in their profession, experts often participate in research and publish articles on the subject in question. Most researchers affiliated with a university now list their publications on their department or faculty Web site; Google Scholar (http://scholar.google.com) also lists some articles. Another database for professional publications is PubMed, a service of the National Library of Medicine (www.pubmed.gov). Scholarly publications in professionally recognized, edited and refereed research journals are, naturally, preferable to newspaper or magazine articles aimed at the lay audience. The latter, while they can be informative, are usually not proof of expertise. Furthermore, because the readers of newspapers and magazines include potential patients, the publication may serve the self-interest of the expert. In scholarly journals, the intended audience consists mostly of fellow researchers. And although there is usually some monetary payment for scholarly books, the compensation for journal articles consists largely of prestige and reputation.

The most reliably representative research ar-

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There are more ways to fake expertise than ever before—and more ways to check bona fides.

(The Author)

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What makes an expert an expert? What other experts think of his or her work. Look for publications in peer-reviewed journals and affiliations with universities and research organizations.

JON FEINGERSH *Getty Images*

FAST FACTS

Find a Reliable Expert

- **Impartiality.** A prospective expert should not have a vested interest in the goods or services he or she is offering; the expert should not be biased.
- **Degree.** The expert should have a degree in the relevant specialty, preferably from a well-established university. Beware of fake degrees from diploma mills.
- **Experience.** The expert should have extensive experience in his or her claimed field of expertise.
- **Affiliations.** The expert's professional reputation should be genuine, current and in good standing. Look for affiliations with hospitals, universities or research institutions.
- **Publications.** Many (though not all) experts publish scholarly research articles in their fields. Articles in peer-reviewed journals are good indicators of expertise.

ticles are those that have been peer-reviewed by other recognized experts in the field. Whereas such studies themselves cannot be replicated in the peer-review process, the referees have knowledge of other studies and articles in the same research area, as well as familiarity with the research methods and controls necessary to exclude errors. The layperson does not have to understand the content of the expert's articles: that the work has passed the peer-review process is itself a good indicator that it meets the rigorous standards of the scientific community. Successful publication also confirms that an expert really has know-how in the subject at hand.

Limits of Advice

Not all medical or psychological questions can be answered definitively. For example, should a person in a permanent vegetative state (PVS) be disconnected from a feeding tube? Should such a person become an organ donor? Medical expertise and information alone, even if trustworthy

Medical expertise cannot always give us the answers. But that does not mean we have no resources.

and accurate, cannot determine the answers to these questions. That does not mean we have no resources to tap, however.

A patient diagnosed with PVS has irreversible damage to one of the hemispheres of the brain, but the brain stem—which regulates basic functioning—is still intact. This pattern of damage is why PVS patients usually breathe on their own and may even open their eyes and appear to cry. But because the part of the brain that is responsible for conscious thought and perception is irreversibly destroyed, the current medical opinion is that these reactions are merely reflexes.

A PVS patient is not considered brain-dead. In a brain-dead patient, the entire brain, including the brain stem, has ceased functioning; brain death therefore constitutes the legal death of a person. As a result, PVS patients, as well as those entrusted with their care, are often placed in a moral limbo. Beyond the diagnosis itself, no amount of expert medical opinion can determine whether or not such a person should be disconnected from a feeding tube. The situation is further complicated if there is no living will, because the patient's own wishes are not obvious.

In such cases, people might consider turning to a "soft expert"—a person who can offer advice based on experience with similar instances or who has studied the moral concerns and other considerations that accompany these cases. A soft expert may be a religious leader or a philosopher—such people often serve on medical ethics advisory boards for precisely those reasons. Other soft experts, such as nurses or care practitioners, can provide context and insights that may not readily occur to laypersons.

When considering our example of the PVS person, a Catholic priest may be aware that Pope John Paul II explicitly spoke out against withholding basic medical care, including nutrition, from such patients. He saw it as nearly impossible to achieve medical certainty that a patient may never recover. A Catholic may thus wish to err on the side of caution and request to disconnect the feeding tube only in those rare instances in which a physician can guarantee that no hope of recovery exists.

In contrast, a soft expert who is trained in philosophy may emphasize the distinction between "killing" (an act of commission) and "letting die" (an act of omission). To use drugs to stop the heart is to kill a person, whereas to disconnect a respirator or a feeding tube is to let unassisted nature take its course. Some philosophers therefore argue that disconnecting a PVS patient from a feeding tube is not morally wrong.

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Science can get us pretty far, but in the most difficult cases our values, beliefs and wishes come into play.

As the challenges of wrestling with these decisions suggest, ultimately no amount of expert advice, however useful, can replace our own reflection on a given subject. Only we are in a position to know the values, beliefs and wishes most important to a loved one or to ourselves. This unique vantage point is especially critical when, and also because, *we* are the ones that must live with the consequences of our actions. Having to defer our choices to someone else limits our autonomy and puts our well-being into the hands of the experts we picked. That is a lot to give up. What we do not have to surrender, however, is the power to choose—and the capacity to choose well—who that person will be. M

(Further Reading)

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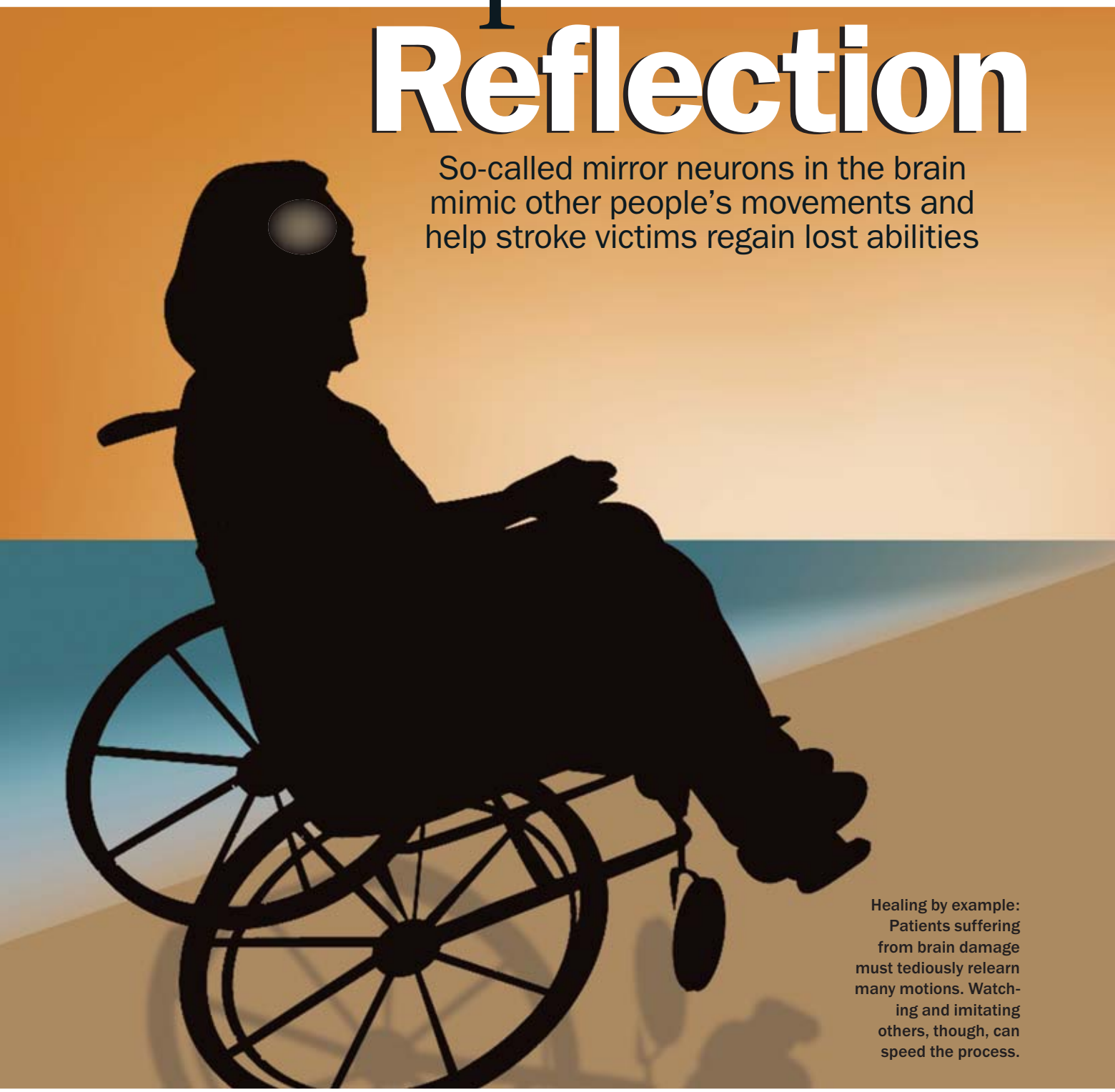
Therapeutic Reflection

So-called mirror neurons in the brain mimic other people's movements and help stroke victims regain lost abilities



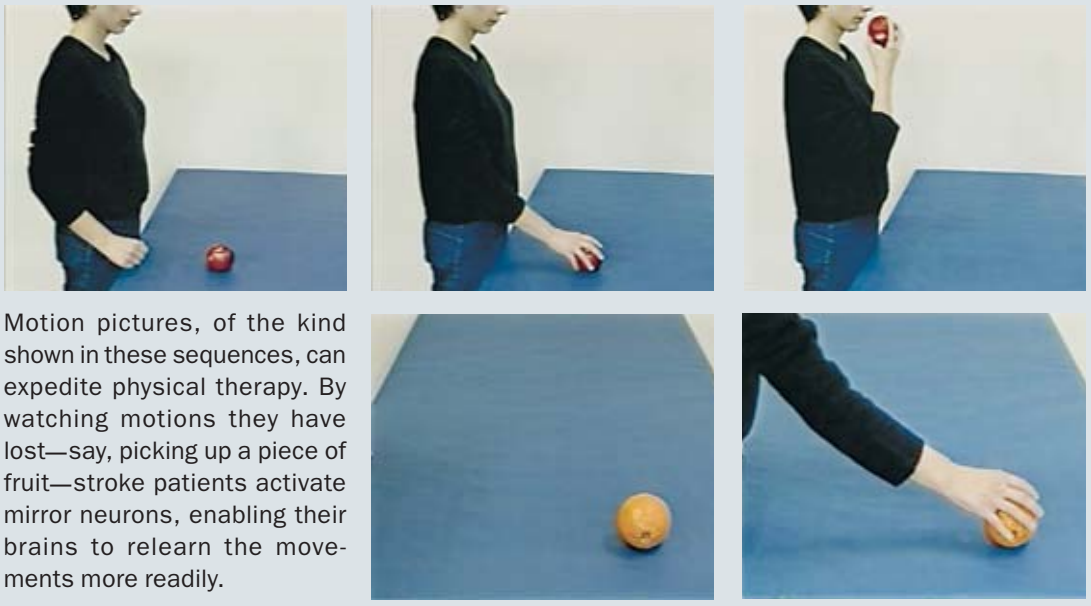
Healing by example: Patients suffering from brain damage must tediously relearn many motions. Watching and imitating others, though, can speed the process.

GETTY IMAGES

By Ferdinand Binkofski and Giovanni Buccino

In 1996 neuroscientist Giacomo Rizzolatti and his co-workers at the University of Parma in Italy published some remarkable findings. They had run an experiment to record electrical activity from neurons specialized for hand movement in two pigtail macaques. As anticipated, these neurons fired when the animals reached for peanuts placed in front of them. What was entirely unexpected, however, was that these same neurons fired when a scientist in the lab reached for the nuts instead. The monkey remained stationary. Nevertheless, watching the scientist move had activated motor areas in the macaque's brain, just as if the animal had carried out the action itself.

Seeing Is Learning



Motion pictures, of the kind shown in these sequences, can expedite physical therapy. By watching motions they have lost—say, picking up a piece of fruit—stroke patients activate mirror neurons, enabling their brains to relearn the movements more readily.

Using functional magnetic resonance imaging (fMRI), Rizzolatti and his colleagues soon documented the same phenomenon in humans and dubbed the responsible nerve cells "mirror neurons" [see "A Revealing Reflection," by David Dobbs; Scientific American Mind, April/May 2006]. These cells look like any other neuron but boast a surprising double function: they become active during any type of directed behavior—chewing food, throwing a ball, performing a dance—whether we do it ourselves or simply watch someone else do it. Indeed, our conscious brain generates an inner simulation of sorts when we follow the actions of another person. Mirror neurons are presumed to be abundant in brain regions responsible for planning and initiating actions, including the primary motor cortex, the premotor cortex and supplementary motor areas.

Since Rizzolatti's discovery, other scientists have revealed that mirror neurons reflect not only the actions of other people but their intentions and emotions as well. The discovery is offering scientists new insight into, among other things, human empathy, language evolution and theories of mind. In addition, mirror neurons may help explain certain neurological conditions. For example, some evidence suggests that autistic children may suffer from mirror neuron deficiencies, leaving them unable to intuit others' emotional states. Our own work indicates that the mirror system can be enlisted to expedite the rehabilitation of hemorrhagic stroke patients.

Monkey See, Monkey Heal

In 2001 another research team at Parma, led by one of us (Buccino), used fMRI to track brain activity in people watching video sequences showing mouth, hand or foot movements. As it turned out, when the subjects watched a mouth move, the part of their brain responsible for controlling their mouth lit up. Likewise, observing hand and foot images engaged the corresponding brain regions. These responses remained below the action threshold—the subjects did not actually move—but they matched the brain responses to video exactly. Given these findings, we speculated that patients who had suffered a cerebral hemorrhage might regain lost movements more readily if, as part of their therapy, they watched others coordinate these actions.

During physical therapy, brain regions near the site of damage do often take on lost functions, but it is a gradual process. It seemed logical that this transfer might happen faster if the neurons in question could rehearse their new role. To test the idea, we recruited stroke patients participating in a 40-day rehabilitation program at

(The Authors)

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FERDINAND BINKOFSKI AND GIOVANNI BUCCINO

Mirror neurons reflect not only other people's actions but their intentions and emotions as well.

the University Medical Center of Schleswig-Holstein in Luebeck, Germany. We asked our subjects to watch a six-minute film showing a series of movements—stretching arms, opening hands, grasping apples and so forth [*see box on opposite page*]. We then asked them to try to imitate the actions. We found that indeed these patients improved their motor abilities considerably faster than those in the control group, who did not watch the videos.

In a recent follow-up study, we documented the same gains among 22 stroke patients who had difficulty using their arms and hands. Physical rehabilitation progressed more rapidly when they watched short films of people demonstrating everyday hand movements before and after each therapy session. With the aid of fMRI, we were able to show that as this motor improvement occurred the areas of the cortex involved became increasingly active. The video observations apparently strengthened those brain areas responsible for planning movements. The inner simulation made it easier for the subjects to carry out the real motions.

Armchair Athletes?

In fact, our mirror neurons react to many movements, but research suggests that their activity level depends on how familiar we are with the actions we witness. Learning to coordinate completely new actions—playing a new sport, for example—demands far more conscious control than is required by a routine task. Buccino and his colleagues showed subjects various video clips depicting a person, an ape or a dog eating or communicating: the person moved his mouth as if speaking, the ape pursed its lips and the dog barked. Of interest, chewing motions universally activated mirror neurons in the subjects. When it came to communication, however, this activation occurred only when the moving lips belonged to a fellow human.

It may well be that our mirror neurons react only to actions that are part of our own motor repertoire. So, too, observers apparently need to understand another's intentions to activate their premotor centers. Neuroscientist Marco Iacoboni of the University of California, Los Angeles, performed an interesting experiment, asking subjects to watch short films of people using identical motions to different ends. In one sequence, a person picked up a cup and drank from it. In another, he picked it up and washed it. Yet another clip showed the motion itself, without any purpose, and another showed simply a set of plates and cups, without any movement. Iacoboni found that neither the motor action nor the environment alone activated the mirror neurons as strongly as the combination of the two did. Motor activity lacking an obvious purpose may be less effective in helping someone relearn a particular movement.

Further research may reveal that mirror neurons lie at the root of many fundamental human traits—from the way we learn to the way we develop distinct cultures. In the meantime, stroke patients stand to gain enormous benefit from harnessing this remarkable system. M

BOB KRIST *Corbis*

Mirror neurons most likely play a significant role in the development of culture, allowing humans to learn through imitation from infancy.

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Why Don't People Change?

How we fail despite our good intentions—and how we can succeed instead

BY HAL ARKOWITZ AND SCOTT O. LILIENFELD

HOW MANY THERAPISTS does it take to change a lightbulb? Hold that thought. We will get to the answer shortly in this column, which addresses how difficult it is to make a change, despite our best intentions. Consider how many people engage in self-defeating patterns of behavior despite negative consequences:

- Smoking, obesity and problem drinking can lead to chronic illness and premature death. Nevertheless, recent large-scale surveys of adults by the Centers for Disease Control and Prevention have found that more than 20 percent of American adults continue to smoke, more than 30 percent are significantly overweight and approximately 15 percent are binge drinkers.
- People do not always comply with medical treatments. Studies indicate that between 50 and 65 percent of all patients do not follow their regimens and that 10 percent of hospital admissions among older adults result from failure to follow doctors' directions. Pauline Vincent, then at Case Western Reserve University, surveyed glaucoma patients in a 1971 study. Some 54 percent of the patients who knew they would go blind unless they used the eye drops as directed still did not adequately comply.
- People who seek psychotherapy for conditions that cause them serious distress often thwart the very help they seek by being uncooperative, frequently missing sessions or dropping out of therapy altogether. One study found that more than 70 percent of patients receiving therapy in a community mental health center dropped out of treatment by the third session!
- Many attempts to change our behavior are unsuccessful. For example, psychologist John Norcross of the University of Scranton found that only 19 percent of those who had made a New Year's resolution to change some problem behavior maintained the change when followed up two years later.
- People continue to engage in patterns of behavior—jealousy, dependency, nagging, anger, violence and withdrawal, for example—that are often destructive to their significant relationships.

Some of the more common explanations for these phenomena blame an individual's characteristics such as stubbornness, resistance, addictive personality and self-destructiveness. This reasoning is largely circular. People infer the explanation from the behavior (for example, "He's not changing because he's stubborn") and then use that very behavior to support the explanation ("He's stubborn because he's not changing"). Clearly, we need a better understanding of why people do not change. That is where research comes in.

Confused about Change

In *Ambivalence in Psychotherapy* (Guilford Press, 2006), David E. Engle, a Tucson psychotherapist, and one of us (Arkowitz) argue that dealing with ambivalence is central. In the authors' view, people who want to change but cannot are pulled in two directions by motivations to change and motivations to maintain the status quo. Several studies have demonstrated that the balance between these opposing forces can predict who changes and who does not. What gets in the way of change? A table on the opposite page summarizes some of the critical factors.

COURTESY OF HAL ARKOWITZ (*top*); COURTESY OF SCOTT O. LILIENFELD (*bottom*); SOREN HALD Getty Images (*left*); GUILHERME MARANHAO Getty Images (*center*); GETTY IMAGES (*right*)

Helping people change means helping them **want to change**—not cajoling them with advice, persuasion or social pressure.

Helping people change involves helping them *want* to change—rather than cajoling them through advice, persuasion or social pressure. Research has demonstrated that such "highly directive" approaches are likely to backfire, making the patient increasingly likely to resist change. For example, a study by William R. Miller, R. Gayle Benefield and J. Scott Tonigan, all then at the University of New Mexico, demonstrated that for problem drinkers, directive-confrontational styles of therapy led to significantly more resistance and poorer outcomes one year later than more supportive approaches did. They found that the more therapists confronted the clients, the more the clients drank. In contrast, more supportive styles were less likely to elicit such reactions and more likely to be successful.

One such approach is motivational interviewing, developed by Miller and fellow psychologist Stephen Rollnick of the Cardiff University School of Medicine in Wales. In this method, the therapist aims to enhance the client's intrinsic motivation toward change by exploring and resolving his or her ambivalence. The goal is to help the client (rather than the therapist) become the advocate for change. In other words, a client's resistance to change is seen by the therapist as ambivalence to be understood and appreciated rather than opposed directly.

To help resolve ambivalence, the therapist provides assistance in several ways. These methods include using a supportive style of therapy and highlighting client statements that reflect conflict between the person's behavior and values ("So it's important to you to be a good mother to your son, but your crack addiction interferes with this"). Such discrepancies create discomfort about the status quo and increase motivation to change. In addition, the therapist pays more attention to the client's talk about changing versus not changing, to help resolve ambivalence and tip the scales toward change. Once those uncertainties are dealt with, behavioral change often occurs.

A considerable body of research shows that motivational interviewing and related approaches are effective in helping people change alcohol and drug addiction, health-related behaviors such as medication adherence and diet, and even anxiety problems. A quantitative review by Arkowitz, Brian Burke of Fort Lewis College and Marisa Menchola of the University of Arizona found a 51 percent improvement rate for motivational interviewing and related procedures compared with 37 percent for either treatment as usual or no treatment.

Apart from its use as a therapy, the ideas inherent in motivational interviewing can be used to help ourselves or a loved one change. These ideas emphasize listening and understanding hesitation about change, not opposing it, and trying to supportively strengthen the side of the person's mind that wants change.

So how many therapists *does* it take to change a lightbulb? By now you may have figured out the answer: "Just one, but the lightbulb really has to want to change." We hope this column will switch on your thinking about change, help you stop short-circuiting your efforts and shed light on watt you can do. M

Forces That Block Change

>> *Diablos conocidos* ("the devils you know"): The status quo is familiar and predictable, even though it may be uncomfortable. In contrast, change is unpredictable and arouses anxiety.

>> People fear that if they fail in their efforts to change, they will feel even worse.

>> Faulty beliefs (for instance, "Unless I am 100 percent successful, I consider it a failure") can impede change. When others push us to change, we often perceive these efforts as threats to our personal freedom. To retain this sense of freedom, we may resist change. Psychologists term such behavior "reactance."

>> The undesirable behaviors may serve important functions (such as the alcoholic who finds that drinking relieves stress and depression temporarily). Changing (stopping drinking) may take away the only means the person has known of dealing with this distress.

—H.A. and S.O.L.

HAL ARKOWITZ and SCOTT O. LILIENFELD serve on the board of advisers for *Scientific American Mind.* Arkowitz is a psychology professor at the University of Arizona, and Lilienfeld is a psychology professor at Emory University. Send suggestions for column topics to editors@sciammind.com

(Further Reading)

- **Ambivalence in Psychotherapy: Facilitating Readiness to Change.** David E. Engle and Hal Arkowitz. Guilford Press, 2006.
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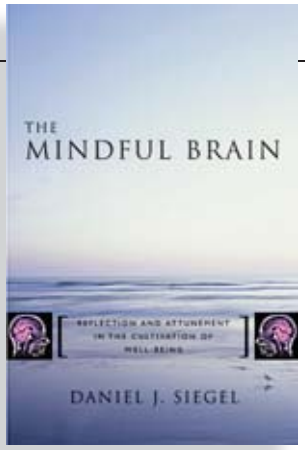
Mind Reads

The Oasis Within

The Mindful Brain: Reflection and Attunement in the Cultivation of Well-Being

by Daniel J. Siegel. W. W. Norton, 2007 ($26.95)



For thousands of years, spiritual traditions around the world have emphasized the importance of living "mindfully"—using prayer and meditation techniques to free ourselves from daily distractions, enabling us to look inside ourselves, to become sensitive to what is happening around us and to live compassionately. Anecdotal evidence has suggested that these practices have a positive influence on people's emotional lives and physical health, but science has only recently begun to investigate their effects. The impact of mindfulness on the brain is, for the most part, still a mystery.

Enter Daniel J. Siegel, a psychiatrist and co-director of the Mindful Awareness Research Center at the University of California, Los Angeles. Siegel has both a meticulous understanding of the roles of different parts of the brain and an intimate relationship with mindfulness. He brings these strengths together in *The Mindful Brain* to come up with insightful proposals, bolstered by preliminary research data, for how mindful awareness might engage parts of the brain in novel ways and lead to permanent neurological changes. His speculations are interesting in and of themselves, and they also may provide neuroscientists with ideas for experiments that could test the effects of mindfulness on the brain.

Throughout the book, Siegel also shares his own deeply personal experiences with mindfulness techniques, such as the challenges he faced the first time he attempted to meditate. To those who are unfamiliar with such experiences, his detailed descriptions might seem overly sentimental and tedious, but those who have similar stories are likely to welcome his wisdom. Toward the end, Siegel—who at times seems to be uncertain about who his audience is—discusses the ways in which mindful awareness can inform education, clinical practice and psychotherapy.

As both a scientist and an avid promoter of mindfulness, Siegel walks a fine line of credibility. But he is to be commended for repeatedly pointing out that his ideas about the mindful brain are just that—ideas. Although he is confident that mindfulness effects beneficial neurological change, he also acknowledges that it could be a long time before science agrees, if indeed it ever does. Nevertheless, in bringing together what we know and have yet to learn about this fascinating subject, Siegel offers an exciting glimpse into an uncharted territory of neuroscience.

—Melinda Wenner

Why We Believe

Six Impossible Things before Breakfast: The Evolutionary Origins of Belief

by Lewis Wolpert. W. W. Norton, 2007 ($25.95)

Humans have been called the believing animal. Obsessed with finding explanations, we fashion viewpoints about the world and then cling to them tenaciously, even if they are self-contradictory and incoherent.

In *Six Impossible Things before Breakfast,* biologist Lewis Wolpert of University College London tries to get to the bottom of why we are such ardent believers, how we form our notions, why they are so often wrong and how we sometimes get them right. (The title comes from Lewis Carroll's *Through the Looking Glass,* in which the White Queen explains to Alice that believing in impossible things merely requires practice.)

Wolpert argues that, unlike animals, humans have "causal beliefs," which address the mechanisms by which a cause leads to an effect. A chimp can learn that wind shakes fruit out of the trees, but, according to Wolpert, only a human will figure out he can shake the branches himself when he is hungry.

So how did we get this way? Wolpert thinks our believing brains arose because of tool use. He argues that people had to understand basic mechanical principles to make and use even simple implements efficiently. Good tool users were more likely to survive than incompetent ones were, resulting in the evolution of humans who could think in terms of cause, mechanism and effect.

Wolpert makes an interesting argument, but he is not completely convincing. Are human ideas about the world really of a different kind than those of other animals, or are we just smarter and better at reasoning things out? Wolpert himself admits that many researchers do not agree with the distinction he draws. Likewise, his argument for tool use as the driving factor seems plausible but not conclusive.

The book also suffers because the author meanders across a number of topics—faulty reasoning, false beliefs, the paranormal, religion and rationalism—which, though interesting, do not cohere into a unified argument.

Although readers will probably wish that Wolpert had managed to better discipline his material, they will find much to enjoy in his fascinating explanations of human and animal reasoning.

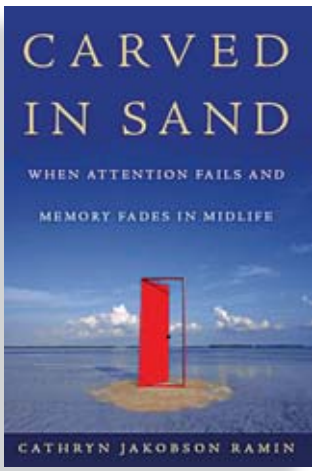
—Kurt Kleiner

Senior Moments

Carved in Sand: When Attention Fails and Memory Fades in Midlife

by Cathryn Jakobson Ramin. HarperCollins, 2007 ($24.95)

We've all had the experience: the name we can't recall, the face we can't place, the lost keys that once lived in the kitchen drawer. Everyone forgets things. But to Cathryn Jakobson Ramin, a seasoned science journalist, these ordinary incidents became unacceptably common shortly after she "crossed the threshold to middle age," in her mid-40s.



"There was no way around it," she writes. "Something was happening to my mind." She felt foggy and forgetful, losing track of dates, names, faces and directions—and she soon felt alone, alarmed and desperate.

Carved in Sand chronicles the quest she embarked on to understand why her memory was fading. Blending personal anecdotes with research literature, Jakobson Ramin delves into such areas as stress, insomnia, diet, menopause, anxiety, depression, substance abuse, attention-deficit disorder and Alzheimer's disease. She also explores why some people remain sharp well into their 90s.

As part of her quest, she subjects herself to a battery of tests, drugs, procedures and studies. She has ECG, MRI and PET scans and undergoes hearing and visual tests. She tries meditating, sleeping, staying awake and exercising. She solves crossword puzzles and plays computer games. She takes antidepressants, stimulants, memory enhancers, hormones and thyroid drugs. She eats more (or less) protein, carbohydrates, fruits, vegetables, meat and fish. She even memorizes poems and goes salsa dancing—activities that reportedly sharpen memory. In short, she tries every strategy that she can think of and that sufferers or professionals recommend.

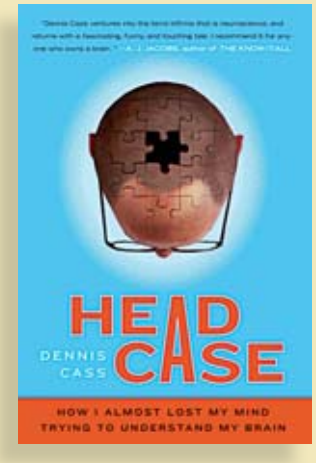
The result: "People ask me all the time if I'm 'better,' and honestly, I can say that I am." Among other things, she learns that a mild traumatic brain injury she suffered early in life (the result of getting whacked on the forehead accidentally by a broom) increased her vulnerability to memory trouble, and she also discovers a thyroid deficiency. Yet, for the most part, she is normal and benefits from a variety of memory-enhancing treatments.

Ultimately, Jakobson Ramin's insightful and well-researched journey through memoryland offers some valuable lessons. For one, forgetfulness is commonplace and need not impair one's life. Moreover, there is no single cause or treatment for forgetfulness, which can arise from a wide variety of biological and psychological causes, ranging from trauma or hormonal imbalances to anxiety or depression. But the good news is that many treatments work. And in her case, "the fog has lifted." —*Richard Lipkin*

Scientific Self-Discovery

Head Case: How I Almost Lost My Mind Trying to Understand My Brain

by Dennis Cass. HarperCollins, 2007 ($24.95)



During a frightful case of writer's block, Dennis Cass had a sudden insight. A simple, clear thought entered his mind: *How can you expect to live by your wits if you have no idea how your wits work?* Delighted with this question, Cass, a journalist who specializes in writing about popular culture, politics and food (and who avoided any topic approaching science), decided to learn as much as he could about his brain.

In *Head Case,* Cass describes his fumbling attempts to visit with scientists, wiggle his way into research studies, perform mind-numbing experiments and play amateur neuroscientist in his office, which he begins to call his lab. Part of the author's charm is that he does not pretend to be an expert. This book is meant to entertain. But as the story unfolds, Cass begins to grapple with questions that lie at the heart not only of science but also of humanity itself.

Cass had never imagined that learning about the brain might be frustratingly difficult or that it could eventually undermine his view of the world and himself. As he begins to understand the science of fear, attention, stress, addiction and consciousness, he relates his revelations to his own experiences and troubled past. With compassion and humor, Cass examines his strained relationship with his stepfather, whose selfish and grandiose ideas sent his family into financial and emotional hardship. He finds solace in the controversial views of evolutionary psychology, realizing at last that everyone shares the same flawed "prehistoric brain" and that his stepfather's lifelong substance abuse problems were the result of mental illness rather than a weak moral character.

Although Cass has come far in understanding how his wits work, he errs on the side of reductionism by explaining almost all the brain's processes as cascades of biochemical reactions triggered by outside stimuli. In doing so, he largely ignores the nuanced ways in which genes and biology interact with experience to influence brain function. By presenting this simplified picture, however, Cass leaves room to show something even more important: the human side of science.

Head Case is a wonderfully entertaining account of Cass's venture into neuroscience, revealing that we all can learn about our brain as long as we put our mind to it.

—*Thania Benios*

ask the Brains

Hypnotic suggestions can modify the way the brain processes information, affecting perceptions such as pain and fear.

Is hypnosis real, and can it be used to help people fight addictions or lose weight?

—Suzanne Napier, Claremore, Okla.

Psychologists Grant Benham of the University of Texas–Pan American and **Michael R. Nash** of the University of Tennessee, Knoxville, reply:

HYPNOSIS IS REAL, but many popular ideas about it are not. When used responsibly by medical professionals as one element in a broader treatment plan, hypnosis can help patients afflicted with various emotional and medical problems.

Hypnosis is a product of sustained, focused attention coupled with suggestions for alterations in subjective experience, perception, emotion, thought or behavior. The degree to which a hypnotized person experiences these alterations depends on his or her natural ability to experience hypnosis rather than on the "power" of the hypnotist or any particular technique. This innate ability does not change much over time: certain people are simply more susceptible to hypnosis than others are.

How hypnosis works is an enduring focus of scientific inquiry. Evidence indicates that hypnotic suggestions can modify the way the brain processes information, thereby affecting perception. If a person hears a hypnotic suggestion that he or she will not feel pain, certain areas of the brain may still register that the body is receiving a painful stimulus, but the brain's normal "emotional" reaction is less than it would be otherwise.

Hypnosis can help some patients who suffer from pain or debilitating anxiety or who wish to curb addictions or lose weight. But hypnosis is almost never a stand-alone treatment, nor is it a foolproof way to cure a person of unhealthy habits. These and other sensationalist claims fail the test of science. For instance, a hypnotized person is not under the control of the hypnotist, and individuals usually remember everything that occurred during hypnosis. Furthermore, memories of past events are not infallibly true.

Why does the outer surface of the brain have folds?

—Tom Laudate, Brighton, Mass.

Neuroscientists Claus C. Hilgetag of Jacobs University Bremen in Germany and **Helen Barbas** of Boston University explain:

PERCEPTION, EMOTION, thought and all other forms of conscious experience arise from the cerebral cortex, the outermost layer of the brain. As animals evolved to use more of these high-level processes, they eventually needed more space for this layer of gray matter than the inside surface of the skull could provide. Folds maximize the surface area available for the cerebral cortex without increasing the size of the head.

Dogs, cats, apes, dolphins and humans have folded brains, whereas animals with smaller brains do not. The tissue sheet of the human cerebral cortex is about three times as large as the inside surface of the skull. Its folding pattern is far from random, however—very unlike a crumpled sheet of paper. In the 19th century scientists proposed that simple mechanical principles might underlie the brain's characteristic structure. They also postulated that the brain's surface shape (morphology) and function were related. For decades, these ideas seemed naive next to emerging genetic theories. Recent studies, however, have given new support to the concept that mechanical factors play a key role in brain morphology and function.

Nerve fiber bundles are tense, like stretched elastic. Regions in the brain that are densely connected are pulled toward one another, producing outward bulges between them—the hills of the cortical landscape. Weakly connected regions drift apart, forming cortical valleys. The stretching and compression of brain tissue also have an effect on the architecture of the cortex and the shape of individual cells, most likely affecting brain function.

One example that illustrates this principle is the asymmetry between the language regions in the left and right hemispheres. A massive fiber bundle connects frontal and posterior language regions in each hemisphere, but the bundle is denser and therefore pulls harder on the left—complementing the idea that in most people the left hemisphere is dominant in language processing. Observations of this type have led scientists to return to the ideas first proposed by anatomists in the 19th century. Modern techniques have shown that the landscape of the brain correlates with brain function after all. M

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

COURTESY OF GRANT BENHAM; COURTESY OF MICHAEL R. NASH; CLAIRE FOLGER (*Hilgetag*); COURTESY OF HELEN BARBAS

Head Games

Match wits with the Mensa puzzlers

1 Take the number of playing squares on a chessboard, divide by the number of railroads in Monopoly, subtract the number of face cards (jacks, queens and kings) in a standard deck of playing cards, multiply by the number of dice in classic Yahtzee, then add the point value of the letter "E" in the U.S. version of Scrabble. What is the final number?

2 If you spell out whole numbers in sequential order (one, two, three, and so on), how high do you have to go before you reach a number that contains the letter "a"?

3 Each letter stands for a different digit. Determine their individual values to solve the subtraction problem.

ARE – ERA = EAR

4 What do the following six words have in common?

cat, owl, meal, mar, over, nub

5 A square that measures four inches on a side has a perimeter of 16 inches and an area of 16 square inches. Find a rectangle with a perimeter of the same value as its area.

6 Based on geographic location, which of these four capitals is the odd one out?

Dodoma Doha Muscat Sana'a

7 Fools inhabit the Foolish Forest. The fools find numbers beginning with the letter "f" to be acceptable, and all other numbers are unmentionable. It is a strict rule that the number of fools in the Foolish Forest be acceptable. On a certain day there was an acceptable number of fools in the forest. Then a few more fools went in foraging for food, and the number in the forest was still acceptable. When four fools fled the forest in fear, the number was still acceptable. A few fools went in to find their friends, and the number was still acceptable. After a while, five fools left to free their families, but the number was still acceptable. A further few fools went in to feast frivolously, and the number was still acceptable. Then 14 fools furiously forsook their forest, and, alas, the number of fools in the forest was not acceptable! Finally, one faithful fool forgot the fury and returned to the forest fold. And the number was once again acceptable.

Assuming that "a few" always stands for the same unmentionable number, how many fools were in the forest to begin with? (Hint: fortunately, there are fewer than 100 fools in the forest.)

8 Fill in the blanks according to the clues.

a) H O _ _ _ _ _ _ T _ _ _ Plant science

b) _ H O _T _ _ A laugh's smaller relative

c) _ H O _ T Vertically challenged

d) H O _ _ _ _ T Superlatively sanctified

e) _ _ H O _ T Accomplice

f) _ H O T _ _ _ _ _ _ Ansel's art

g) H O _ T _ _ _ A type of takeover

h) H O _ _ _ T A former Charlotte hoopster

i) _ H O _ _ _ T _ _ _ Considerate

American Mensa is at www.us.mensa.org/sciamm

Answers

1. 64/4 = 16; 16 – 12 = 4; 4 × 5 = 20; 20 + 1 = 21.
2. One thousand.
3. E = 4, R = 5, A = 9.
4. They have three things in common. 1) Their first letters spell the word "common." 2) You can make new words by changing each word's last letter to "n." 3) Each word has an anagram (act, low, lame, arm or ram, rove, bun).
5. A three-inch by six-inch rectangle has a perimeter of 18 inches and an area of 18 square inches.
6. Dodoma, Tanzania. The other capitals are in the Arabian Peninsula: Doha, Qatar; Muscat, Oman; and Sana'a, Yemen.
7. 53. "A few" means exactly "three." 53 + 3 = 56, 56 – 4 = 52, 52 + 3 = 55, 55 – 5 = 50, 50 + 3 = 53, 53 – 14 = 39, 39 + 1 = 40.
8. a) HORTICULTURE
   b) CHORTLE
   c) SHORT
   d) HOLIEST
   e) COHORT
   f) PHOTOGRAPH
   g) HOSTILE
   h) HORNET
   i) THOUGHTFUL

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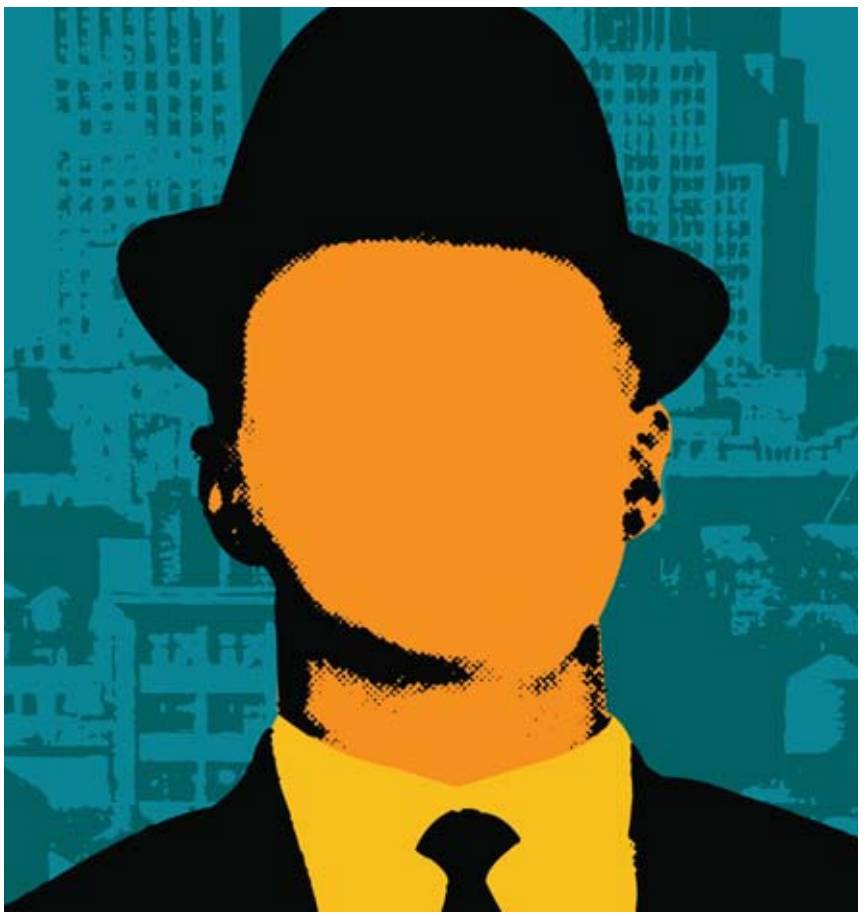

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Therapy 2.0

Computer simulations in virtual reality offer patients with anxieties the ability to face—and eventually master—their fears.

PLUS:

Ask the Brains Experts answer your questions.
Illusions Play tricks on your brain—and gain insights about mental functions.
Head Games Brain teasers and puzzles.

GETTY IMAGES (*left*); ROB HOWARD *Corbis* (*right*)