TIPS TO RESIST YOUR TEMPTATIONS *page 45*

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March/April 2013
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Stress and the City
page 58

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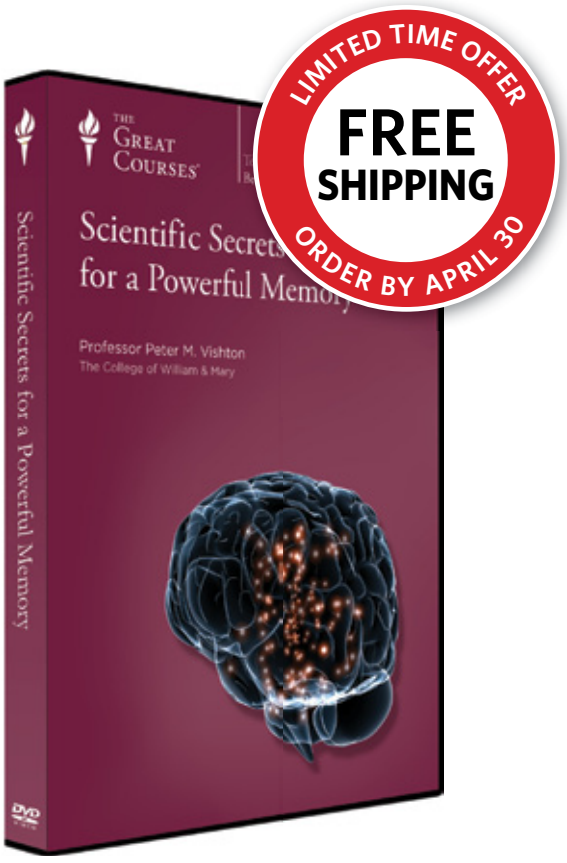

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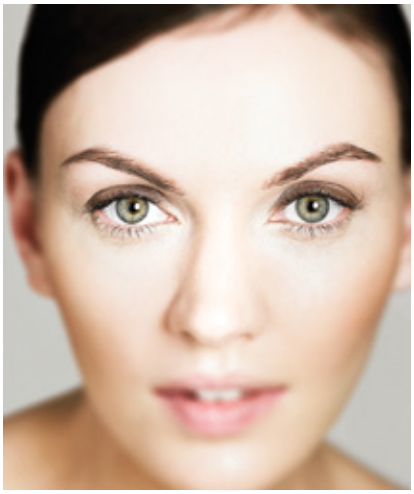


Powers of Attention

Jon Kabat-Zinn, a tireless advocate of mindfulness meditation, sees parallels between the mind and the Pacific Ocean. Waves of emotion may roil the surface, but 30 feet down, all is peaceful. By tuning in to every breath as it travels through your body, you can dive into that basal oasis.

Mindfulness, or being keenly aware of the present moment without judging what is happening, can lift moods, hone focus and improve health. As psychologist Amishi P. Jha writes in her cover story, "Being in the Now," on page 26, this cognitive cure-all may work by strengthening the brain's attention mechanisms.

Living in the present, of course, is not the same as ignoring the future. Yet that is what we do when we cave in to a fast-food hamburger or bust our budgets with a shopping spree. In "Time-Warping Temptations," journalist David H. Freedman explores why we overrate the treats of today and cheat our future selves. Turn to page 45.

It's easy to lose our cool, especially in a metropolis, with the stress of congested streets, crowded sidewalks and the loneliness that can emerge amid thousands of strangers. Urban living can harm the brain—notably by increasing the risk of developing schizophrenia. Psychiatrist Andreas Meyer-Lindenberg explains why in "Big City Blues," on page 58. Fortunately, emerging therapies for schizophrenia are helping patients overcome the disorder's often ignored social and cognitive deficits, which make building friendships and living independently so tough. See "A Social Salve for Schizophrenia," by psychologist Matthew M. Kurtz, on page 62.

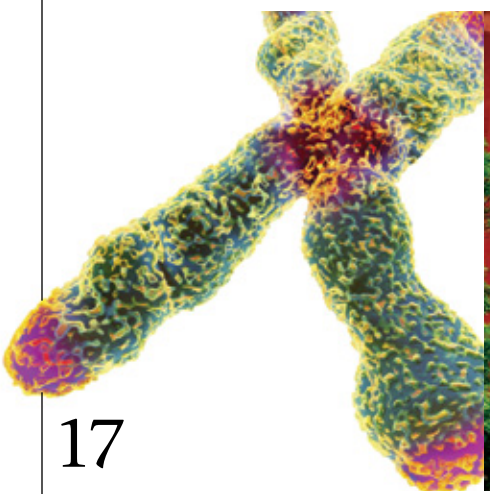
But first, take a look at the lively design we're unveiling for Head Lines. We've packed it with fresh features. In a new column, How to Be a Better…, we share tips for upping your performance; this issue focuses on driving skills. And the first installment of Pharma Watch, which highlights trends in drug research, looks at old medications that are finding new life as brain treatments. Check out the ticker along the bottom, too, to pick up some fascinating facts. We hope you love what you find.

Sandra Upson
Managing Editor
editors@SciAmMind.com

SCIENTIFIC AMERICAN MIND
Volume 24, Number 1, March/April 2013

FEATURES

DEPARTMENTS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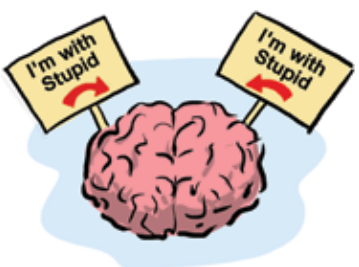

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GENIUS, UNPROCLAIMED

Tonight the hoary caveman contemplates
Not just tomorrow's risky hunting fate,
But he has indeed resolved our origin
And where the stellar heavens did begin.
He depicts no record of any kind
And so this genius is lost in time.

What are the rules for genius-designates?
Somewhere today a genius contemplates
The deepest mysteries of the human mind.
Yet, for the laws of Science, she is blind.
How is her silent genius measured then
As this mother toils and her children tends?
Not a word of what she thinks
Is written or said to provide a link
To the thoughts in her prodigious mind
Where her august genius resides sublime.

Is genius only a transient state
Fulfilling what current standards dictate
Today, for those who fill this select class
With timely words and deeds which
they amass?
Even though we do not understand
The mindful genius in another man,
Should we concede the conceivable chance
His genius is tempered by circumstance?
That he too might forge a unique thought
Which no one else has ever sought?

For every genius that is recognized
A thousand geniuses remain disguised
Or unexpressed or indeed unproclaimed.
Or, that fleeting moment is not sustained
For the circumstance requisite to find
The fertile substrate for the genius mind.

Clarence Madhosingh
Ottawa, Ontario

GENIUS REQUIRES EFFORT

Thank you for the excellent article by Dean Keith Simonton, "The Science of Genius." I would agree that true genius is the merging of intellect, creativity and outstanding achievement. For this to happen, mastering domain expertise is crucial, confirming the "10-year rule." Brilliant creativity requires the necessary knowledge, versatility and skill in order to have a scholarly academic or artistic breakthrough. Only then can we be truly original, achieving unpredicted goals, never before dreamt of.

Greg Westlake
Norfolk, England

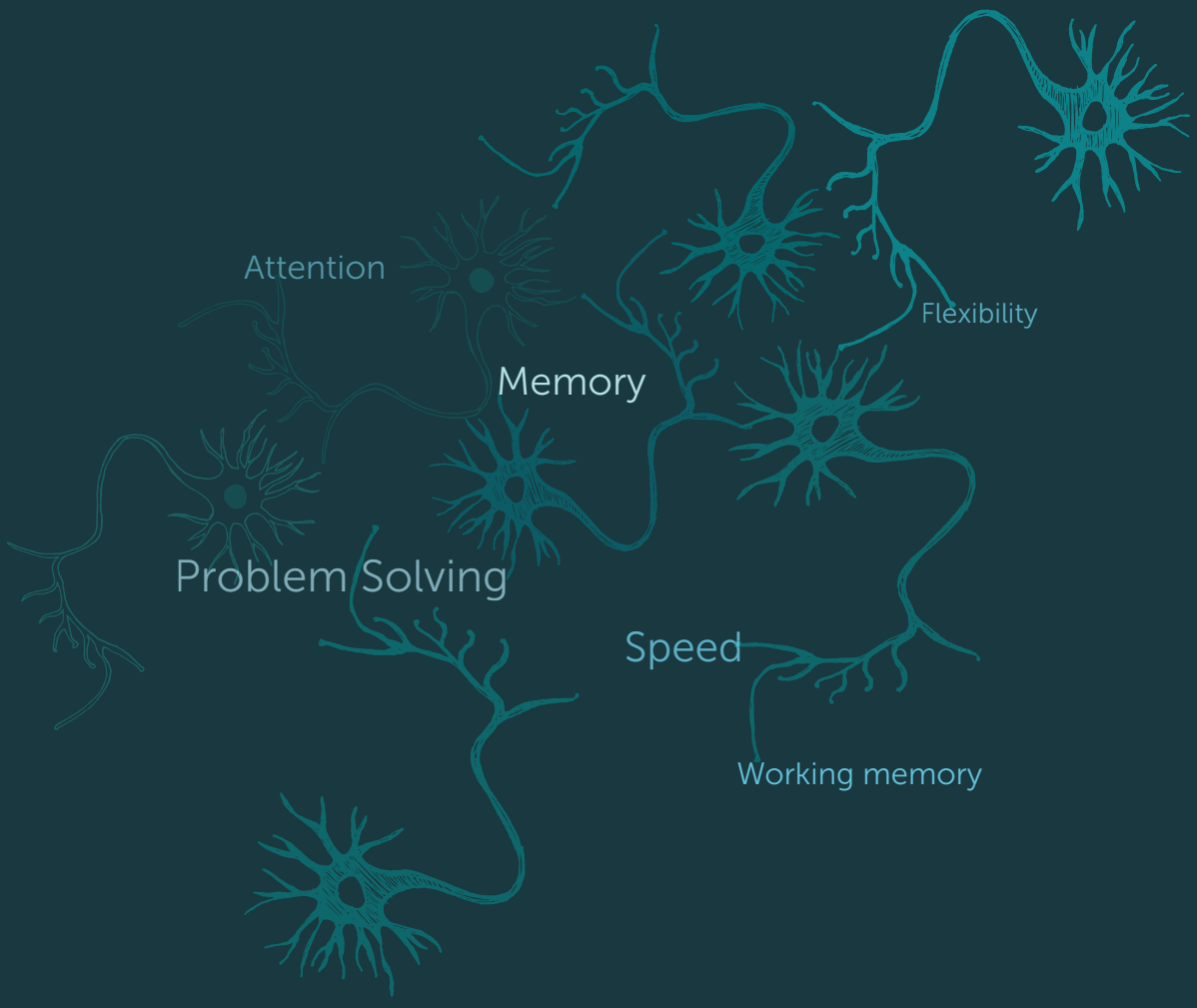
ACCIDENTAL SEXISM?

I subscribe to *Scientific American Mind*. In the November/December 2012 issue, you primed me on page 8 [Head Lines] with the information that only 5 percent of Nobel laureates are women. I am interested in educational trips so I later read the SA Travel advertisement and discovered not even one female lecturer! With 10 lecturers named in four pages! And of the 12 people on *Scientific American*'s Board of Advisers, only two are female. Maybe you need blind auditions. Come on, *Scientific American*, you can do better!

"Bailey" (female)
via e-mail

DRINKING WHILE PREGNANT

"A Daily Glass of Wine Is Okay during Pregnancy," by Stephani Sutherland [Head Lines], discusses a study published by Danish scientists who examined the drinking habits of pregnant women and the cognitive outcomes of 1,600 five-year-old children. The authors of the study report that drinking up to eight alcoholic drinks per week during pregnancy has no effect on children's intelligence or attention span, but they caution that drinking during preg-



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nancy is generally not safe. Nevertheless, the headline of your article and messages such as "Expecting moms can relax, it appears, and have a drink now and then, guilt-free," alongside other similarly egregious abbreviated headline messaging in the national media, suggest that drinking during pregnancy is unequivocally safe. This undermines years of research to the contrary and directly challenges public health messages that urge pregnant women to abstain from alcohol.

Countless scientific studies have shown that alcohol is dangerous to the developing fetus. In response to the misleading messages delivered by *Scientific American Mind* and elsewhere by the media, scientific experts, advocacy groups and national medical organizations have released statements to the effect that no amount of alcohol consumed during pregnancy can be considered safe. We urge *Scientific American Mind* to act now and do the same.

Do we discount geniuses who do not fit our expectations?

Nina Di Pietro, Judy Illes, James Reynolds, Joanne Weinberg, Albert Chudley, Eric Racine and Emily Bell
National Core for Neuroethics
University of British Columbia
Vancouver

THE EDITORS REPLY: *A short news article is by its nature never as detailed as a feature; we regret any misunderstandings. To better analyze the existing research, we commissioned a more extensive treatment of this topic, which you may find on page 22.*

THE SLEEP CURE

David Levine writes in "Treating Sleep Improves Psychiatric Symptoms" [Head Lines]: "Investigating their patients' sleep health might allow doctors to alleviate mental disturbances early—perhaps even before patients try psychiatric drugs."

I think this point is so spot on and very important. Psychiatric drugs are overly prescribed without asking basic questions about factors such as sleep patterns. Other initial questions should include how much water and caffeine are consumed. Staying hydrated and limiting one's caffeine intake is important to overall health and helps to improve one's sleep.

"war4tek"
commenting at
www.ScientificAmerican.com

Psychiatric disorders are not the only ailments made worse by sleep disturbance. Chronic inflammatory diseases and pain syndromes are much more difficult in patients with sleep apnea and other sleep problems. All patients should be screened for sleep disturbance.

"ssm1959"
commenting at
www.ScientificAmerican.com

Hippocrates, the founder of medical principles, wrote much the same thing back in 400 B.C. He often would cure his patients by improving their sleep. Nothing new in 2,400 years, eh?

"samil"
commenting at
www.ScientificAmerican.com

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PLAY IT AGAIN, SAM

Regarding "Why You Like to Watch the Same Thing Over, and Over, and Over Again," by Sunny Sea Gold, I agree that it sparks contemplation about personal growth. And I love the Heraclitus quote about never crossing the same river twice. I've been watching *Gone with the Wind* since I was seven years old (for more than 50 years), and every time my perspective has changed.

"voice"
commenting at
wwwScientificAmerican.com

OPEN YOUR EARS

To the closing tips in "How to Use Your Ears to Influence People," by Tori Rodriguez, I would add, "Practice listening without thinking ahead to what you're going to say when someone stops talking." Perhaps assume you will be asking a question and trust that the "right" question will come to the surface.

I love the point about striking a balance between listening and talking. Being a better listener means when you do speak, it will have more meaning and relevance.

Truly listening to someone is one of the greatest gifts you can give that person. On a fundamental human level, most people simply want to be seen and heard. If you can do that for someone (sincerely, without manipulative intent), you'll build trust, respect and influence.

"IntrovertEntrepreneur"
commenting at
www.ScientificAmerican.com

ERRATUM

In problem number 9 in Head Games [November/December 2012], the middle box in the top row should contain the number 206, not 205.

Head Lines

THE LATEST SCIENCE ON BEING HUMAN

GETTY IMAGES

Is This Kid Doomed?

Studies of delayed gratification say yes, but new research suggests he may just be rational

M News from our Web site Whether reading French words or Chinese characters, people harness the same brain regions.

Nature vs. Nurture

A Marshmallow in the Hand

Delaying gratification is not always the rational choice

A four-year-old girl sits at a table in a featureless room. A friendly researcher places a marshmallow in front of her and tells her that if she can resist eating it for 15 minutes, he will be back with another one and she can then eat both. He leaves, and what she does next will predict her success and mental health for the rest of her life. Such is the power of the now classic marshmallow study, long thought to be a measure of self-control.

The initial research began in the late 1960s, and follow-up work has suggested that the length of time a child waits before eating the marshmallow is a better predictor than intelligence of success as an adult. A new study published last October in *Cognition*, however, indicates that children's behavior in such situations may not always reflect only their innate self-control. A child may also be making a rational decision on whether to trust that the second marshmallow is indeed coming soon.

Celeste Kidd, a doctoral candidate in brain and cognitive sciences at the University of Rochester and lead author of the new study, suspected there might be a common misconception about the classic marshmallow study—namely, that waiting is always the right choice. While volunteering years ago at a homeless shelter for families in Santa Ana, Calif., she realized that all the kids around her would eat their marshmallows straight away, living as they did in an environment where anything they had could be taken away at any time. "Delaying gratification is only the rational choice if the child believes a second marshmallow is likely to be delivered," Kidd says.

Although previous marshmallow-type studies have acknowledged that external factors might influence kids' ability to wait for the bigger reward, none had directly tested for those factors' effects. So Kidd and her colleagues ran a study in which they manipulated the reliability of their young participants' environment. A researcher gave children with an average age of four years some poor-quality art materials and told them if they could wait, she would return with better supplies. In a "reliable" condition, she did exactly that, but in an "unreliable" condition, she returned to explain she did not have any better materials after all. A marshmallow test followed. Those in the reliable condition lasted an average of 12 minutes, whereas those in the unreliable condition lasted only three.

With that in mind, the findings of the many decades of follow-ups to the marshmallow study [*see timeline at right*] are cast in a different light. The studies invariably point to a strong association between how long a child was able to wait before eating the marshmallow and various measures of mental health, competence and success in later life. A recent imaging study of the kids in the original study, now in their 40s, even found differences in the activity of key brain areas between those who could and could not resist temptation as children.

If Kidd is right, these differences may be the result of more than just innate self-control, such as socioeconomic status, parenting quality and other environmental factors that influence decision making. "It's incorrect to presume lack of willpower is the only relevant factor in determining children's wait times and, subsequently, the primary driver of children's successes later in life," she says.

—Simon Makin

MARK DOUET *Getty Images (hand)*; MICHELE CONSTANTINI *Corbis (marshmallow)*; PENELOPE MATHERS *(illustrations)*

The Myth of the Family Meal

Eating together might not be as magical as researchers thought

Regular family meals have been touted as a preventive for all kinds of problems, including teen pregnancy, smoking and obesity. Recent research in the *Journal of Marriage and Family*, however, found that most of the benefits of regular family meals were not actually the result of eating together. Rather, social scientists Kelly Musick and Ann Meier found, they stemmed from other factors in the family environment that facilitated regular meals, such as sufficient income, strong family relationships and authoritative parents.

Instead of fixating on family dinners, Musick and Meier suggest, moms and dads should focus on building relationships with children at any opportunity, such as while driving in the car. A 2010 report by the National Center on Addiction and Substance Abuse at Columbia University noted that teens were more likely to talk to their parents in the car than almost any other place. Being involved in a kid's life is extremely beneficial, scientists say, even if it doesn't happen over placemats.

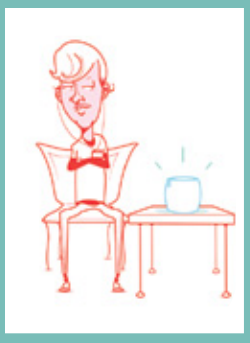
—Carrie Arnold

M A mother's brain can harbor cells that originated in a fetus. If a woman conceives a boy, she can end up with male cells in

1972: Walter Mischel's classic "marshmallow study" is published. Preschoolers were given a treat and told that waiting 15 minutes to eat it would earn them a second marshmallow. They waited, on average, six minutes. Children who hid the marshmallow from view or who distracted themselves were able to delay gratification much longer.

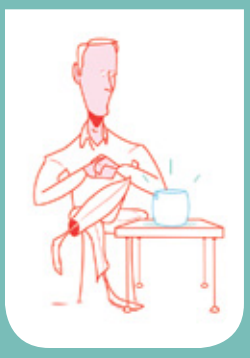
1981: An experiment in pigeons produces similar results—distractions and visual obstruction helped the birds delay gratification.

1988: The children, now teenagers, who were better able to delay gratification in preschool show greater academic, emotional and social competence, including higher SAT scores.



1999: Mischel proposes a framework for willpower: a rational "know" system promotes self-control, and an emotional "go" system undermines it.

2005: At age seven children begin to understand being "of two minds," called the Ulysses conflict. The Greek hero's conflicting desires led him to strap himself to his ship's mast so he could hear the Sirens' song without succumbing to it.



2009: Failing to delay gratification at age four increases the risk of being overweight at age 11.

2011: The differences in Mischel's original subjects' ability to resist temptation remain evident four decades later.

2012: A child's ability to exert self-control is also influenced by environment, a new study shows.

Placebos Work Better for Nice People

Agreeable personalities produce more of the brain's natural painkillers

Having an agreeable personality might make you popular at work and lucky in love. It may also enhance your brain's built-in painkilling powers, boosting the placebo effect.

Researchers at the University of Michigan, the University of North Carolina and the University of Maryland administered standard personality tests to 50 healthy volunteers, identifying general traits such as resiliency, straightforwardness, altruism and hostility. Each volunteer then received a painful injection, followed by a placebo—a sham painkiller. The volunteers who were resilient, straightforward or altruistic experienced a greater reduction in pain from the placebo compared with volunteers who had a so-called angry hostility personality trait.

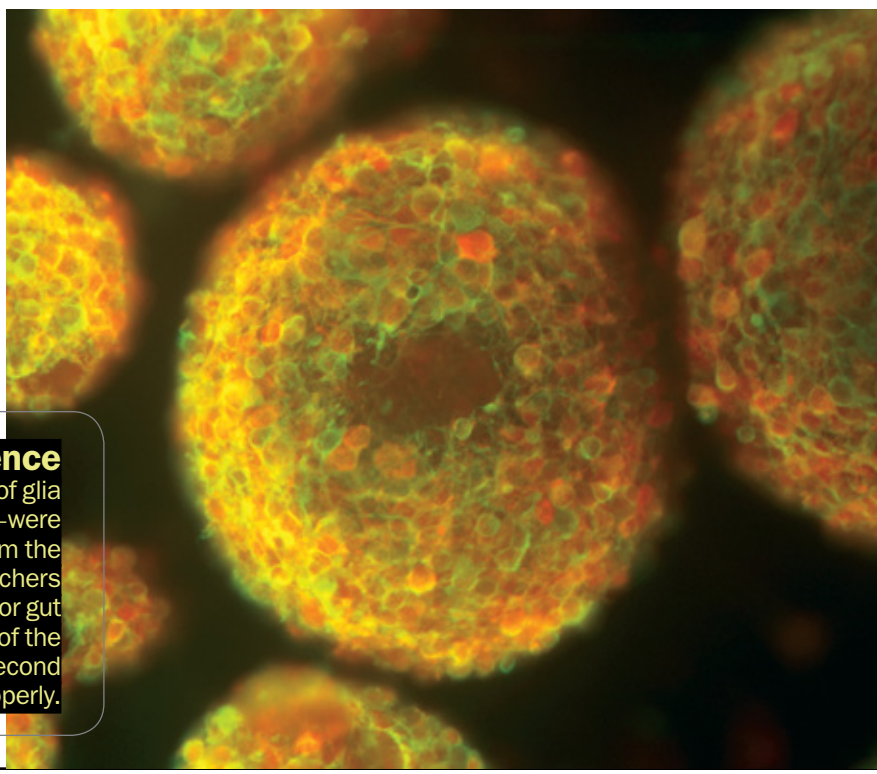
The difference was not just psychological. The researchers, led by Jon-Kar Zubieta of the University of Michigan, used PET (positron-emission tomography) scans to measure levels of mu-opioids—the brain's own painkilling chemicals—in the volunteers' brains during the placebo procedure. The brains of volunteers with "more agreeable" personalities, according to Zubieta, released more of these natural painkillers, thus enhancing the placebo effect.

"The regions where we see these changes are all engaged in taking sensory information from outside, integrating it and giving it an emotional content," Zubieta says. "Personality traits like straightforwardness and altruism are part of an overall capacity to be open to new experiences and integrate that information in a positive fashion. That's probably what drives the placebo effect."

The findings could help make clinical trials for new drugs, which depend heavily on placebo testing, more accurate.

—John Pavlus

For more on the placebo effect, see page 34.



Sphere of Influence

These neurospheres—free-floating balls of glia (*red*), neurons (*green*) and stem cells—were cultivated in a lab from stem cells taken from the intestine or stomach of a mouse. Researchers use the neurospheres to test treatments for gut motility disorders, in which portions of the intestine, sometimes referred to as the second brain, lack sufficient nerve cells to function properly.

CLIVE STREETER *Getty Images (top)*; COURTESY OF DIPA NATARAJAN *University College London* AND RANIA KRONFLI *Royal Hospital for Sick Children (bottom)*

her brain. | After blending 30 odors, researchers dubbed their new nondescript scent "olfactory white," akin to white light and white noise.

VELVET IMPROVES OLDER ADULTS' WELL-BEING

Touching the soft material may bring back positive memories

It's no surprise that soft materials are more pleasing to the touch than rough ones, but a recent study found that they can actually improve the cognitive and emotional skills of older adults. In the research, published in the October 2012 issue of *Geriatrics and Gerontology International*, participants were divided into three groups, each of which completed twice-weekly activities that involved working with either a piece of velvet, canvas or Velcro. After 10 weeks, participants in the velvet group had increased verbal fluency and emotional competence and decreased negative emotions, whereas those in the Velcro group had the opposite results. (There was no change in the canvas group.)

This study is the first ever to look at how touching different materials affects well-being, so the researchers do not yet know how the phenomenon works, but they hypothesize that the association between soft materials and positive memories may be to thank.

—Tori Rodriguez

Television Romance and Real-Life Marriage

People who believe that TV relationships are realistic are less likely to stay true to their spouse

Expectations for marriage come from many places—family life, past relationships, observations of other married couples. Now a study published last September in the journal *Mass Communication and Society* finds that television may also affect how we feel about marriage and our spouse.

Researchers at Albion College surveyed 392 married individuals, analyzing their television-viewing habits, belief in the portrayal of television relationships, expectations for relationships and feelings toward their own marriage. They found that participants who believe that couples on TV are true to life are less committed in their own marriage: their survey responses indicate they are more likely to cheat and less likely to stay in the marriage.

In addition, these participants measured their relationship "costs" as much higher than those who did not believe that TV portrayals are realistic. Relationship costs include feelings of lost personal time and an increased emphasis on a partner's unattractive qualities, explains Jeremy Olson, study author and assistant professor of communications at Albion.

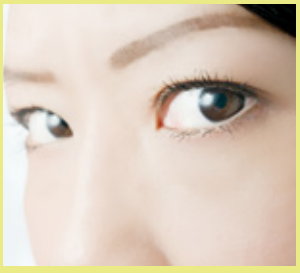
This is the first study to assess how attitudes toward television reveal feelings about one's own marriage, although previous research has suggested that television viewing is related to general perceptions of marriage and romance. In a study published in 2006 in the *Journal of Communication,* researchers found that college students who frequently watch romantic-themed shows are more likely than other students to believe that their partners should know their innermost feelings and that their wedding day will be the happiest day of their life.

Olson hopes his research helps couples take a hard look at where they are getting their expectations for their relationship and whether television is reinforcing unreasonable beliefs. "The biggest factor contributing to divorce is going into marriage with unrealistic expectations," Olson says.

—Monica Rozenfeld

Mental Mirrors Reflect Hatred

Mirror neurons distinguish between those we like and those we do not



Mentally simulating the actions of others is thought to be a key component of empathy. Yet new research suggests that our so-called mirror neurons may also expose hidden divisions. A study published in October in the journal *PLOS ONE* reveals that these copycat neurons do not reflect all people equally.

Mirror neurons were discovered in the early 1990s, and their existence was a neuroscientific revelation: brain cells not only fire when we perform a given action, they also fire when we see someone else doing the deed. Much subsequent work has suggested that mirror neurons undergird social cognition. Now emerging research is finding that our mirror neuron system distinguishes between people who are physically and culturally similar and those who are not. The new work probed these differences further. In the study, investigators asked 17 young adult Jewish men to review the biographies and photographs of eight individuals who physically resembled the participants. Half these characters, portrayed by actors, were identified as neo-Nazis. The subjects reported they strongly disliked the anti-Semitic characters but not the others. Next, the participants underwent functional MRI scans while watching a video of each character drinking from a water bottle. The researchers focused on the ventral premotor cortex, a region typically active when we carry out an action or watch someone else do so. They found that neurons in this region activated differently when subjects viewed detestable and likable characters.

Because mirror neuron activity is thought to be a very basic part of brain function—and it can be seen in many animals besides humans—the new finding supports the notion that our brain is predisposed to distinguish "us versus them." This distinction can be beneficial, encouraging caution around those with harmful intentions, or dangerous, further entrenching prejudices. To weaken unwelcome biases, lead author Lisa Aziz-Zadeh, a cognitive neuroscientist at the University of Southern California, suggests that exposure and perspective taking could go a long way.

—Daisy Yuhas

SVETLANA SYLENKO *iStockphoto (top);* SAWAYASU TSUJI *Getty Images (bottom)*

M Humans are innately good at deducing what someone else is thinking. A single location in the brain, the right temporoparietal junction, tucked

(PHARMA WATCH)

OLD DRUGS, NEW TRICKS

Developing new drugs is no easy feat. As much as 95 percent of new compounds fail along the path to becoming clinically available. Attrition is especially high for drugs treating the central nervous system. The ones that do succeed rack up an average cost of $1.8 billion. So researchers are increasingly turning to the bottles already on the shelf. Proved safe for human consumption and often understood at a molecular level, today's familiar pills might just be tomorrow's medical discovery. Sometimes one man's side effect is another man's cure.

—Daisy Yuhas

Drugs, Reinvented	How It Works	Strength of the Evidence	Next Steps
Bexarotene: from **Chemotherapy** for skin lymphomas to **Alzheimer's** treatment	■ Bexarotene activates a chemical receptor in the body that affects how cells develop. In the brain, activating this receptor promotes activity that both attacks Alzheimer's characteristic plaques and clears proteins that cause neuron death		Human studies are commencing
Mifepristone: from **Abortifacient** to **Antidepressant**	■ Mifepristone was originally developed to block the neurotransmitter glucocorticoid to treat depression. Scientists discovered a useful side effect: the drug blocks progesterone, a neurotransmitter necessary in pregnancy. Abortion controversy mothballed research for decades, but now the drug is being reexamined as an antidepressant		Large trials thus far have not found the drug very effective. Yet evidence suggests that at the correct dosage, more patients will respond. Researchers are also investigating new drugs that mimic mifepristone without inhibiting progesterone
Gabapentin: from **Epilepsy** seizure prevention to **Addiction** withdrawal relief	■ Gabapentin appears to mimic certain neurotransmitters. One of its functions is normalizing activity in the amygdala, which can relieve addicts' symptoms of withdrawal. A major side effect is drowsiness—a blessing in disguise for addicts trying to quit, for whom insomnia is common		A study of 150 marijuana users aims to replicate a smaller study's finding of reduced withdrawal symptoms. Other trials are also under way for other types of dependency
Minocycline: from **Acne** medication and **Arthritis** reducer to **Schizophrenia** stabilizer	■ Minocycline is an anti-inflammatory drug that easily crosses the blood-brain barrier, so scientists wondered if it also helps to protect brain cells. They found that it diminishes some symptoms of schizophrenia, including social withdrawal and apathy—perhaps because it blocks glutamate, a neurotransmitter implicated in psychosis		A study with 175 subjects seeks to replicate previous findings and incorporate neuroimaging to better understand changes in the brain associated with treatment
Amantadine: from fighting the **Flu** to pulling patients out of a **Vegetative State**	■ Amantadine can cross the blood-brain barrier and alter neurotransmitters, so scientists have long sought to use it to treat brain disorders. The most exciting outcome: it helps patients in low-consciousness or vegetative states recover awareness, perhaps by ramping up dopamine activity, which reawakens the brain's drive and arousal system		Amantadine's success in disorders of consciousness has led to investigations for other traumatic brain injuries, including injury-induced irritability and aggression
Propranolol: from relieving **Anxiety** to diminishing **Racism**	■ Propranolol reduces blood pressure and anxiety because it blocks noradrenaline, part of the body's stress response. Its calming effects also lower scores of subconscious racial bias		The researchers—currently setting up a larger study—are interested in the neurobiology behind bias, not a racism cure. Their work also raises ethical questions about how the side effects of medication might influence personal attitudes

ISTOCKPHOTO (*pills and people*); SVETLANA ALYUK *iStockphoto* (*mice*)

behind the right ear, is where this reasoning is centered. | Humans and katydids—but no other known insects—have remarkably similar ears.

» Sleep *New molecular discoveries tackle troubled slumber*

An Internal Sedative

New insights into the relentless exhaustion suffered by people with a rare disorder may help treat several sleep conditions

Imagine you get nine hours of sleep every night, squeeze in long naps whenever you can, and yet every waking hour is a blur of exhaustion, poor focus and longing for the next time your head will hit the pillow. That is the reality for people with primary hypersomnia, a poorly understood, rare condition of perpetual sleepiness and lethargy.

The dogma in sleep science has been that unexplained sleepiness is caused by underactive brain regions involved in wakefulness and attention. This view has done little to provide relief for many of the chronically tired. Yet the opposite hypothesis—that the body might be producing a natural brake or sedative—has been controversial. Now scientists at Emory University have found just such a sedative in patients with primary hypersomnia, providing hope for the weary and perhaps even pointing to a new type of sleep-aid drug.

The Emory team discovered the sleep-promoting substance in the patients' cerebrospinal fluid, the watery liquid that cushions the brain and surrounds the spinal cord. In a study appearing in *Science Translational Medicine* last November, the researchers demonstrated that the compound enhances the activity of the same signaling pathway in the brain that is spurred on by sedatives such as the commonly prescribed benzodiazepines Valium and Ambien. The pathway involves gamma-aminobutyric acid (GABA), which is an attention-dampening neurotransmitter.

The researchers took spinal fluid from 32 patients with primary hypersomnia and applied it to human cells while measuring their electrical activity. They found the spinal fluid ramped up GABA receptor activity by some 84 percent, when GABA was also present (as it is in the brain). Spinal fluid from unaffected individuals enhanced GABA receptor activity, too, though to a lesser extent. There the boost was closer to 36 percent—similar to the effect elicited by patients' spinal samples after researchers removed the natural sedative.

The compound's chemical identity remains a mystery; thus far the researchers have determined that it is probably a peptide, which is a small protein. Future work will focus on identifying and perhaps even synthesizing the substance, to act as a sleep aid for people with insomnia.

For the perpetually sleepy, the recent work offers hope. Because their internal sedative acts in the brain like a benzodiazepine drug, the investigators reasoned that its action could be blocked by flumazenil, a drug given intravenously to treat benzodiazepine overdoses.

In seven hypersomnolent patients, flumazenil did restore alertness and reaction times for several minutes to a few hours, depending on the dose. For one of these patients—a woman who has managed to obtain an ongoing supply of the drug in tablet and cream forms—that relief has lasted four years.

Getting enough flumazenil to treat multiple individuals with hypersomnia may be tricky—the entire North American supply would be enough for only four hypersomniacs at the doses likely needed to maintain alertness all day, every day. Even so, Emory researchers have begun initial trials exploring the possibility of using the drug, or another like it, to awaken those living with internal sedation.

—Andrea Anderson

THIS PAGE: VINCENT BESNAULT *Getty Images*; OPPOSITE PAGE: GEORGE RETSECK (*brain*); PETEK ARICI *iStockphoto* (*pillow*)

SLEEP STATS

70 million Number of Americans who have a chronic sleep disorder.

$16 billion Estimated medical costs associated with sleep disorders in the U.S., which do not include indirect costs associated with lost productivity.

70 Number of sleep disorders described to date.

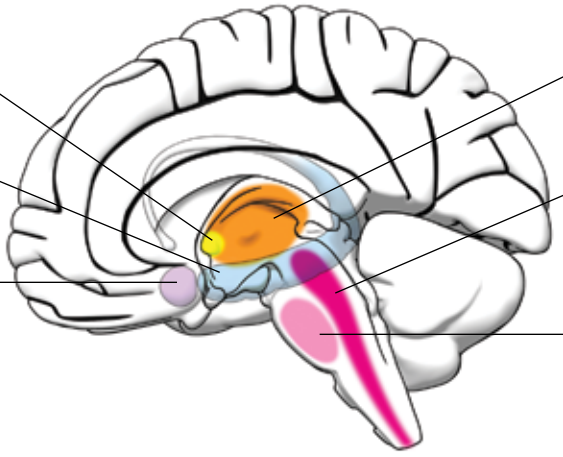
15 minutes Average time it takes a person to fall asleep.

2 Number of drugs on the market for treating sleep disorders.

600 milliliters Amount of cerebrospinal fluid produced by the brain each day. This liquid keeps the brain buoyant and may also transport a newly discovered internal sedative.

M Fluoxetine, the active ingredient in Prozac, can end up in waterways. The drug can cause male fathead minnows to ignore—or even kill—females.

Central Brain Regions Involved in Sleep



NAPPING IMPROVES MEMORY

Study subjects who took a short nap retained 85 percent of cards memorized pre-nap compared with 60 percent of those who stayed awake.

Don't Sleep It Off

Dozing immediately after trauma might make the memories worse

It may be tempting to seek solace in slumber after a traumatic event, but a study from the October 2012 issue of *Neuropsychopharmacology* found that sleeping too soon after trauma might lead to increased post-traumatic stress disorder symptoms. Two groups of rodents were exposed to a predator's scent, a traumatic event for a mouse. For six hours afterward, one group was prevented from sleeping, whereas a control group was not. The sleep-deprivation group displayed fewer physiological markers of stress than the control group and less PTSD-like behavior, such as freezing and a heightened startle response.

Researchers believe that sleep deprivation disrupts the consolidation of trauma memories—a hypothesis that jibes with the current understanding of the role of sleep in strengthening emotional memories. (Once that memory is ingrained, however, sleep could provide an opportunity for treatment; see the story at the right.)

Sleep deprivation can also reduce the impact of traumatic brain injury (TBI), according to a study published in the November 2012 issue of *Neuroscience Letters*. Rats with TBI sustained less damage when they were kept awake for 24 hours after the injury. Taken together, these findings suggest that after a violent, traumatic event—such as a car accident—staying awake for a while could afford both physical and mental protection.

—Tori Rodriguez

Desperate to Forget

Traumatic memories persist when our nighttime memory-erasing process fails

Scientists have long known that once we nod off, certain memories grow stronger. One recent theory suggests that forgetting, too, is an essential function of sleep [see "Sleep's Secret Repairs," by Jason Castro; Scientific American Mind, May/June 2012]. Researchers now suspect that post-traumatic stress disorder (PTSD) may emerge from flaws in sleep's forgetting process. Two studies presented at the 2012 meeting of the Society for Neuroscience in New Orleans indicate that sleep might offer a window of opportunity for weakening memories and providing relief from lingering reminders of trauma.

Neuroscientists believe that during sleep, a memory-elimination routine cleans out obsolete information by physically weakening synapses, the junctions between communicating neurons. Gina Poe, a neuroscientist at the University of Michigan, found in mice that for synapses to lose strength, levels of the neurotransmitter noradrenaline must drop. Noradrenaline levels typically fall during REM sleep in rodents and humans, but in people with PTSD the amount stays high throughout sleep. Normalizing noradrenaline with pharmaceuticals, Poe says, "could absolutely be a key target to actually cure PTSD through normal sleep."

In a separate experiment, researcher Asya Rolls of Stanford University hijacked memory remodeling in sleeping mice to make a traumatic association less scary. Rolls and her colleagues conditioned mice to fear the scent of jasmine flowers by pairing the smell with a foot shock. When the mice slept, they released a puff of jasmine. Under normal circumstances, the smell would reactivate and bolster the memory, a process that requires newly made structural proteins. The researchers gave some mice a drug that prevented the manufacture of these building blocks in a key fear-memory area. When these mice woke up, they no longer responded to the odor with fearful behavior, indicating that the memory had been successfully disrupted. The findings might someday translate to a new kind of sleep-based therapy in people whose traumatic experiences are tied to specific sounds and smells—such as the noise of a bomb going off—that can be presented to their sleeping brain.

Current treatments for PTSD—and other persistent negative memories—often rely on exposure therapy, which inoculates patients against their fear trigger by creating a new, safe memory that springs to mind more often than the old, frightening memory. But the old memory remains. To truly diminish its power, this research suggests, we must target the unconscious mind and help the brain forget. *—Stephani Sutherland*

Parrots parroting parrots: In the wild, parrots purposely mimic the calls of a specific individual to elicit a response from that other bird.

Blunting Pain with Magnets

Altering brain activity with magnetic fields may relieve chronic pain

Treating the brain with magnets went mainstream a few years ago, when the technique proved successful at relieving major depression. Now the procedure, repetitive transcranial magnetic stimulation (rTMS), shows promise for another mysterious, hard-to-treat disorder: chronic pain.

Until now, pain seemed out of reach for rTMS because the regions involved in pain perception lie very deep within the brain. The other disorders helped by rTMS all involve brain areas close to the skull. To treat depression, for example, a single magnetic coil directs a magnetic field at the dorsolateral prefrontal cortex, a region of the brain's outer folds. When aimed at different areas of these outer folds, rTMS improves the motor symptoms of Parkinson's disease, staves off the damage of stroke, lessens the discomfort that follows nerve injury and treats obsessive-compulsive disorder. The magnetic field affects the electrical signaling used by neurons to communicate, but how exactly it improves symptoms is unclear—scientists suspect rTMS may redirect the activity of select cells or even entire brain circuits.

To extend the technique's reach, David Yeomans, a neuroscientist at Stanford University, and his colleagues used four magnets rather than one and employed high-level math to steer the resulting complex fields. Their target was an area called the anterior cingulate cortex (ACC), an area active in the experience of all types of pain, regardless of its source or nature.

The researchers aimed the magnetic impulses at the ACC of healthy volunteers for 30 minutes. Immediately afterward, subjects underwent a PET scan of brain activity. During the scan, subjects reported minute-by-minute pain sensations from a hot plate applied to their arm. After rTMS, subjects rated their pain nearly 80 percent lower than they had before treatment, and the PET scan revealed blunted activity in the ACC.

Next the researchers tested the treatment on chronic pain in people with fibromyalgia, a mysterious pain syndrome that causes pain and tenderness all over the body. Patients received a daily dose from the magnets for four weeks and saw a reduction in their daily pain by almost half, which lasted for four weeks beyond treatment.

The study, presented at last October's meeting of the Society for Neuroscience in New Orleans, shows the potential of rTMS for many kinds of pain. The procedure has become increasingly common and available since 2008, when the Food and Drug Administration approved it for treating major depression. "More psychiatrists are bringing it into their armamentarium," Yeomans says. Now that it appears this noninvasive technique "can affect pain without putting new molecules into your body," he adds, relief may be close for people for whom drug therapies have failed or simply do not exist. —*Stephani Sutherland*

$300 Cost of a typical transcranial magnetic stimulation (TMS) session. TMS therapies often include 20 to 30 sessions, at a total cost of between $6,000 and $10,000.

12/08 Date the FDA approved TMS in the U.S. to treat major depression in adults who had failed to improve on an antidepressant regimen. Canada had granted the same approval six years earlier.

1 Number of conditions TMS is approved to treat: major depressive disorder. Research suggests the technique can also help people with posttraumatic stress disorder, bipolar disorder and Parkinson's disease, among other ailments.

387 Number of recent clinical trials testing TMS for a variety of conditions, including schizophrenia, anorexia, Alzheimer's disease, autism and cerebral palsy.

1985 Year TMS was first developed and tested. Anthony T. Barker of Royal Hallamshire Hospital in Sheffield, England, used the machine to noninvasively stimulate the cerebral cortex.

Rational Thought Can Override a Generous Intuition

Our instinct is to give, until we think about it logically

Cooperation eases our way in the world, contributing to extraordinary and mundane human achievements alike. Yet even the nicest do-gooders sometimes act with self-interest. A study published recently in *Nature* sought to understand the mental processes that tip a person from generous to greedy. "By default are we selfish animals who have to exert willpower in order to cooperate?" asks David Rand, a psychologist at Harvard University who led the study. "Or are we predisposed to cooperate, but when we stop to think about it the greedy calculus of self-interest takes over?"

To peer into this aspect of human nature, Rand and his colleagues gave study participants 40 cents, then asked them to decide how much to keep for themselves and how much to donate to a common pool that would later be doubled and split evenly among those who donated. Those who quickly made up their minds donated more than those who took longer, suggesting that quick decisions based on intuition were more generous than slower, deliberative decisions.

In a follow-up study, researchers prompted participants either to trust their instincts or to mull them over when deciding. Consistent with the earlier finding, donations were higher for the intuition group.

This result suggests that our first impulse is to cooperate, but it does not necessarily mean we are genetically hardwired to do so, Rand says. Instead it may reflect a habit learned from a lifetime of fruitful cooperative experiences. The work also suggests that donation seekers would do well to leave their facts and statistics behind when courting potential donors—that pitch could backfire by promoting a ruminative, miserly mind-set. —***Michele Solis***

SCOTT GOLDSMITH *Aurora Photos*

M Apes experience a midlife crisis, too. Captive chimps and orangutans show a dip in well-being in their late 20s to mid-30s, their middle age,

A GUIDE TO MASTERING YOUR WORLD

When we think about the things we do every day—driving, working, parenting—we realize that even with tasks we are generally good at, there is always room for improvement. Luckily, scientists are on the case. Visit this column in every issue to find tips for acing life.

—The Editors

How to Be a Better **Driver**

#1 **Take up meditation.** Driving is the ultimate multitasking activity. Your brain constantly switches among actions—looking for brake lights ahead, checking the mirrors, watching for pedestrians, listening for horns and sirens, glancing at the speedometer (and watching for cops in the rearview mirror if you're speeding). A recent study at the University of Washington found that people who trained in mindfulness meditation two hours a week for eight weeks were better able to focus during multitasking tests than those who never meditated. The training appeared to help them notice interruptions (in the study, a computer alert) without totally losing focus on the task at hand. Although these findings cannot be directly extrapolated to the open road, improving your brain's ability to be focused and nimble is bound to help.

#2 **Put your cell phone in the trunk.** You already know texting while driving is deadly, but chances are you feel pretty safe using a hands-free cell to chat. After all, it's legal. But those policies are misguided and deceptive, says Paul Atchley, a psychologist in the Transportation Research Institute at the University of Kansas. "All the studies that have been done by cognitive psychologists or that have looked at phone records have found that hands-free and handheld [phone use] lead to the same amount of risk while driving." It's the conversation, not the act of manipulating a phone, that distracts the brain, Atchley explains. (In-person conversations are much less problematic because the passengers are usually tuned in to driving conditions and able to hold their tongue if necessary.) "It's very difficult for your brain to ignore social input," Atchley says—we are wired to attend closely to messages coming in from our peers. That's why he recommends you put your phone in the trunk (or turn it off): "If it's within arm's reach, you're going to go for it. Even if the phone's in the glove box. I've seen people engage in all sorts of acrobatics." You're better off if you just can't hear it.

#3 **Drive more.** Any complicated activity requires your prefrontal cortex, a high-level control area of the brain, to understand the task's rules and to prioritize information. "Training has a big effect on that," Atchley says. Younger adults and other less experienced drivers, for instance, are not as good at deciding where to place their attention—they may spend too much time staring at the bumper in front of them instead of looking several cars ahead to anticipate slowing or sudden stops. Frequent driving trains the brain to focus on the right things, Atchley explains. If your experience is lacking, logging some hours behind the wheel will help you sharpen your skills.

#4 **Do some downward dog.** Good drivers rely on their keen visual perception to avoid sudden obstacles in the roadway and react to shifts in traffic. As strange as it may sound, several studies in India have found that yoga practice may improve exactly that type of visual acuity. In one such report, published in the *Journal of Modern Optics* in 2007, children and adults who practiced yoga for two months were able to detect that a flashing light was pulsing, rather than held steady, at significantly higher frequencies than control subjects. The meditative qualities of yoga (as per the first suggestion above) are very likely responsible for the improvement.

#5 **Assume the worst.** At any given time you can assume that at least 10 percent of other drivers are distracted, Atchley says, which studies have found makes them even more dangerous than drunk drivers. Defensive driving courses suggest you pay attention to the cars around you and be prepared for sudden stops or swerves. Atchley says he drives all the time "under the assumption that everyone else is out there to kill me" and doing so, he reports, has saved him from wrecks twice in recent memory.

—Sunny Sea Gold

Head vs. Heart in Negotiations

When to empathize and when to see things through another's eyes

In table tennis matches, marital spats and job negotiations, you are advised to get inside the other person's head. But that can mean one of two things: to cognitively take that person's perspective or to emotionally empathize. New research reported in the January issue of *Personality and Social Psychology Bulletin* explores these two approaches and shows that there is a time and a place for each.

In a complex war game, players decided in each round whether to disarm or attack. The game models any ongoing relationship with conflicting goals, including "a lot of work life, really," says the paper's lead author, Debra Gilin of Saint Mary's University in Nova Scotia. Subjects who scored higher on a perspective-taking scale—those who typically try to see the other side of an argument—fared well. But those high in empathy—who feel another's pain acutely—suffered for their soft-heartedness.

In a second experiment, undergraduates interacted in groups of three, then secretly picked a partner for a money-making round; the goal was a mutual match. In this coalition-building task—modeling real-life networking or relational disputes—empathy paid off more than perspective taking. In a third experiment, using the same setup as the second, researchers instructed the volunteers to focus on empathy rather than perspective taking, which made them more emotionally responsive and doubled their chances of a match.

"What I'm very excited about with this work is the inherent trainability of each of these mental activities," Gilin says—no matter what your natural tendencies, you can choose to wield the mind-set the situation calls for. She emphasizes, however, that in many complex interactions, you are better off using your head *and* your heart.

—Matthew Hutson

PAUL PANTAZESCU *iStockphoto (top left)*; ANDREY KRASNOV *iStockphoto (top right)*; CAROL YEPES *Getty Images (bottom)*

before rebounding in old age. | Guppies bred to have bigger brains also had smaller guts and fewer offspring than their dumber counterparts.

Is Cocoa the Brain Drug of the Future?

By Daisy Yuhas

Cognition-Boosting Compounds

It's news chocolate lovers have been craving: raw cocoa may be packed with brain-boosting compounds. Researchers at the University of L'Aquila in Italy, with scientists from Mars, Inc., and their colleagues published findings last September that suggest cognitive function in the elderly is improved by ingesting high levels of natural compounds found in cocoa called flavanols. The study included 90 individuals with mild cognitive impairment, a precursor to Alzheimer's disease. Subjects who drank a cocoa beverage containing either moderate or high levels of flavanols daily for eight weeks demonstrated greater cognitive function than those who consumed low levels of flavanols on three separate tests that measured factors that included verbal fluency, visual searching and attention.

Exactly how cocoa causes these changes is still unknown, but emerging research points to one flavanol in particular: (-)-epicatechin, pronounced "minus epicatechin." Its name signifies its structure, differentiating it from other catechins, organic compounds highly abundant in cocoa and present in apples, wine and tea. The graph below shows how (-)-epicatechin fits into the world of brain-altering food molecules. Other studies suggest that the compound supports increased circulation and the growth of blood vessels, which could explain improvements in cognition, because better blood flow would bring the brain more oxygen and improve its function.

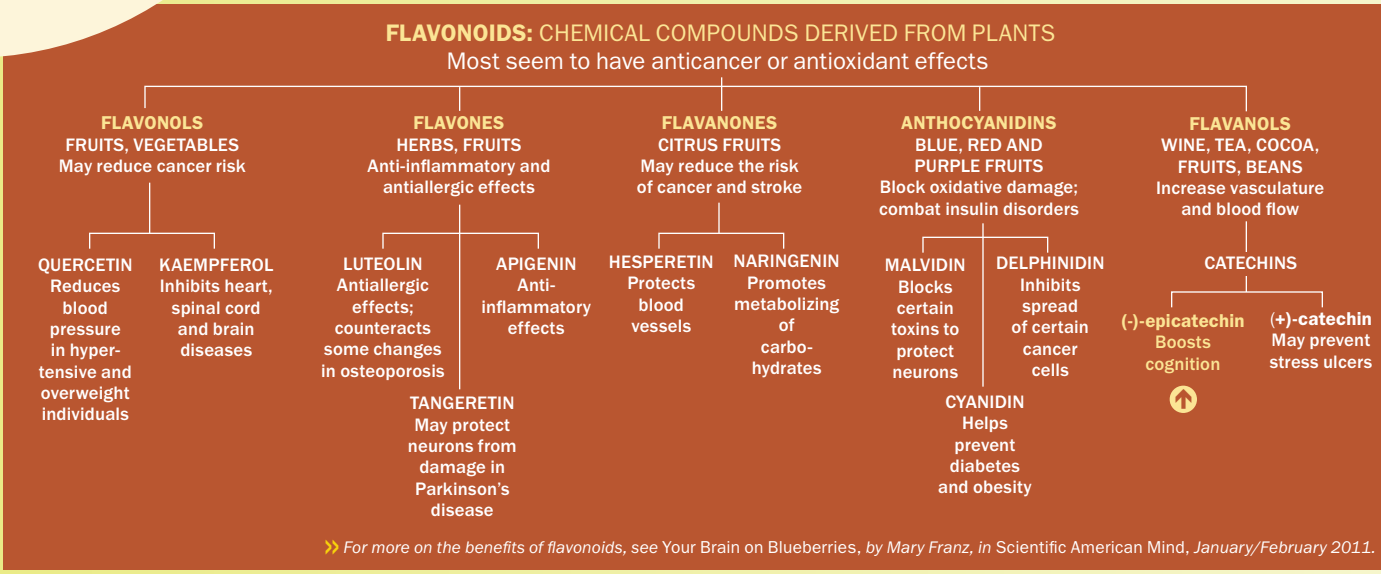
Animal research has already demonstrated how pure (-)-epicatechin enhances memory. Findings published last October in the *Journal of Experimental Biology* note that snails can remember a trained task—such as holding their breath in deoxygenated water—for more than a day when given (-)-epicatechin but for less than three hours without the flavanol. Salk Institute neuroscientist Fred Gage and his colleagues found previously that (-)-epicatechin improves spatial memory and increases vasculature in mice. "It's amazing that a single dietary change could have such profound effects on behavior," Gage says. If further research confirms the compound's cognitive effects, flavanol supplements—or raw cocoa beans—could be just what the doctor ordered.

So, Can We Binge on Chocolate Now?

Nope, sorry. A food's origin, processing, storage and preparation can each alter its chemical composition. As a result, it is nearly impossible to predict which flavanols—and how many—remain in your bonbon or cup of tea. Tragically for chocoholics, most methods of processing cocoa remove many of the flavanols found in the raw plant. Even dark chocolate,

The Kuna-Cocoa Connection

The Kuna Indians who live on the San Blas Islands off Panama drink an average of five cups of high-flavanol cocoa daily. The island population is also remarkable for extremely low rates of hypertension, unlike the Kuna on the mainland, who consume processed cocoa mix low in flavanols. Researchers, suspecting the island Kuna's staggering cocoa consumption might account for their superior health, began investigating the health effects of cocoa's raw compounds. This investigation led to the finding that (-)-epicatechin, one particularly abundant cocoa compound, supports circulation.



» *For more on the benefits of flavonoids, see* Your Brain on Blueberries, *by Mary Franz, in* Scientific American Mind, *January/February 2011.*

M Sleep medications are the second most common drug taken by astronauts, after painkillers. Most astronauts are sleep-deprived, averaging

MATTHIAS HOFFMANN Getty Images (*left*); PHOTO RESEARCHERS, INC. (*right*)

touted as the "healthy" option, can be treated such that the cocoa darkens while flavanols are stripped.

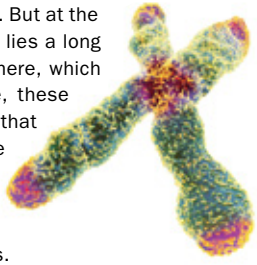
Researchers are only beginning to establish standards for measuring flavanol content in chocolate. A typical one and a half ounce chocolate bar might contain about 50 milligrams of flavanols, which means you would need to consume 10 to 20 bars daily to approach the flavanol levels used in the University of L'Aquila study. At that point, the sugars and fats in these sweet confections would probably outweigh any possible brain benefits. Mars Botanical nutritionist and toxicologist Catherine Kwik-Uribe, an author on the University of L'Aquila study, says, "There's now even more reasons to enjoy tea, apples and chocolate. But diversity and variety in your diet remain key."

Smart People Eat Chocolate?

The more chocolate a population consumes, the more Nobel Laureates it has: Columbia University's Franz Messerli discovered a positive correlation between annual chocolate consumption per capita and a country's number of Nobel Prize winners per 10 million people. The study is not meant to seriously imply that brilliance is the result of chocolate consumption—although Messerli believes chocolate probably has some benefits, his analysis was inspired purely by whimsical curiosity and exemplifies the hazards of reading too much into a correlation.

Clues about Aging from Chromosome Caps

Chronic pain and anxiety may prematurely age our DNA



When we think of the DNA that makes up our chromosomes, we usually focus on our genes. But at the end of every chromosome in our body lies a long chain of repetitive DNA called a telomere, which acts as a protective cap. As we age, these caps get shorter. Now studies find that chronic pain and phobic anxiety are linked with shorter telomeres, which suggests that sufferers of these ailments may be aging prematurely and points to ways to reverse that process.

Time naturally shortens telomeres because whenever a cell divides, a portion of the telomere is not replicated. But telomere length can be reduced by other stressors, too, including depression, trauma and obesity. A recent Harvard University study adds anxiety to the list. People with high phobic anxiety, such as that characteristic of panic disorder and agoraphobia, had shorter telomeres, according to the paper published in *PLOS ONE*.

Shortened telomeres have been observed in several types of cancer, coronary heart disease, hypertension, diabetes and arthritis. Thus, telomeres offer insights into an individual's cumulative exposure to and ability to cope with stress—a measure of biological rather than chronological age, says Afton Hassett, a principal investigator at the University of Michigan's Chronic Pain and Fatigue Research Center. "Accelerated telomere shortening can signal vulnerability to disease, premature aging or even death," she says.

In a study co-authored by Hassett that appeared in the October 2012 issue of the *Journal of Pain*, higher levels of chronic pain in women with fibromyalgia were strongly associated with shortened telomeres. In addition, participants with shorter telomeres had increased pain sensitivity and decreased gray matter volume in pain-processing areas of the brain. Fibromyalgia patients with high levels of both depression and pain had telomeres that looked approximately six years older than those of patients who had lower levels of depression and pain.

Researchers do not know whether the stress of living with chronic pain caused telomere shortening or whether telomere shortening, caused by other factors, made the participants more sensitive to pain. "Our feeling is that both possibilities are likely at work," Hassett says. "Either way, our findings suggest that chronic pain is a more serious condition than is often presumed, with consequences extending into health and longevity."

Fortunately, the findings of many other studies point to ways people can prevent and reduce shortened telomeres, including taking steps to reduce chronic stress and work-related exhaustion, improving diet (a December 2012 study found the Mediterranean diet to be protective), minimizing exposure to air pollution, exercising consistently, moderating alcohol consumption, and viewing stressful situations as challenges instead of threats.

—Tori Rodriguez

six hours of sleep a night. New LED fixtures could help prevent their insomnia. For full stories: ScientificAmerican.com/Mind/mar2013/stories

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Truer Than Truth

Trompe l'oeil illusions challenge your perception

BY SUSANA MARTINEZ-CONDE AND STEPHEN L. MACKNIK

> "I always tell the truth.
> Even when I lie."
> —*Al Pacino in* Scarface, *1983*

IN THE STUDIO of sculptor Tom Eckert, life appears to imitate art. A new snow shovel—Eckert cannot get much use of it in Tempe, Ariz.—hangs on the back wall, covered by a sheer piece of fabric. We had seen photographs of Eckert's art before our visit, so we suspect that the translucent curtain is carved out of wood. But the trick is on us. Eckert reveals that the shovel is wood as well, as is the "plastic" hook holding it and the two not really galvanized metal nails securing the curtain to the wall. Instead a metal fastener hidden in the back supports the entire piece, and the shovel's filmy silhouette is spray-painted onto the solid wood block that is the faux silk curtain. Elsewhere in the studio, we mistake wood sculptures for balled-up used work rags, and vice versa. Is the rag abandoned on the workbench a model for a sculpture, or are we looking at the carving instead? Only after touching it can we decide. M

SUSANA MARTINEZ-CONDE and STEPHEN L. MACKNIK are laboratory directors at the Barrow Neurological Institute in Phoenix. They serve on *Scientific American Mind*'s board of advisers and are authors of *Sleights of Mind: What the Neuroscience of Magic Reveals about Our Everyday Deceptions,* with Sandra Blakeslee, now in paperback (http://sleightsofmind.com). Their forthcoming book, *Champions of Illusion,* will be published by Scientific American/Farrar, Straus and Giroux.

MURAL: DEREK BESANT; PHOTOGRAPH COURTESY OF TOMAS ROSENFELD

BEHIND THE CURTAIN

The Flatiron Mural is artist Derek Besant's milestone outdoor public trompe l'oeil mural for the city of Toronto in Canada. The back end of the Gooderham Flatiron Building, a magnificent 1893 Victorian triangular structure with turrets and coned rooflines at the heart of Toronto's Theatre District and St. Lawrence Market, was knocked down to create a park, and five windows were punched into the firewall facade, creating an aesthetic problem. "My solution was to apply aspects of the surrounding five blocks of architecture into a sculptural facade that appears to be a giant curtain," Besant says.

TRUE LIES

According to legend, trompe l'oeil ("to trick the eye," in French) originated in a competition between artists Zeuxis and Parrhasius in ancient Greece. Zeuxis painted such lavishly appetizing grapes that birds tried to eat them. Sure of his victory, he attempted to unveil Parrhasius' painting but was crushed to realize that the curtain he tried to pull aside was the art itself. Such illusions work because your visual system uses position, shading and even the interplay of light on an object's surface to build a mental representation of the world around you. Tom Eckert, a modern-day Parrhasius, does not consider himself a trompe l'oeil artist. "Trompe l'oeil implies mimicry," Eckert says. "I create illusions." Indeed, pieces such as *The Raising of the Sphere* appear to defy the laws of nature rather than emulate them. The "silk" cloth raising the ivory ball is not fabric but wood. The thinness, detail and luster of the carving deceive our visual neurons, and we conclude that the material must lack the structural integrity to support a large, heavy object, despite what we see. The end result is not the perception of a masterful wood carving but of magic and the impossible.

ATTACK OF THE GIANT ARACHNIDS

One way to achieve spectacular trompe l'oeil illusions is through the use of anamorphic perspective. Artist Marlin Peterson painted harvestmen (which, although they are arachnids, are not actual spiders) on a Seattle rooftop. The images are stretched so as to optimize 3-D perception for viewers at the observation level of the Space Needle; other vantage points diminish the illusion. As in many trompe l'oeil illusions accomplished by painting, the expert use of shadows is critical. Peterson needed six gallons of house paint and a full-body harness to create this artwork. You can see the major steps of the process in a short video at http://marlinpeterson.com/2-minute-video-of-the-whole-mural

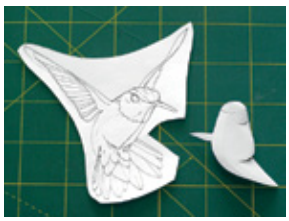
CLONES AND MIRAGES

As a young child in the backseat of the family car on a long hot Arizona highway, Eckert was struck by the persistent sight of water on the road. His parents told him it was a mirage, an illusion. He was stunned. The epiphany marked the beginning of a lifelong fascination with the boundaries of reality and our perception of it. Today Eckert is a producer of mirages. The shovel propped up against the wall is the real-world prototype of a hanging carved wood sculpture. Road mirages work because blue photons from the sky refract from the surface between cool and hot air just above the asphalt. Similarly, Eckert uses paint and carving techniques in such a way that light helps to evoke materials other than wood. Your brain sees luster and interprets it as the sheen of metal, for instance. Eckert's shovel also exemplifies the perceptual principle known as amodal completion, by which we infer a whole object even if some of its parts are occluded. Eckert did not need to carve a shovel handle, or even a full blade, to create the illusion of the complete tool. Just a touch of spray paint over the fabric "veiling" the implement, and our amodal completion mechanisms take care of the rest.

COURTESY OF TOM ECKERT (*top and bottom*); MARLIN PETERSON (*middle*)








OUTSIDE THE BOX

Consummate trompe l'oeil artists make their creations jump out of the frame, sometimes literally, as in Spanish Catalan painter Pere Borrell del Caso's *Escaping Criticism.* Paper sculptor Calvin Nicholls pulls off the illusion by creating actual 3-D objects from small pieces of paper. He starts with a 2-D detail drawing, which becomes a pattern for all the paper pieces he will cut. Then he traces individual pieces from the drawing and transfers them to the actual paper used in the sculpture, attaching them with minute amounts of glue.

HANDCRAFT

Painter Annie Ralli and photographer Ray Massey give new meaning to the term of handwriting. If you have not seen the illusion yet, look again: *There. Is. No. Pen.* The illusion is part of a series for Ecclesiastical Insurance, a company using the byline "You're in good hands." Notice how cleverly the pen's "metal" clip disguises the index finger's first knuckle. The perceptual principle known as good continuation (our perception that the paint lines defining the pen make up a single uninterrupted object) plays a big role in the deception.

PENCIL ME IN

Portuguese lawyer and self-described art hobbyist Samuel Silva creates astonishing photorealistic drawings with regular ballpoint pens. *Redhead Girl,* based on a photograph by Russian photographer Kritina Taraina, took approximately 30 hours and seven ballpoint pen colors to complete. "It takes me forever to do my works," Silva writes on his Deviantart page. He crosshatches in layers to create blending and the illusion of colors that he does not actually use and cleans his pen every minute or two to prevent ink blobs.

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COURTESY OF PERE BORRELL DEL CASO (*top, far left*); COURTESY OF CALVIN NICHOLLS/CALVINNICHOLLS.COM (*top, center and right*); RAY MASSEY (*bottom left*); COURTESY OF SAMUEL SILVA (*bottom right*)

To Drink or Not to Drink

For pregnant women, is that still a question?

BY MELINDA WENNER MOYER

GETTY IMAGES

ON THE NIGHT of my 32nd birthday, my husband and I enjoyed a delicious dinner while on vacation in Orvieto, Italy. To complement my pasta, I drank a single glass of red wine, my first since learning I was pregnant four months earlier. Even now my indulgence that evening inspires periodic pangs of guilt: Did I stunt my son's potential by sipping that Sangiovese?

Nobody questions the notion that heavy drinking during pregnancy is harmful. It can cause facial abnormalities, central nervous system problems and stunted growth. But evidence regarding the effects of light or occasional drinking is mixed. In five epidemiological studies published in 2012, medical psychologist Erik Mortensen of the University of Copenhagen and his colleagues found that five-year-old children born to women who had one to four drinks a week during pregnancy displayed no deficits in general intelligence, attention or other types of higher-order thinking. On the other hand, in 2011 psychiatrist Nancy Day of the University of Pittsburgh and her colleagues reported that teens born to women who averaged more than one drink a week during pregnancy were twice as likely as those born to nondrinkers to have conduct disorder, a condition characterized by theft, deceit or violence.

The truth is hard to discern because research on the issue is fraught with problems. The ideal type of experiment is not ethical: scientists cannot randomly assign one group of women to drink during pregnancy and compare the outcome with those instructed to abstain. As a result, they must compare what happens to women who *choose* to drink during pregnancy with those who do not, and these women often differ in important ways. All things considered, having an occasional drink during those nine months—say, one or two a week—probably poses little, if any, harm. Still, some experts warn, light or sporadic drinking may have effects we do not know how to measure.

Messy Methodologies

The thorniest problems with this research involve the ways in which women who drink during pregnancy differ from those who do not. A woman who drinks moderately or heavily is more likely to smoke, use drugs and physically abuse her child than a nondrinker, all of which could worsen her son's or daughter's prognosis independent of alcohol. This woman might also have a genetic background predisposing her—and her children—to behavioral problems.

Meanwhile women who drink lightly while pregnant may have protective characteristics. Compared with abstainers, they "are often the more affluent moms, the more educated moms, and the smarter moms as well," perhaps

because they belong to a higher socioeconomic class than teetotalers, says epidemiologist Ron Gray of the National Perinatal Epidemiology Unit at the University of Oxford. This effect could explain why, in a 2010 study, clinical psychologist Monique Robinson and her colleagues at the Telethon Institute for Child Health Research in Perth, Australia, discovered that children of mothers who drank two to six drinks a week while pregnant were *less* likely to have behavioral problems in the first 14 years of their lives than were children of mothers who abstained. As with most such studies, the researchers tried to account for systematic differences in the groups, but as Robinson acknowledges, "these unmeasured factors may have influenced our results."

Another complexity: most studies assess maternal drinking through interviews, and pregnant women might lie about or underestimate their consumption out of embarrassment or shame. Lower estimates can mask harmful effects if they cause light drinkers to be incorrectly categorized as abstainers and put in the comparison group. They might, however, *inflate* the perceived risk if heavy-drinking mothers of children with deficits get incorrectly categorized as light drinkers.

Moreover, definitions of light, moderate and heavy drinking can vary enormously. Investigators who consider light drinking to be up to a drink a day tend to conclude that the practice is more harmful than those who say light drinking means up to one drink a week. (The alcohol content in "one drink" can also differ.) And many studies are based on an "average" number of drinks per time interval, which can lump together dramatically different drinking patterns—for example, imbibing one a week and bingeing on five in one night in a month.

And yet, Day says, "there's a lot of literature that shows that binge drinking may have a bigger effect." One 2009 study, for example, tied a single binge during pregnancy to hyperactivity and attention problems in children. Most studies of periodic light drinking, on the other hand, find that it has no effects.

Teasing Out the Truth

Because individual studies so often conflict, coming to a consensus about how much alcohol—if any—is safe for an expectant mother is a tall order. Nevertheless, one psychologist couple, Sandra and Joseph Jacobson of Wayne State University, has assessed a good deal of the published literature in an attempt to answer the question. They say that no obvious neurobiological deficits have been detected in children whose mothers consume less than one drink a day during pregnancy. Still, the data do not prove that a drink a day in pregnancy is without effect, Sandra Jacobson warns; it could be that researchers have not been looking at the right outcomes or that their tools are too insensitive to pick up any changes.

Gray believes the latter to be true. Although he and his colleagues have found that moderate drinking during pregnancy (which they define as an average of two to six drinks a week) has no overall effect on child IQ at age eight—the kids of the drinking moms in his cohort actually had higher IQs than the abstainers' kids—they did find, using a new genetic technique, some potential for harm.

Humans have multiple genes for proteins that break alcohol down into harmless by-products. Some people have variations in these genes that cause alcohol to linger in their bloodstream. In a November 2012 paper Gray and his colleagues reported that the more changes in these genes children of maternal drinkers have, the lower their IQs are. (The effect is weak; the IQs of children with four genetic differences were only 3.5 points lower than those of kids with two.) More important, however, the gene variations have no effect on the IQ of children born to nondrinking women, suggesting that there is at least a minimal danger to prenatal drinking for certain individuals.

Because of such findings and all the other uncertainties, policy makers are unlikely to ever give the green light to occasional drinking during pregnancy. "We will never, ever, ever know how much is safe for every individual," says biologist Kathleen K. Sulik of the University of North Carolina at Chapel Hill. What is harmless for a woman of one race, weight, nutritional status and genetic background may be dangerous for another. That said, the literature is reassuring to the many women who socially drank before realizing they were pregnant and to those who, like me, had one celebratory glass. M

No obvious deficits have been detected in children whose mothers **consume less than one drink a day** during pregnancy.

MELINDA WENNER MOYER is a science journalist based in New York City and an adjunct assistant professor at the City University of New York Graduate School of Journalism.

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A Consciousness Meter

An electromagnetic gadget to measure the level of consciousness

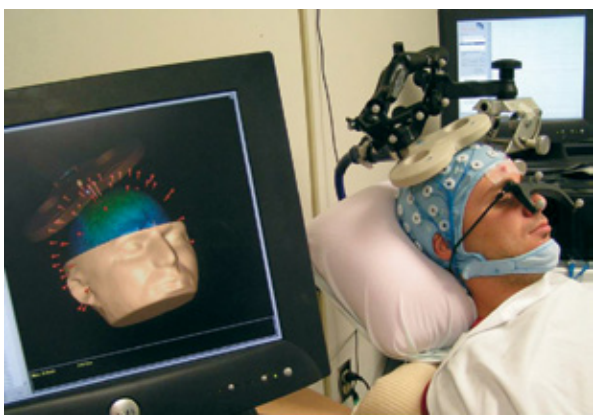
BY CHRISTOF KOCH

Measure what is measurable, and make measurable what is not so.

THIS QUOTE FROM Galileo Galilei, one of the founding fathers of science, is a call to arms for ingenious bench scientists, clinicians and theoreticians to render consciousness measurable: to build an instrument that can tell whether that prone person who is nonresponsive or behaving in a reflexlike manner is actually conscious of something—of anything. Such a "consciousness meter" should reliably distinguish between a sleeper who is experiencing a vivid dream—even if she does not recall most of its content later on—and one who is in a dreamless, deep sleep, not feeling anything. Not just black but nothing, *nichts, nada, rien*. Or between a patient who is deeply anesthetized, and oblivious to the abdominal surgery being performed on him, and the rare cases of "awareness under anesthesia." Such a device should also be able to tell whether a grievously brain-injured patient, whose electroencephalograph (EEG) might be flat but who is moaning and occasionally moving his head or limbs, is experiencing pain or distress or is truly not conscious—alive but oblivious to the world.

Most scholars of consciousness aver that to be aware of something is to have a single, integrated experience. When looking at a sunset, for instance, you cannot separate the garish purple-orange hues from the bright globe about to sink below the horizon. Unless you are colorblind, color is a holistic aspect of your experience. When you are looking out at the world, you cannot make yourself be only conscious of the left or the right half of your visual field. You experience both. Whatever information you are conscious of is wholly and completely presented to your mind; it cannot be subdivided.

Underlying this unity of consciousness is a multitude of causal interactions among the relevant parts of the brain that create the mind. If areas of the brain start to disconnect or become fragmented and balkanized, as occurs in deep sleep or in anesthesia, consciousness fades and might cease altogether. Giulio Tononi, a neuroscientist, psychiatrist and expert on sleep and consciousness at the University of Wisconsin–Madison, has made this phenomenal aspect of consciousness the centerpiece of his Integrated Information Theory of consciousness [see "A 'Complex' Theory of Consciousness," Consciousness Redux; July/August 2009].



To assess the level of consciousness, a coil-like electromagnetic device (*shown above the head*) applies a pulse; the brain's responses are recorded via EEG electrodes.

Tononi, together with his colleague Marcello Massimini, now a professor at the University of Milan, Italy, and a few others set out to measure the extent to which the brain is integrated during sleep and during various pathological states.

The Bell of Consciousness

In a series of experiments, the researchers delivered a single, high-field pulse of magnetic energy via a technique called transcranial magnetic stimulation (TMS) to the heads of volunteers. Discharging a plastic-enclosed coil of wire held against the scalp induces a brief electric current in the gray matter underneath the skull (the subject feels a slight sting from stimulation of the skin). This pulse excites brain cells and nearby fibers of passage that will, in turn, engage synaptically connected neurons in a cascade of activity that reverberates inside the head. This electrical activity quickly dies out.

Tononi and Massimini rigged the subjects' scalp with 64 electrodes for recording the EEG while subjects were either quietly resting or asleep. When awake, the volunteers' EEG following the TMS pulse showed a typical waxing and waning pattern of fast, recurrent brain waves, lasting a third of a second or so. A mathematical analysis of the EEG signals revealed that a hotspot of high-amplitude potential traveled from the premotor cortex, above which the TMS coil was positioned, to the matching premotor cortex in the other hemisphere, to the motor cortex and to the posterior parietal cortices in the back. Think of the brain as a large church bell and the TMS device as the clapper. Once struck, a well-cast bell will ring at its characteristic pitch for a considerable time. And so does the awake cortex, buzzing between 10 to 40 times a second.

In contrast, the brain of a deep sleeper acts like a stunted, badly tuned bell. Whereas the initial amplitude of the EEG is larger than when a subject is awake, its duration is much shorter, and it does not reverberate across the cortex to other connected regions. Although the neurons remain active in sleep, as evidenced by the strong, local response, integration has broken down. Little of the spatially differentiated and temporally variegated

CHRISTOF KOCH (*Koch*); COURTESY OF MARCELLO MASSIMINI *University of Milan (apparatus and patient)*

sequence of electrical activity that is typical for the awake brain is present. The same is also true of subjects who volunteered to undergo general anesthesia with propofol or xenon. The TMS pulse invariably produces a simple response that remains local, indicative of a breakdown of cortico-cortical interactions and a lessening of integration.

drawn out over hopeless decades in hospices and nursing homes, is mirrored and amplified by the love—and the resources—her family expends on her care, always hoping for a miraculous recovery.

You may recall Terri Schiavo in Florida, who lingered for 15 years in a persistent vegetative state until her medically induced death in 2005. Because of the

versity Hospital in Liège, Belgium, Massimini, Tononi and their colleagues measured the span of brain integration in such patients. They applied TMS pulses to the parietal or frontal lobes of patients who had their eyes open. The result was unambiguous. Patients in a vegetative state had simple and local EEG responses—usually a slow, single positive-negative wave (when they had any response at all)—resembling the deep sleep and anesthesia response. Contrariwise, in minimally conscious patients, the magnetic pulse triggered the complex electrical responses expected of healthy, awake subjects. Five patients were additionally recruited from intensive care as soon as they awoke from coma. Three eventually recovered awareness, and two did not.

> Think of the brain as **a large church bell** and the transcranial magnetic stimulation device as the clapper.

Probing the Mind of a Patient

When severe injury strikes the brain, consciousness may not return. A car accident, a fall, a combat wound, a drug or alcohol overdose, a near drowning—any of these can lead to profound unconsciousness. Thanks to rescue helicopters and emergency medical technicians, who quickly deliver the victim to the care of a team of specialized trauma nurses and physicians, many patients can be plucked back from the edge of death. Although this is a blessing for most, it is a curse for a few. They remain alive for years, never recovering consciousness, undead.

Impaired states of consciousness include coma, the vegetative state and the minimally conscious state. Overall arousal fluctuates from complete absence in coma, to periodic sleep-wake transitions in the vegetative state, to conscious awakenings with purposeful movements in the minimally conscious state, to more or less continual awareness.

In the U.S. alone, as many as 25,000 patients hover for years in a persistent vegetative state. What makes the situation almost unbearable is that they can look and act as if they are fully present. Indeed, such patients have daily sleep-wake cycles. When they are "awake," their eyes are open and they may move reflexively; they may grimace, turn their head, groan. To the naive observer, these movements and sounds suggest that the patient is awake, trying to communicate with loved ones. The tragedy of the ruined patient's blank and empty life,

nasty, public fight between her husband, who advocated discontinuing life support, and her parents, who believed that their daughter had some measure of awareness, the case was litigated up and down the judicial chain, and eventually drew in then president George W. Bush. Medically, her case was uncontroversial. She had brief episodes of automatisms: head turning, eye movements and the like, but no reproducible or consistent, purposeful behavior. Her EEG was flat, indicating that her cerebral cortex had shut down. Her condition failed to improve over many years. The autopsy showed that her cortex had shrunk by half, with her visual centers atrophied; thus, contrary to public reports at the time, she could not have seen anything.

In contrast to Schiavo, minimally conscious patients have fluctuating signs of nonreflexive reactions, such as pursuing a target with their eyes or making verbal or hand responses to simple commands. Whereas consciousness has fled patients in a vegetative state, it is partially preserved in minimally conscious ones. It is, of course, absolutely critical to tell the difference between one and the other. Yet this is often not possible with purely behavioral-based measures.

Neurologist Steven Laureys of Uni-

The onset of consciousness in those patients who did recover was preceded by a lengthening and complexification of the EEG response to the magnetic pulses—they progressed from a single localized wave to a much richer spatiotemporal pattern. In other words, this method can act as a crude consciousness meter. A miniaturized TMS coil in combination with an EEG device with a handful of electrodes can easily be assembled into an instrument.

In this way, theoretical insights into consciousness are married to clinical practice that benefits many. **M**

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A focus on the present, dubbed mindfulness, can make you happier and healthier. Training to deepen your immersion in the moment works by improving attention

By Amishi P. Jha

BEING IN THE NOW

Pulling into a parking spot at work, you realize you have no recollection of the drive that got you there. On reaching the bottom of a page in a book, you are frustrated that you have failed to understand what you just read. In conversation, you suddenly become aware that you have no idea what the person speaking to you has said.

These episodes are symptoms of a distracted mind. You were thinking about a vacation while reading a report or reliving a hurtful exchange with a friend instead of paying attention to the road or conversation. Whether the mind journeys to the future or the past, whether the thoughts that whisked

Photoillustration by Aaron Goodman

Modern mindfulness practices have their roots in customs that have been integral to Eastern cultures for millennia.

you away were useful, pleasant or uncomfortable, the consequences are the same. You missed the present, the experience of the moment, as it was unfolding. Your mind was hijacked into mental time travel.

Distinct from deliberate daydreaming, our mind gets offtrack in this fashion almost half the time, according to studies in which people report by smartphone what they are doing, feeling and thinking throughout the day. Such mental meandering is tied to negative mood. Chronic psychological stress, suffered by millions, may be built on a mind consumed by rumination, worry or fear about many topics. This type of diffused and unstable focus impairs performance, too. In moments that demand quick decisions and action, the consequences of diverted attention and perception could be deadly.

The opposite of a wandering mind is a mindful one. Mindfulness is a mental mode of being engaged in the present moment without evaluating or emotionally reacting to it. Hundreds of articles lay out evidence showing that training to become more mindful reduces psychological stress and improves both mental and physical health, alleviating depression, anxiety, loneliness and chronic pain [*see box on page 33 for a sample exercise*]. More than 250 medical centers worldwide now offer mindfulness-based therapies for mood and other disorders.

Now findings from my laboratory and others have revealed a surprising mechanism for these benefits. Mindfulness training works, at least in part, by strengthening the brain's ability to pay attention. Although video games and medication can also sharpen focus [see "Brain Changing Games," by Lydia Denworth; Scientific American Mind, January/February 2013], mindfulness training uniquely builds the ability to direct attention at will through the sea of internal and external stimulation while also allowing for greater awareness of what is happening in the moment. Whether research findings in small groups of individuals can be scaled up to society at large remains to be seen. Yet the overarching message seems to be that the more people engage in such training, the happier and healthier we all will be.

Salve for Sadness

For millennia Eastern cultures have proffered various forms of what we now call mindfulness meditation as a solution to the conundrum of human suffering. Ancient texts detail precise training exercises to cultivate attention to ongoing perceptual experience rather than conceptual trains of thought. People have been engaging in mindfulness exercises ever since, claiming they improve mental clarity and calm and even promote longevity.

One broad category, referred to as focused attention practices, guides individuals to select a specific sensation, tied to breathing, for example, on which to focus. Instructions encourage the practitioner to notice when his or her mind goes astray and simply return attention back to his or her immediate sensations. Another type, called receptive or open-monitoring practices, coaches participants to watch what enters, then drops out of, consciousness moment by moment. Think of hearing the faint sound of a fire truck siren in the distance. The sound becomes louder as the truck approaches, then fainter again as it passes. You may notice that initially the siren is part of a vast sea of sounds, later that it is the most salient sound, only to fade into the background again. Thoughts, emotions and other sensations may similarly grow and diminish as we remain in a watchful monitoring mode. Many sages, beginning with Buddha Siddhartha Gautama, have advocated repeated engagement in these forms of meditation as a route to increasing mindfulness in daily life.

It was not until the late 1970s that research on mindfulness began to get traction in the psycholog-

ALISON WRIGHT *Getty Images*

FAST FACTS

Pausing on the Present

1» **Mindfulness is a mental mode of being engaged in the present moment without evaluating or emotionally reacting to it.**

2» **More than 250 medical centers worldwide now offer mindfulness-based therapies for mood and other disorders.**

3» **Mindfulness training works, at least in part, by strengthening the brain's ability to pay attention.**

LESLEY MAGNO Getty Images

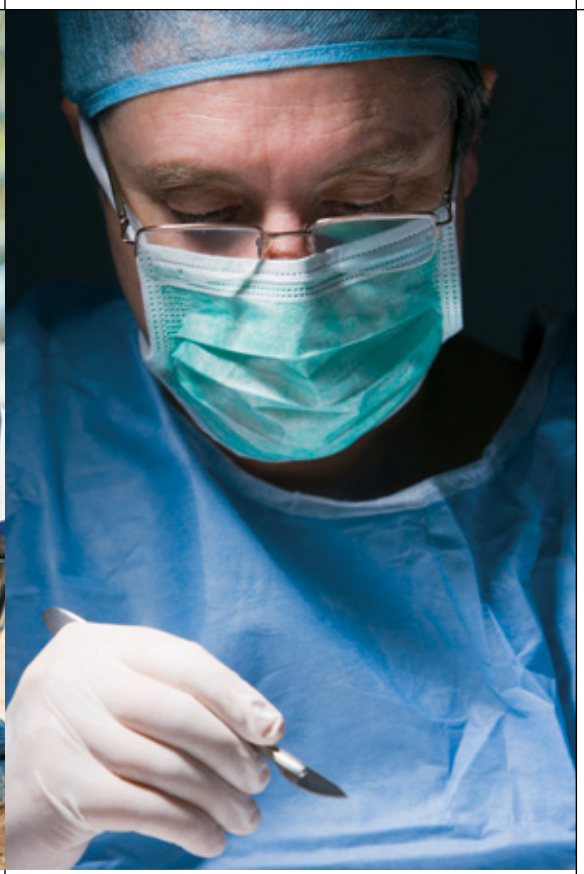
Learning to be more mindful, or aware of what is happening now, is an antidote to rumination, worry and fear—and their effects on mental health.

ical and medical sciences. At that time, biologist Jon Kabat-Zinn of the University of Massachusetts Medical School developed a secular outpatient program called Mindfulness-Based Stress Reduction (MBSR) that includes a manual for trainers. The eight-week program emphasizes two aspects of attention: the ability to voluntarily *focus* attention, narrowing our thoughts to keep out distractions, and to *monitor* ongoing thoughts, feelings and sensations—without getting caught up in them—a phenomenon called meta-awareness. Working together, focusing and monitoring prevent our mind from wandering without our knowledge and escaping our control.

In the past decade researchers have established that MBSR and similar techniques can be used to successfully treat a wide variety of illnesses. In 2011 graduate student Jacob Piet and professor of psychology Esben Hougaard of the University of Aarhus in Denmark published a meta-analysis (quantitative review) of six studies with a total of 593 patients, who were given mindfulness-based cognitive therapy to prevent relapse into depression. This technique, developed by psychologist Zindel Segal and his colleagues at the University of Toronto, is modeled after MBSR but emphasizes the idea that the negative thoughts that can spark a depressive episode are fleeting mental events. Their transitory nature means that patients can choose to attend to them or not.

After receiving mindfulness-based cognitive therapy, patients often report noticing that the experience of sadness fluctuates moment to moment and that negative thoughts lose their power over

■ After receiving mindfulness-based cognitive therapy, patients report noticing that negative thoughts lose their power over time.



By improving the ability to direct and monitor attention, mindfulness meditation could enhance people's performance in pursuits as diverse as sports and surgery.

time. Indeed, Piet and Hougaard report that depressed patients with three or more episodes of major depression who undertook this cognitive mindfulness training had significantly lower relapse rates than those given the usual care or a placebo. Mindfulness training in its various forms has similarly helped alleviate suffering from psychological illnesses such as anxiety, panic disorders and phobias.

Mindfulness exercises can ameliorate bodily ills as well—most notably chronic pain. Because these exercises can lessen psychological stress, they can reduce the emotional contribution to pain, which is often quite significant. In fact, one of MBSR's first clinical uses was for the treatment of chronic pain. In 1985 Kabat-Zinn and his colleagues enrolled 90 patients with chronic pain in his eight-week program, measuring their levels of pain, negative mood and anxiety before and after their participation. The researchers saw significant reductions in these negative symptoms after the program ended but found no beneficial changes in 21 patients who received traditional treatment methods such as nerve blocks, physical therapy and antidepressants. Strikingly, the benefits from Kabat-Zinn's exercises were maintained for up to 15 months, and patients reported continuing the exercises on their own.

Recent data suggest that mindfulness training can also help with less severe, but still significant, psychological issues such as job-related burnout in medical professionals and teachers. Although the training may not reduce the number of job-related stressors, it helps to change a person's relation to these stressors and renew his or her sense of curiosity and connection with patients or students.

Social stressors, such as loneliness in elders, can also diminish with the practice of mindfulness. In 2012 psychologist J. David Creswell and his colleagues at Carnegie Mellon University assigned 20 people between the ages of 55 and 85 to participate in an MBSR course and another 20 such individuals to receive no therapy. Creswell's team found that self-reported loneliness, as assessed by a questionnaire, dropped among those receiving MBSR but remained unchanged in the others. Loneliness is not directly related to the number of social contacts

GETTY IMAGES

(The Author)

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a person has. In fact, programs to increase social engagement among older people do not necessarily lessen their feelings of disconnectedness. Mindfulness training may make loneliness less distressing by helping people recognize that, although they feel alone, their loneliness does not define them.

What is more, in Creswell's study this psychological improvement was accompanied by changes in immune function. The mindfulness course reduced blood levels of pro-inflammatory proteins, suggesting that this training may also lower the risk in older adults of inflammatory diseases such as lupus and rheumatoid arthritis. Other studies indicate that mindfulness training can relieve symptoms of ailments that stress can exacerbate, including psoriasis, dermatitis, fibromyalgia and irritable bowel disease.

Being mindful may even relate to a biological indicator of longevity. In a study published in 2012 psychologist Elissa S. Epel and her colleagues at the University of California, San Francisco, found that people who have a greater propensity toward mind wandering were found to have shorter caps, called telomeres, at the ends of their chromosomes than those whose minds were more often anchored in the present. Shorter telomeres are associated with a shorter life span for an organism. As a result, the authors suggested in their paper that "a present attentional state may promote a healthy biochemical milieu and, in turn, cell longevity."

■ Mindfulness training can relieve symptoms of ailments that stress can exacerbate such as psoriasis and fibromyalgia.

Finding Focus

As mindfulness training was gaining traction as a wellness-promotion and stress-reduction tool in the early 2000s, I began to consider, from a cognitive perspective, how it might work. As late as 2007 my field—cognitive neuroscience—had yet to weigh in on what is happening in the brain when people practice mindfulness. I wondered if my own expertise on the brain bases of attention might be able to fill the gaps in our understanding. After all, there were striking parallels between current theories of distinct brain systems supporting attention and accounts from ancient texts describing practices to cultivate calm focus and open, accepting curiosity of events as they unfold.

Physician Michael Baime of the University of Pennsylvania, psychologist Jason Krompinger, now at Harvard Medical School, and I set out to investigate this link by asking 34 medical and nursing students to perform a test of visual attention. They had to detect a target appearing at one of two locations on a computer screen. Sometimes they were told where and when the target would appear; other times they were either alerted only to when it would appear or given no warning at all. Then for eight weeks, half the subjects engaged in mindfulness exercises that required concentrated focus for 30 minutes a day. When they took the test again, these volunteers were 5 percent faster at responding during the trials in which they were told both where and when the target would appear, indicating that they were better at directing their attention to the cued location than the untrained participants, who showed no improvement. The results were the first hint that we were on the right track in linking mindfulness training with a person's ability to willfully orient his or her attention in space.

We then separately tested the effects of the open-monitoring approach on attention by recruiting another 17 individuals with previous experience in mindfulness training to participate in a one-month intensive mindfulness retreat. The retreat included receptive, open-monitoring practices in addition to focusing exercises. At the end of the month, the participants had improved their ability to detect the target when there was no warning. Their responses were 7 percent faster than other groups receiving only concentrated exercises or no training, suggesting that open-monitoring practices tune bottom-up attention, making people more aware of what is going on around them. Since this study, experiments from various research teams have found similar benefits on attention from these two types of mindfulness exercises.

Mindfulness training can tune our ability to attend to tactile as well as visual stimulation. In 2011 psychologist Catherine Kerr and her colleagues at Harvard enrolled eight people in an eight-week MBSR course, requiring 45 minutes of daily practice. The researchers then flashed a word on a computer screen denoting a body part—say, "hand" or "foot"—that might soon be getting a light, barely detectable tap. While the participants watched the

Amishi P. Jha and Brigadier General Walter Piatt review brain-wave recording procedures, along with a memory test military service members take before and after mindfulness training.

words and felt the taps, Kerr and her colleagues measured ongoing seven- to 10-hertz magnetic signals at the scalp from neurons representing the hand in the somatosensory cortex, a region of the brain that registers sensations from various body parts. Among the participants who took the course, but not in eight untrained individuals, the researchers saw greater signal power in the hand area of the brain after seeing "hand" compared with "foot," reflecting an increased readiness of neurons to fire, a brain signature of attention. This anticipatory activity, before the hand was tapped, suggests that MBSR tunes people's ability to generate high-resolution representations of their hand or other body parts at will, sharpening body awareness.

(Further Reading)

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These results may help explain how MBSR may alleviate the psychological impact of chronic pain. If a person can willfully direct attention to specific body parts that are experiencing pain, he or she may notice subtle fluctuations in sensations at those locations, to the point where the idea of pain as a monolithic "thing" may fall apart into ever changing sensations. As a result, the pain may become less distressing. Similar mechanisms tied to attention may be at play for psychological and social stressors. In these cases, present-moment focus and monitoring of sadness, say, or loneliness, may help minimize the perceived significance of these forms of suffering.

Recently my colleagues and I have connected mindfulness training to both a sharpening of focus and improved mood. In a study published in 2010 we tested 51 U.S. marines, 34 of whom engaged in mindfulness exercises involving focused attention developed by Elizabeth A. Stanley, a professor of security studies at Georgetown University. We asked marines to remember letters that appeared on a computer screen before and after simple math problems, which they were supposed to solve. This task assessed their working memory, the ability to hold and manipulate selected information over a few to several seconds. Working memory, akin to a mental white board, works hand in hand with attention, which puts the information onto the board and keeps distractions off of it.

People with higher working memory capacity—think of a bigger whiteboard—are better able to regulate mood and prevent their minds from getting offtrack. Unfortunately, working memory capacity shrinks under stress, which marines experience as they prepare for military deployment. Indeed, we found that marines who did not receive mindfulness training had lower working memory capacity, more itinerant minds and worse mood at the end of the eight weeks than they did when the study began. Marines who engaged in mindfulness exercises for 12 minutes or more every day, however, kept their working memory capacity, focus and mood stable over the eight weeks. The more an individual practiced, the better he or she fared, with those who practiced the most showing improvements in memory and mood by the end of the study. These results are in line with other findings that suggest that better control of attention is the most effective way to regulate mood.

Several groups of researchers have found that these improvements in performance correspond to tractable changes in brain structure and function. In the brain, a network of regions, including certain

COURTESY OF AMISHI P. JHA LAB *University of Miami*

sections of the prefrontal and parietal cortex (at the front and top surface of the brain), support voluntary or top-down selective attention. Meanwhile other parts of the prefrontal and parietal cortex, together with the insula, form a network that monitors what is happening in a bottom-up fashion. In 2012 neuroscientist Eileen Luders and her colleagues at the University of California, Los Angeles, reported that certain parts of this bottom-up network—prominently the insula—are more intricately and tightly folded in people who have engaged in mindfulness training for an average of 20 years compared with otherwise similar untrained individuals. The additional folds are very likely to indicate more efficient communication among neurons in these regions, which may underpin better bottom-up attention.

Cultivating Consciousness

Attention is almost certainly not the only way mindfulness training works. Mindfulness techniques are most likely to alter and strengthen many other brain networks and processes. Several studies suggest, for example, that such exercises shift the mind from a narrative mode of viewing the self, in which the central character in the story is you, to a more experiential view, in which you observe the unfolding of your thoughts, feelings and sensations over time. Other studies indicate that emotional changes or the calming of stress-induced physiological symptoms may drive psychological improvements. Whether better attention relates to these other suggested mechanisms is not yet clear.

Whatever the mechanism, efforts to become more mindful could make a considerable dent in human suffering. Working mindfulness practices into your daily routine can bring benefits similar to those of physical exercise. As an antidote to an ambling mind, negative mood and stress, such mental workouts can help virtually everyone live a happier, healthier and more fulfilled life. Students or athletes who want to boost their performance, for example, and parents, teachers or caregivers wishing to be more attentive to others' needs may all find mindfulness training useful. Such training may be particularly essential, however, for people such as soldiers, surgeons and air traffic controllers whose ability to control and monitor their attention may be a matter of life or death.

As we learn to grab a hold of our own attention, we gain control of our own happiness and health. Perhaps the time is *now* for us all to consider cultivating greater awareness of our moment-to-moment experiences and the contents of our consciousness. M

Capturing Attention

DAVID TROOD Getty Images

Mindfulness, a focus on the present moment without judgment, has proven benefits for health and happiness. Engaging in daily mindfulness workouts can help you assume this mental mode more often in your daily life. The following 10- to 15-minute mindfulness exercise is designed to train two types of attention: concentrative focus, a narrowing of your attention, and open monitoring, a broad awareness of sensations and surroundings.

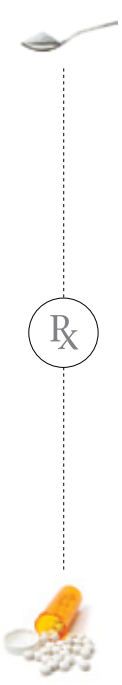
Here's what to do:

- Sit in an upright, stable position, hands resting on your thighs or cradled together.
- Lower or close your eyes, whichever is more comfortable for you.
- Attend to your breath, following its movement throughout your body.
- Notice the sensations around your belly as air flows into and out of your nose or mouth. You have been breathing all day—all of your life—and in this moment, you are simply noticing your breath.
- Select one area of your body affected by your breathing and focus your attention there. Control your focus, not the breathing itself.
- When you notice your mind wandering—and it will—bring your attention back to your breath.
- After five to 10 minutes, switch from focusing to monitoring. Think of your mind as a vast open sky and your thoughts, feelings and sensations as passing clouds.
- Feel your whole body move with your breath. Be receptive to your sensations, noticing what arises in the moment. Be attentive to the changing quality of experience—sounds, aromas, the caress of a breeze … thoughts.
- After about five more minutes, lift your gaze or open your eyes.

—Scott Rogers, director of Programs and Training, Mindfulness Research and Practice Initiative, University of Miami

When Pretending Is the Remedy

Scientists are dissecting the placebo effect in hopes of deploying its active ingredients as treatments | **By Trisha Gura**



Back in the 18th century, German physician Franz Mesmer peddled a concept called animal magnetism. Creatures contain a universal fluid, he asserted, that when blocked in flow, caused sickness. Mesmer used magnetized objects to redirect that flow in patients, initiating unusual body sensations, fainting, vomiting or violent convulsions that ended in profound salubrious effects.

Skeptical, Benjamin Franklin and French chemist Antoine-Laurent Lavoisier simulated one of Mesmer's typical sessions in 1784. They asked people suffering from ailments ranging from asthma to epilepsy to hug "magnetized" trees. The people swooned and shook, as expected. But then the researchers divulged that the trees were never magnetized. And everyone realized that something else was inducing the reactions to the trees. That something was later dubbed the placebo effect.

In the centuries since, the placebo response—that is, the beneficial result in a patient from an inert substance or bogus procedure—has emerged repeatedly in many forms. Researchers have shown that sugar pills reverse insomnia, fake injections relieve pain and sham surgeries treat Parkinson's disease.

Responses to such dummy treatments can be surprisingly powerful. Studies on placebos for depression show, for example, that they can reproduce more than 80 percent of the positive effects of antidepressants. That potential power has motivated a growing cadre of researchers to study the placebo, backed by an abundance of support from federal agencies, foundations, pharmaceutical companies and advocates for alternative health. "Right now we are overfunded," says Ted J. Kaptchuk, director of the newly launched Program in Placebo Studies at Beth Israel Deaconess Medical Center in Boston. "We have a lot of NIH projects. We are actively courting the pharmaceutical industry, and we have no problem getting entry."

One big challenge, however, is that placebo responses remain unpredictable. People given the same

OKTAY ORTAKCIOGLU *iStockphoto (spoon)*; ISTOCKPHOTO *(medicine)*; AARON GOODMAN *(sugar cube)*

The power of the placebo is most prominent in mental illness and other ailments in which improvement is subjective. In disorders such as asthma, placebos may make people feel better even if objective measures indicate they do not work.

pill or potion may show wildly different reactions. The effects can vary widely by illness. Pain, insomnia, fatigue, nausea, and disturbances to bowel, urinary or sexual function seem the most amenable to placebo treatments; broken limbs the least. Attempts to explain such variation have led scientists to delve deeper into the nature of the placebo effect. They have found that it shows up most prominently in illnesses that have a strong psychological component or when improvement is measured using subjective reports from patients.

With better neuroimaging tools and more sophisticated experimental designs, investigators are deconstructing placebo responses in the brain. They are finding that placebos can tap circuits governing expectation, attention and emotion. A placebo's power in these realms depends on social and environmental cues that act around the dummy pill, prick or potion. The doctor's behavior, for example, plays an essential role. "The placebo is about the terrain of medicine," Kaptchuk observes. "What things are said; how the doctor behaves. It's the rituals and symbols—sitting in the waiting room, the patient exam, et cetera. And then, at the psychological level, it is the active ingredients of hope and trust and imagination, which are really antithetical to a scientific world."

Doctors hope to use this antithetical collection of findings to predict when and where a placebo will work and enhance its benefits in the clinic—ideally without deception. As the data reveal the biological mechanisms behind these "sham" remedies, placebos may become standard medical fare, used to augment and, in some cases, replace approved drugs and therapies. Incurable conditions, such as chronic pain, asthma and Alzheimer's disease, may one day yield to placebos, Kaptchuk suggests. Mesmer's idea of animal magnetism may have been bunk, but what he inadvertently tapped was not.

FAST FACTS

Something behind Nothing

1» **Dummy treatments can be surprisingly powerful. Placebos for depression can reproduce more than 80 percent of the positive effects of antidepressants.**

2» **In the brain, placebos tap circuits governing expectation, attention and emotion.**

3» **Doctors may someday routinely use placebos to augment and, in some cases, replace approved drugs and therapies.**

Subjective Salve

Placebos debuted in contemporary medical research, not as objects of study but as tools for clinical experiments. In 1955 Harvard Medical School physician Henry K. Beecher published a landmark report in which he estimated that 35 percent of any treatment group responded to a placebo. Entitled "The Powerful Placebo," the study offered evidence from 15 clinical trials of 1,082 patients to back up his claims of the existence of a placebo effect. He pushed for trials that compared patients taking drugs with those taking placebos. Only in 1968 did the Food and Drug Administration formally usher placebos into standard clinical trials as a way of ensuring that drugs worked as manufacturers claimed.

Meanwhile astute practitioners such as Kaptchuk were noticing something mysterious happening with their patients. Perhaps the most unusual associate professor at Harvard Medical School, Kaptchuk holds no Ph.D. or M.D. Instead, after graduating from Columbia University in 1968, he took off for Macao, China, earned a doctor of Oriental medicine (OMD) degree in 1975 and began to practice acupuncture a year later. Af-

BEAU LARK *Corbis (left)*; IAN HOOTON *Getty Images (right)*

ter 15 years, he realized that the needles themselves could not account for the curative effects of his practice. He quit and set out to explore what else was helping his patients feel better.

In studies conducted over two decades, Kaptchuk and others found that Beecher's initial estimates were flawed. For starters, Beecher had not separated patients' responses to the placebo from other phenomena, such as the fact that some patients simply got better with time. Even more curious, different placebos worked optimally for different ailments. Pills worked better for insomnia, for example, whereas shots provided the best pain relief. And placebo effects could occur by proxy. For instance, parents can help their child get better simply by feeling positive about their child's prescription.

As data reveal the mechanisms behind these "sham" remedies, placebos may become standard medical fare. Incurable conditions such as chronic pain, asthma and Alzheimer's disease may one day yield to placebos.

Just as placebo studies seemed to be gathering force, in 2001 a Danish group dropped a bombshell. Epidemiologist Asbjørn Hróbjartsson of the Nordic Cochrane Center in Copenhagen and his colleagues conducted a meta-analysis in which they reviewed 114 trials that investigated 40 clinical conditions. In each, patients randomly received either a placebo or no treatment. Investigators found little evidence that placebos had significant clinical effects. Yet in that study, entitled "Is the Placebo Powerless?" and in two others published in 2004 and 2010, Hróbjartsson also found incredible variability in placebo responses. "We are seeing a dramatic effect in some laboratories and trials but lack of effect in others," he says.

One source of that variability was in how researchers tracked improvement. If doctors measured success by medical, objective measures such as blood pressure, placebos did not appear to work. But in certain settings, if researchers tracked recovery by how patients reported they felt, then placebos revealed their potency, especially in conditions such as pain and nausea.

Indeed, in 2002 Harvard psychologist Irving Kirsch found results consistent with the idea that the power of placebos is evident mostly when improvement is subjective, as it is in mental illness. In a meta-analysis of 47 trials of six of the most widely prescribed antidepressants, Kirsch and his colleagues discovered that 82 percent of the improvement in mood, as measured by a standard questionnaire, could be duplicated by giving patients a placebo pill instead of an antidepressant. In a similar study published in 2008, Kirsch and his colleagues found that the only people in whom antidepressants worked significantly better than placebo pills were patients with the most severe cases. He reached a controversial conclusion: "Unless your patient is extremely depressed, you shouldn't be prescribing an antidepressant."

Placebos also seem to work on a subjective level in nonpsychiatric conditions, such as asthma. In a 2011 study Kaptchuk, Kirsch and their colleagues gave 46 volunteers with asthma either an inhaler with a drug (albuterol), an inhaler with saline, sham acupuncture or nothing. During each of 12 visits, researchers measured how much air the patients could inhale and exhale, both before and after treatment. The respiratory scores of those treated with albuterol rose by 20 percent, whereas all the others got just a 7 percent bump, suggesting the placebos had no effect.

But when the researchers asked the asthma sufferers to rank their respiratory discomfort on a scale of 0 to 10, everyone except those who got no treatment reported a 50 percent improvement. Even though the drug was causing a "robust" medical effect, as compared with the placebo, patients could not reliably detect the difference. Perhaps the placebo activates a mechanism that is distinct from the pharmaceutical's targeted pathway but, in some respects, is equally effective. "A medical treatment has two components: the actual pharmacological effect and the placebo component of the active treatment," Kirsch says.

The Brain against Pain

To further unravel that placebo component, neuroscientists have also been mapping the brain's response. In a pioneering 2002 study psychiatrist Predrag Petrovic of the Karolinska Institute in Sweden and his colleagues investigated the placebo's brain signature in pain relief, something scientists had previously linked to changes in the body's endorphin system. Petrovic and his colleagues told nine healthy volunteers that they would be receiving two potent painkillers, but only sometimes did the injection consist of the opioid remifentanil; in other cases, it was saline. Forty seconds after an injection, the team stimulated a subject's left hand with an electrode that either heated to the point of pain, gave off benign warmth or provided no sensation at all. Meanwhile the researchers scanned subjects' brains using positron-emission tomography.

(The Author)

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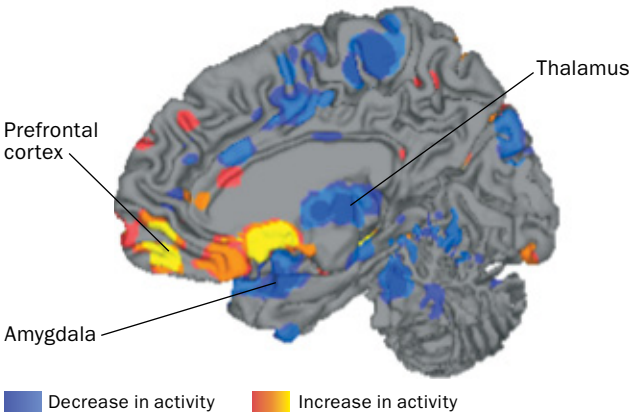
CLIVE STREETER *Getty Images (sugar cubes)*



Belief can bring pain relief. When people thought they were getting a painkiller, the prefrontal cortex, which attaches meaning to pain, suppressed emotion areas such as the amygdala and pain perception hubs such as the thalamus, bringing respite.

Both the opioid and the saline activated a network of brain regions consisting of the brain stem, a seat of the opioid system that mediates pain relief, and the rostral anterior cingulate cortex, which is rich in opioid receptors and part of the body's reward system. Petrovic proposed that placebos, as with opioids, might be working by triggering cortical areas such as the anterior cingulate that, in turn, exert control over the analgesic systems of the brain stem.

In 2004 neuroscientist Tor D. Wager of the University of Colorado at Boulder and his colleagues further dissected the painkilling effect of a placebo using MRI and found that it involved additional brain regions. (The researchers also chose pain because it is easy to manipulate in a scanner.) The researchers administered a placebo cream while giving people painful shocks or putting intense heat on their forearms. In one experiment, they gave subjects a warning cue, a red "get ready" sign, just before those subjects received the painful stimulus. With that signal, participants expected pain, unless the cream was applied, in which case they expected relief. That expectation of relief first activated a cognitive "executive" center of the brain called the prefrontal cortex. After that, activity in the pain response areas of the brain declined, and subjects reported relief. This temporal pattern of brain activity suggested that placebo pain relief involves an expectation signal from the prefrontal cortex that tells the midbrain to release opioids to meet the expectation of reprieve. "There is a cognitive mechanism driving the opioid system," says Petrovic, who, in a reanalysis of his 2002 study, also pinpointed regions of the prefrontal cortex as drivers.

The placebo effect seems to involve emotions, too. Wager went on to reanalyze his 2004 data with a computer technique that searches for patterns of brain activity that predict the best placebo responses. Wager and his colleagues reported in 2011 that a robust placebo effect was usually accompanied by changes in activity in regions of the brain that are charged with emotional appraisal, such as the insula, orbitofrontal cortex and amygdala.

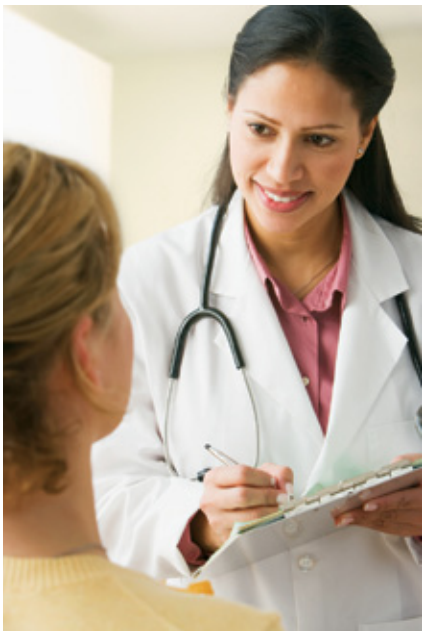
This pattern is consistent with what Wager calls "endogenous regulation," the ability of humans to reinterpret their situation. In addition to boosting expectations of respite, placebos may somehow give people a better perspective on their predicament. Under the influence of a placebo, Wager speculates, people reevaluate what their pain means, reducing its emotional significance—say, deciding the pain will abate rather than cause persistent disability. During a placebo response, "our brain is likely doing a lot of the work without our real conscious input or even in spite of our conscious desires," he says. That is, people are unconsciously engaging brain mechanisms that serve to soothe.

Surprisingly, that self-soothing process may require focusing on the pain more than thinking about something else. Wager and his colleagues conducted another study, published in 2012, in which they tried to distract individuals away from experimentally induced pain by giving them another task. But the distraction did not help the participants feel better. Instead when the researchers coaxed subjects to pay attention to the heat on their arm by asking them to rank its intensity, the subjects experienced greater relief. This outcome is consistent with "acceptance" or "relaxation response" therapies in which people surrender to their pain to better tolerate it.

Distraction from the pain did not help participants feel better. On the contrary, they felt more relief when scientists made them pay attention to the heat on their arm by asking them to rank its intensity.

Together these results suggest the placebo response consists of a particular pattern of brain activity that can be differentiated from that triggered by an active medication. Wager's team gathered backing for that idea in another study published in 2012. This time the investigators carefully separated expectation of pain relief from the effects of a medication (remifentanil). The team found that both the drug and expecting to get the drug (but actually receiving a saline placebo) reduced people's self-reported pain. More important, the expectation component worked via a separate mechanism, increasing activity in the prefrontal cortex and reducing it in emotion areas, whereas drugs influenced the pain-processing brain areas more directly and did so later, when levels of remifentanil had a chance to reach their peak in the brain. Given these findings, placebo responses could add to the effective-

FROM "DISSOCIABLE INFLUENCES OF OPIATES AND EXPECTATIONS ON PAIN," BY LAUREN Y. ATLAS ET AL., IN *JOURNAL OF NEUROSCIENCE*, VOL. 32, NO. 23; JUNE 6, 2012



Attention from a doctor can be an effective placebo. In one study, the more care and concern for a patient a doctor expressed, the more likely the patient was to report relief from irritable bowel syndrome.

ness of a painkiller—or a drug for depression, nausea or rheumatoid arthritis.

Dosing the Doctor

If placebos offer a separate brand of therapy, doctors might like to explicitly add them to a treatment regimen or enhance their effects—ideally, without having to trick patients. "The ethical problem in practice is feeding your patients the presumption that in order for a placebo to be effective," Kirsch says, "the person had to be deceived into thinking he was getting a real medication."

One way to circumvent deception is to invoke the doctor-patient relationship. In a 2008 study of 262 patients with irritable bowel syndrome (IBS), Kaptchuk's team assigned the patients to either placebo acupuncture or a waiting list. The researchers further subdivided the placebo group into those offered no conversation with the acupuncturist and those who received a heavy dose of attention, empathy and interaction from the practitioner. He or she actively listened to each patient's problem, repeated his or her words, expressed confidence, touched the patient and lapsed into 20 seconds of thoughtful silence. "We laid it on," Kaptchuk says.

The special care paid off. Researchers found a dose-response relation between the degree of doctoring and the proportion of patients who got better. Of the group sitting on a waiting list, 28 percent of people reported that their bowel symptoms improved. Of those receiving the bare-bones doctor-patient ritual, 44 percent reported significant relief. Among those who received a lot of attention from their doctor, 62 percent said they felt better. Thus, by simply manipulating a physician's bedside manner, the placebo can be dosed.

In as yet unpublished results, Kaptchuk's group discovered evidence that another aspect of this manner could be calibrated: empathy. The team gathered 12 physicians and put them in MRI scanners while the doctors thought they were offering a patient relief from the pain of a hot electrode strapped to his or her wrist. (The "patient" was really a confederate of the researchers.) In a doctor's brain, the act of providing pain relief looked a lot like the response in a patient's brain when he or she expected and perceived pain relief in previous experiments: an increase in activity in both the prefrontal cortex and the anterior insula, an indicator of empathy for pain. Doctors also reported feeling relief. "You do sort of bond and feel some kind of responsibility to the patient," says Michelle Dossett, a general practitioner in Boston who participated in the study. Finding ways to boost a doctor's empathy and ability to transmit that feeling to patients might thus lead to an effective placebo.

Physicians might also be able to productively deliver fake pills and procedures without deception. In a 2010 study Kirsch, Kaptchuk and their colleagues gave 40 patients with irritable bowel syndrome pills they described truthfully as "placebo pills made of an inert substance, like sugar pills, that have been shown in clinical studies to produce significant improvement in IBS symptoms through mind-body self-healing processes." After taking these "open label" placebos twice daily for 21 days, patients reported feeling better overall and having less severe symptoms than the 40 patients who received no treatment.

Researchers are working to better understand and manipulate both the softer, environmental and harder, brain-based aspects of placebo responses. Perhaps one day physicians will be explicitly trained to express empathy or to use language that creates hope and expectation—with the placebo effect in mind. Someday, too, MRI scans might be used to predict placebo responses for individuals in advance. "It is really turning the art of medicine into a science of the art," Kaptchuk says. "Can we really understand what is usually considered intangible, fringe or ignored and elevate it to a level of serious scientific inquiry?" Doing so, he says, would advance science and improve health. M

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JOSE LUIS PELAEZ *Getty Images*

A LIFELINE FOR ADDICTS

Restoring the brain's flexibility may help addicts act on their desire to quit

BY MICHELE SOLIS

Reid had been drinking hard since 1994, when sickness, his father's death and business troubles had him reaching for more alcohol than usual. Eventually he was knocking back 10 or more drinks a day. In 2009 his family leveled an ultimatum. He had to give up alcohol or get out.

"That choice sounds real simple, but it's very, very hard," says the 58-year-old college-educated businessman, whose last name has been withheld. "I've got a wife to die for and two of the greatest kids in the world, and I'm sitting there looking in the mirror, asking myself, 'You're going to give all this up for that drink?'" he remembers. Still, he drank, secretly downing miniature bottles of vodka while walking the dog, hiding out in the bathroom or going through the car wash.

An alcoholic's sense of being trapped in old habits reflects an underlying resistance to learning that scientists are now documenting at the molecular level. Over the past five years researchers have turned up evidence that using drugs and alcohol causes a loss of flexibility in the brain, including in the regions needed for changing habits. Even brief periods of drug use damage the junctions between neurons, known as synapses. Their healthy operation is critical to translating will into action. The very structures needed to dig a person out of addiction are eroded by drug use.

Researchers are now looking for ways to replenish this flexibility with compounds that adjust how the neurotransmitter glutamate, a chemical messenger in the brain, operates at the synapses. "We're trying to restore the brain machinery that allows a person to regain more control over their behavior," says Peter W. Kalivas, a professor at the Medical University of South Carolina, who studies the role of glutamate in addiction.

Returning the brain to a state where it is open to change, rather than resistant to it, could kick-start recovery. "This is not going to cure addiction, but it's definitely going to help," says Nora D. Volkow, director of the National Institute on Drug Abuse.

Drug-Induced Learning Problems

In the past scientists had focused primarily on how drugs take hold of the brain's reward regions. The new research on glutamate seeks to explain not how addiction sets in but why it is so hard to beat.

Even when addicts desperately want to stop, for fear of losing a job, a spouse or their life, they often still persist in taking drugs. Experts suspect this disconnect happens because drug use impairs a person's capacity to learn. Although scientists have long known that drug use induces a variety of cognitive shortcomings, during the past 10 years the learning deficit has emerged as a key reason why addicts stay addicted. In particular, addicts struggle to break old habits—even those not related to drug use.

This difficulty with developing a new routine can be measured in laboratory tests of "reversal learning" that ask a person to change how he or she responds to a familiar prompt. Addicts can learn an initial rule perfectly well, but they run into trouble when the rules change. In a 2006 study, for example,

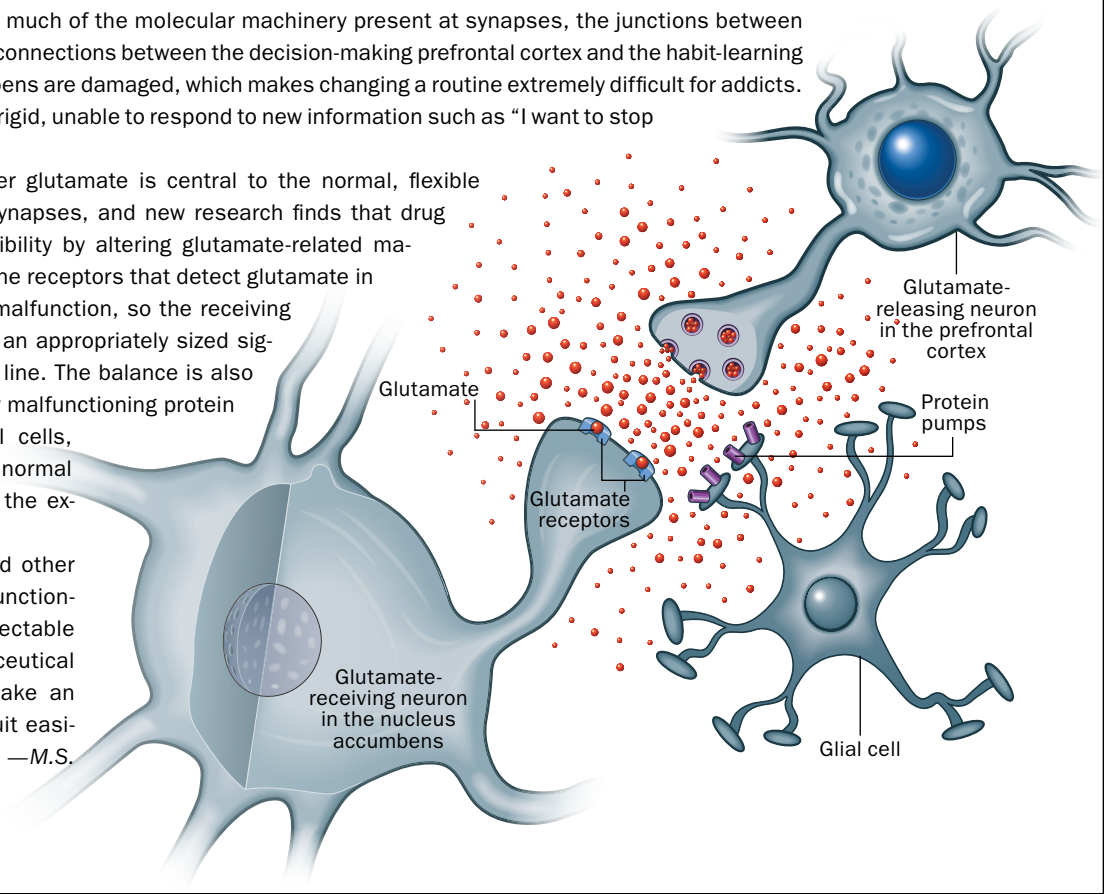
ISTOCKPHOTO (*left*); DANIELLE STOLLÉ (*right*)

Rigid Synapses

Addiction affects much of the molecular machinery present at synapses, the junctions between brain cells. The connections between the decision-making prefrontal cortex and the habit-learning nucleus accumbens are damaged, which makes changing a routine extremely difficult for addicts. The synapses become rigid, unable to respond to new information such as "I want to stop using drugs."

The neurotransmitter glutamate is central to the normal, flexible functioning of these synapses, and new research finds that drug use destroys that flexibility by altering glutamate-related machinery. For example, the receptors that detect glutamate in the synapse begin to malfunction, so the receiving neuron does not send an appropriately sized signal to the next cells in line. The balance is also thrown out of whack by malfunctioning protein pumps in nearby glial cells, which fail to keep up normal levels of glutamate in the extracellular space.

These problems and other types of synaptic malfunctioning seem to be correctable with common pharmaceutical drugs, which could make an addict's decision to quit easier to implement. —*M.S.*



cocaine and alcohol abusers were asked to press a key each time they saw a green rectangle on a screen. After 500 repetitions, the rules changed so that the green rectangle signaled they were *not* to press the key. Healthy control participants soon withheld their key presses, but the addicts kept on pressing. Even when given feedback about their mistaken key pressing in a follow-up study, addicts still stuck with the old responses.

Addiction itself can be viewed as impaired reversal learning, says David Jentsch, a neuroscientist at the University of California, Los Angeles. A person first learns the rule: "When I use drugs, I feel good." Over time, as negative consequences accumulate, the rule changes to: "When I use drugs, bad things happen." "They know the new rule, they know things are getting bad, they know the drug isn't as positive as it once was," Jentsch says. "But they're unable to update their behavior." Reid, for instance, would convince himself that he could handle just one drink, despite plentiful evidence to the contrary. "I'd think one beer won't hurt, but next thing you know, I'd have blacked out," he says.

Animal studies indicate that this inability to update is a result of drug use rather than, say, an inherent trait of those likely to try drugs. In 2002 Jentsch and his colleagues reported that daily injections of cocaine for two weeks impaired reversal learning in vervet monkeys. Nine days after the last injection, monkeys learned by trial and error which of three objects hid a food treat underneath it. Once they figured it out, the food was hidden underneath a different object, and the monkeys had to discover the new location. Cocaine-naive monkeys readily adapted their choices, but cocaine-treated monkeys did

FAST FACTS

How Addiction Takes Hold of the Brain

1» **Drug use impairs the brain's flexibility, making it difficult to change habits.**

2» **Neural communication is impaired by broken machinery at the synapses—the connections between brain cells.**

3» **Repairing this machinery with pharmacological treatment can restore flexibility, allowing an addict's desire to change to triumph over his or her habit.**

JIM KOPP

not, continuing to select the object that had first hidden the food. Similar effects have since been found in rats and mice for cocaine, methamphetamine and alcohol.

Strung-Out Circuitry

Impairments in reversal learning reflect a brain working on automatic pilot. Behaviors ingrained as habits—whether looking in the same place for food or taking drugs—begin largely subconsciously until some surprise or consequence necessitates a change. The plan to change is then hatched in the brain's supervisory regions, within the prefrontal cortex, and implemented through that area's connections to regions that drive habitual behaviors, such as the nucleus accumbens, a sugar cube–size area buried underneath the cortex. "It's a self-control circuit," Jentsch says. "Think of it as where knowing meets doing."

Drug-free monkeys readily adapted their choices when the food was hidden under a different object, but cocaine-treated monkeys did not.

These areas communicate by way of the synapses between neurons [*see box on opposite page*]. To send a message, a neuron in the prefrontal cortex releases glutamate onto the receiving end of a neuron in the nucleus accumbens. There the glutamate molecules bind to proteins on the cell called receptors, like keys fitting into locks. The receptors then trigger a discharge of electricity from the neuron in the nucleus accumbens, which releases more neurotransmitters through its synapses, and the message is passed on. Strong synapses translate this glutamate message into a big electrical signal, whereas weak synapses convey only blips.

Researchers are finding that these synapses are unusually rigid in addiction, as though the nucleus accumbens receives the messages from the prefrontal cortex but cannot heed the instructions. Normally a synapse's strength varies over time, depending on the pattern of previous messages sent through it. For example, the rapid-fire release of glutamate leads to long-lasting boosts in electrical output. Yet in animals exposed to cocaine, no matter how much glutamate is released or how quickly it floods the synapse, the receptors trigger the same amount of electrical activity. Similar disruptions in synaptic plasticity are also found in animals exposed to methamphetamine, nicotine and heroin.

Kalivas and Volkow propose that this loss of flexibility prevents addicts from fully using information coming from the prefrontal cortex to curb their drug habits. "It's not like the connections have been burned out completely," Kalivas says about the lost flexibility at these synapses. "It's more subtle than that, which gives us hope we can fix it."

Refurbishing Synapses

Armed with the knowledge that restoring these synapses to their original, malleable state might help addicts, researchers began trying to figure out exactly which parts of the synapse are broken by addiction. Although a synapse is only a tiny point of contact between two neurons, it relies on a vast array of molecular machinery responsible for releasing and detecting glutamate messages.

The latest research suggests that several of these synaptic components are damaged by addiction. For example, in 2003 Kalivas's team found that cocaine decreases the amount of glutamate floating outside the neurons in the nucleus accumbens, in the space that surrounds brain cells and their tiny synapses. The lack of this signaling chemical ultimately distorts the glutamate messages sent through synapses by the prefrontal cortex.

Cocaine appears to cause this deficiency by reducing the number of glutamate-supplying protein pumps located on nearby support cells called glia. These pumps work by importing an amino acid called cysteine from the extracellular space and exporting glutamate into that space. Kalivas and other researchers wondered if supplying more cysteine to the brain could bump up the glutamate supply. They turned to a common compound used to treat a Tylenol (acetaminophen) overdose and included as a mucus buster in some cough syrups. In 2009 Kalivas showed in rats that this compound, called N-acetylcysteine (NAC), spurred the brain's remaining glutamate pumps into overdrive and returned glutamate levels to normal, restoring plasticity to the synapses.

In 2011 Kalivas's group linked this NAC-induced flexibility to less relapselike behavior in rats. In these experiments, rats initially learned to press a lever to receive cocaine intravenously, but they then learned to stop pressing after the lever started delivering saline instead. When given a small "reminder" dose of cocaine or a cue associated with the drug, the control rats began pressing the lever again. The rodents treated with NAC pressed the lever substantially less often than controls.

Drugs do more than interfere with glutamate pumps, however. They also change the synaptic machinery responsible for detecting glutamate—which means another possible target for

(The Author)

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N-acetylcysteine treatment reduced consumption in both adult pack-a-day smokers and teen marijuana users.

Restoring the brain's flexibility will not cure addiction by itself. Drug users will still need to nurture their desire to quit in positive environments such as support groups.

treatment. There are several types of glutamate receptors, each of which shapes the ensuing electrical signal in distinctive ways. These receptors interact, meaning that drug-induced changes to one receptor can affect other receptor types, causing a kind of domino effect of molecular adjustments. "I don't think there's one monolithic thing that's broken at this synapse, but rather one thing after another is somewhat shifted," says Marina Wolf, a neuroscientist at the Rosalind Franklin University of Medicine and Science.

In 2008 Wolf and her team found that prolonged access to cocaine spurred a long-lasting increase in an unusual kind of glutamate receptor in rats that matched an uptick in the rodents' drug cravings. In 2011 they reported that pharmacologically stimulating another type of glutamate receptor reversed the effect, possibly by instigating the removal of the unusual receptors.

Recovery Fast Track

Many of the drug-induced changes in glutamate signaling can be targeted with compounds that doctors already use for other ailments. Some glutamate receptor drugs are approved for treating disorders such as migraines or Parkinson's disease, and NAC is even sold in health food stores as an antioxidant.

Preliminary studies in humans suggest that taking NAC does indeed reduce drug use. Kalivas and his colleagues reported in a series of recent studies that three days of NAC treatment decreased—but did not eliminate—cocaine users' desire for the drug, and a similar treatment regimen halved craving intensity for cocaine, as reported by frequent users. Other studies have also found that NAC treatment in adult pack-a-day smokers and teenage marijuana users reduced consumption in both groups.

Kalivas calls his results in humans "modest" compared with the strength of the rat studies, however. NAC may need more time to recondition the synapses in people, and it may work best when ongoing drug use does not interfere. To test this idea, he has begun a study in which participants will abstain from drugs while receiving NAC in the hospital for six weeks.

Even with new pharmacological remedies on the horizon, behavioral therapies that teach coping strategies to an addict will still form a crucial part of treatment. "Restoring the synaptic machinery will not do anything on its own," Kalivas says. "A person has to have other input that will help guide him or her away from the drugs." Although people can and do beat addiction solely through therapies such as 12-step programs, restoring the synapses pharmaceutically may ease the way for the plans formulated in the prefrontal cortex to hold sway over behavior.

This type of treatment could speed up recovery for people such as Reid, who tried and failed several times to get sober. After a humiliating arrest for driving under the influence, he began taking a drug that blocks the metabolism of alcohol, so that if he has a drink he becomes sick. That threat, combined with counseling and a 12-step program, has helped him stay sober since January 2011. He says it is the hardest thing he has ever done, however, and his old habits continue to haunt him. A drug that directly targets these habit-forming areas of the brain, such as NAC, might have made his recovery easier. "There will be a time today when I think a cold beer would really be nice," he says. "But I just have to get through it and move on." M

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GETTY IMAGES

Time-Warping Temptations

Impulsivity arises from a tendency to want small imminent rewards more than big future benefits. How can we correct our skewed values to care for our future selves?

By David H. Freedman Illustration by Josue Evilla

The popularity of fast food speaks to the human tendency to value what we can have now more than larger payoffs that would accrue to us down the road.

GETTY IMAGES

Walk into any fast-food restaurant, and you can watch a small crowd of ordinary people doing something that is utterly irrational: eating junky, excess-weight-inviting food likely to leave them feeling bad about their bodies and open to a host of serious ills. We literally line up to trade our health and self-image for a few minutes of pleasant mouth feel and belly comfort—because the latter is right here, right now, whereas the former is months, years and decades away.

FAST FACTS

Upturned Priorities

1» Temporal discounting is our tendency to view small rewards available now as more desirable than even much bigger rewards we would get down the road.

2» The lure of immediacy plays out in overeating, overspending, abusing drugs, and more.

3» The drive to instant gratification appears to be hardwired in humans. But researchers are coming up with strategies for counteracting this impulse and changing shortsighted behavior.

This foolish exchange reflects a glitch in our brains that may wreak more havoc in our lives and in society than any other. Known as temporal discounting, it is our tendency to view small rewards available now as more desirable than even much bigger payoffs down the road. Scientists think this trait may have been programmed into us by evolution at a time when the environment, with its many threats to our survival, favored those who grabbed whatever they could whenever they could get it.

Today this tendency plays out in overeating, overspending, abusing drugs, and more. "Because the rewards for our good behavior are off in the future where they seem less important, we are almost guaranteed to often act against our own

interests," says Laurette Dubé, a psychology and marketing researcher at McGill University.

The drive to instant gratification appears to be hardwired in humans. But that fact does not mean we are destined to grab immediate rewards we will later regret. "It was long thought that impulsiveness was fixed," says psychologist Samuel M. McClure of Stanford University. "Now there's a lot of evidence it can be moved."

The drive to instant gratification appears to be hardwired. But we are not destined to grab rewards we will later regret. "It was long thought that impulsiveness was fixed," says Stanford University psychologist Samuel M. McClure. "Now there's a lot of evidence it can be moved."

New insights into the psychological subtleties of temporal discounting have suggested ways to counteract the distorted thinking behind the phenomenon and change shortsighted behavior. If these strategies work, we will be more likely to eat more healthfully, exercise, stay out of debt, and even avoid drug and alcohol addiction.

A Matter of Time

Temporal discounting has long been seen as the triumph of feelings or impulses over reason. To go beyond that imprecise insight, several groups of neuroscientists, including teams led by Paul Glimcher of New York University and B. J. Casey of Weill Cornell Medical College, have scanned people's brains using functional MRI while they were tempted to grab immediate rewards. They found that this urge seems to originate in the brain's limbic system, a set of cerebral regions charged with emotion, along with the ventral striatum, a hub for reward, among other areas associated with feelings and impulsivity.

Thoughtful decisions to resist temptation, on the other hand, appear largely rooted in the prefrontal cortex, the seat of executive functions such as working memory, attention and inhibitory control. In people who have lesions in the prefrontal cortex or in whom prefrontal responses are diminished by other means, the urge to grab at what is offered becomes more intense. If we can make the sooner, smaller reward seem less compelling or get the larger, later reward to attract more attention, researchers have discovered, activity shifts from the limbic system to the prefrontal cortex—and we make wiser choices.

Important clues about how to combat rash behavior come from studies of how we perceive time when making decisions in which immediate desires conflict with longer-term goals. Some of the same brain systems involved in temporal discounting also contribute to our ability to estimate spans of time. Researchers at the University of Pennsylvania, the University of Minnesota and elsewhere have shown over the past 10 years that these estimates become skewed when comparing sooner versus later rewards. That is, the later benefit feels further off than it really is, diminishing its appeal.

What is more, that perceived gap between the value of sooner and later rewards grows as the time to the sooner reward approaches, according to a number of recent studies. For example, in a study published in 2009 marketing professor Gal Zauberman of the University of Pennsylvania and his colleagues showed that students placed much less value on a gift certificate that they had to wait a relatively short time to use as compared with one they could use right now. On the other hand, the students perceived only a minimal difference in the worth of two certificates when one required waiting a long time and the other, even longer. Thus, an ice cream sundae may seem like a health- and figure-destroying bomb when contemplated a few days before it appears at a party, but as the party approaches the price of eating it will recede further into the future, even as the sundae becomes ever more appealing.

Finding ways to delay the more immediate reward can counteract this time-skewing effect. Research has shown that requiring people to wait just

ANNA BRYUKHANOVA *iStockphoto*

If you are forced—or can force yourself—to wait, even just five minutes, before splurging on something you cannot afford, you are more likely to forgo the indulgence and thereby avoid its negative consequences.

If you think of your future self as a person who is dependent on you, you are more likely to behave in ways that benefit you later, such as making large contributions to a retirement account.

five minutes for a treat cuts the appeal of the treat in half. Thus, if you are about to order a double cheeseburger at the fast-food counter or if you are eyeing an unaffordable new watch, persuade yourself to run a few errands before deciding whether to indulge. You can also think of the later benefits as coming more quickly. Imagine seeing a lighter reading on the scale that evening or a lower balance on that credit-card account when you look online. Such tactics will make the temporal playing field a bit less tilted and give the better decision a fighting chance.

Certain environmental cues can also trick the brain into judging time in ways that mitigate temporal discounting. Students in McClure's laboratory at Stanford have observed that subjects exposed to a slow audio rhythm are less likely to overestimate the time to distant events and more likely to opt for later rewards than those who hear sounds at a swifter pace. That result suggests that faster-paced sensory cues might speed up our internal clocks, making time of the essence. Conversely, it implies that a calming environment may temper temporal discounting—that a mellow McDonald's might sell more salads and fewer Big Macs.

Additional research supports the notion that the hustle and bustle of fast-food chains may magnify our desire for a faster payoff. In a study published in 2010 organizational behavior researchers Chen-Bo Zhong and Sanford E. DeVoe of the University of Toronto found that people who were asked to think about their last visit to a fast-food chain or shown logos of those companies tended to opt for immediate (over longer-term) rewards to a greater extent than did those not given the fast-food triggers. Those made to think about fast food also read faster and expressed more interest in time-saving products, hinting that the sensory cues of fast-food establishments may serve to speed up our internal clocks. Thus, staying away from fast-food restaurants can have a double bonus: avoiding being plied with less healthy food and easing the pernicious effects of temporal discounting on your health- and wealth-related decision making.

Details, Details

Another approach to combating temporal discounting involves collecting detailed data. A range of findings show that our brains tend to grasp events that are further in the future in vaguer terms than events close at hand. Gathering specific information

LIAM NORRIS *Getty Images*

(The Author)

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about more distant rewards, therefore, may help far-off goals effectively compete for attention with more immediate wants.

Psychologist Michael Cameron of Pacific Child and Family Associates, a group of behavioral health clinics headquartered in Santa Paula, Calif., has applied this concept to antiobesity programs. He asks clients to document exactly how much weight they gain when they slip and then how long it takes to get back to their previous weight. This ritual causes people to place greater value on the eventual downsides of eating too much. "Because of temporal discounting, people focus on how much they're going to enjoy the binge, and they're on autopilot when it comes to the consequences," he says. "I found that if you give people specific information about those consequences and get them to say it out loud, they go into the decision with their eyes wide open and start wondering if they really want to go through all that."

Cameron's clinical observations strongly suggest that generic statements about consequences do not work. "It has to be information that's specific to the individual and directly connected to a particular decision," he says. So if you are tempted to drop more than you can afford on that flashy high-end model the car salesperson is pushing, take a breather and remind yourself out loud that the hefty monthly payments on that vehicle would downgrade your restaurant and vacation privileges for the next five years.

Psychologist Christopher J. Bryan of the University of California, San Diego, has a different approach to boosting the perceived significance of more remote gains. He and other psychologists have speculated that one reason temporal discounting can be so strong is that we do not like to think about ourselves in the distant future, perhaps because we do not like to imagine ourselves as old. (Never mind studies showing that people tend to get happier as they age.) "If we don't want to think of our older selves, we're less likely to worry about doing things that will pay off for our older selves," he says.

In 2011 Bryan hypothesized that we might be able to circumvent this aversion by tapping into our sense of obligation to people who depend on us. To test that theory, he and marketing researcher Hal E. Hershfield of N.Y.U. encouraged two groups of Stanford faculty and staff members to increase their pension deductions. One group was told that the benefits of doing so would accrue to "you" down the road; for the other group, Bryan and Hershfield described the beneficiary in the third person as a future self who was dependent on the subject's behavior now. Sure enough, many in the latter group actually ended up boosting their deductions, whereas few in the former group did. "When you evoke people's moral obligation to take care of a future self who is dependent on them, in the same way we take care of our children and elderly parents, they make better choices," Bryan says. To enlist this effect when you are about to give in to a costly temptation, think of the long-term damage you will be doing to that trusting person under your care who happens to be your future self.

People who were asked to think about their last visit to a fast-food chain or shown logos of those companies tended to opt for immediate over longer-term rewards to a greater extent than did those not given the fast-food triggers.

If these kinds of seemingly simple tweaks prove effective and can be rolled out to society at large, the world 30 years from now could be one in which obesity epidemics, personal debt crises and other mass ills of poor choice seem like relics of another time. "By getting ourselves to understand how awful the prospects are for us in the future if we choose short-term rewards," Bryan says, "we may actually be able to avoid that future." M

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A Transparent, Trainable Brain

New imaging methods allow people to observe their brain activity in real time. This technology could help combat brain-based disorders and improve learning

By Heather Chapin and Sean Mackey
Illustration by Vivienne Flesher

Melanie Thernstrom lies motionless inside the large, noisy bore of a functional MRI scanner at Stanford University. She tries to ignore the machine's loud whirring as she trains her attention on a screen mounted inside the scanner, right in front of her eyes. An image of a flame bobs and flickers, shifting subtly in size. To her, the flame is a representation of the searing pain in her neck and shoulder, with its fluctuations reflecting the rise and fall of her discomfort. To the neuroscientists scrutinizing her through a window from the control room next door, the flame is a measure of the activity in a part of her brain.

As Thernstrom's pain increases, so does the amount of activity in part of this brain area, called the anterior cingulate cortex (ACC). This boomerang-shaped region, located in the frontal lobes, straddles the brain's midline between the ears and the forehead. Thernstrom's task is to will the flame to shrink, thereby reducing the neuronal hubbub in that region and the sensation of pain. With software rapidly parsing the machine's data to update the image of her ACC, Thernstrom can peer inside her own mind. She can observe, fuzzily, her brain's inner workings almost in time with the conscious manifestation of her discomfort.

Pain is your brain's way of telling you that your body is facing impending or actual damage to your tissue. To send that signal, the brain constructs an unpleasant sensory and emotional experience. When you get a paper cut, for example, the nerves in your finger shuttle a message to your brain, which interprets that incoming missive to beget the experience of pain. The ACC helps to modulate the pain response. The prickling sting of a sliced fingertip serves as an internal red flag alerting you to an attack or threat, and it vies for your attention with your other perceptions and cognitive states—musings about lunch, the ping of an incoming e-mail, a co-worker's pungent cologne.

The brain is not an unerring interpreter of the body's maladies. For Thernstrom, chronic pain was impeding her ability to get on with life, and she often felt as if her pain was draped like a veil over her thoughts. If she could lift the veil, she would be able to resume the daily activities she had relinquished. To do so, we and our collaborators hypothesized, she had to learn how to gain conscious control over her ACC.

Marshaling one's neurons to behave in a certain manner is no easy feat. Much as a baby might learn how to manipulate her fingers and toes through trial and error, Thernstrom has to discover what patterns of thoughts stoke the fire versus snuffing it out. First, she tries to convince herself that the burning sensation is soothing warmth, as if she is on a beach basking in the sun or relaxing in a Jacuzzi. The flame amplifies. The flickering image reminds her of scenes in a recent theological book she had read, in which religious martyrs were being burned at the stake. This gives her an idea.

She calls to mind the story of Akiba ben Joseph, who was said to have joyfully surrendered to his tortuous fate as a way of asserting his devotion to God. As she imagines herself taking on a similar role, she notices the flame begin to dwindle, along with her pain. As long as she concentrates on the feeling of surrender, the aches in her neck and shoulders lose their edge.

Much as a baby might learn how to manipulate her fingers and toes through trial and error, Thernstrom has to discover what patterns of thoughts stoke the fire versus snuffing it out.

Thernstrom is one of several chronic pain sufferers who have volunteered to help our laboratory investigate an emerging technology called real-time fMRI (rtfMRI) neurofeedback. Imaging technologies, widely used to produce snapshots of the brain in action, are now gaining traction as tools for rehabilitation, therapy and brain training more broadly. This neurofeedback technique builds on the idea that exposing a person to his or her own patterns of brain activity could help that individual modify harmful or undesirable cognitive processes. Rather than training someone's brain to adopt new habits by teaching a new task—say, learning to juggle to improve hand-eye coordination—this approach aims to alter brain activity directly, through a person's own process of discovery.

For certain disorders, among them chronic pain and the loss of movement in Parkinson's disease, scientists have identified key brain regions implicated in the ailment. By showing a person how that target area is behaving in the present moment, a recipient of neurofeedback can experiment with mental strategies to alter the brain's behavior. As the technology develops, rtfMRI has the potential to help sufferers of numerous brain-based disorders exert greater control over their disease process. Our latest work has investigated using it to modulate the brain in depression, and it may also assist with anxiety, phobias and physical rehabilitation after a stroke.

It might enhance cognition for healthy people, too, by identifying when key brain regions are primed to learn or by helping individuals internal-

FAST FACTS

Mind Control

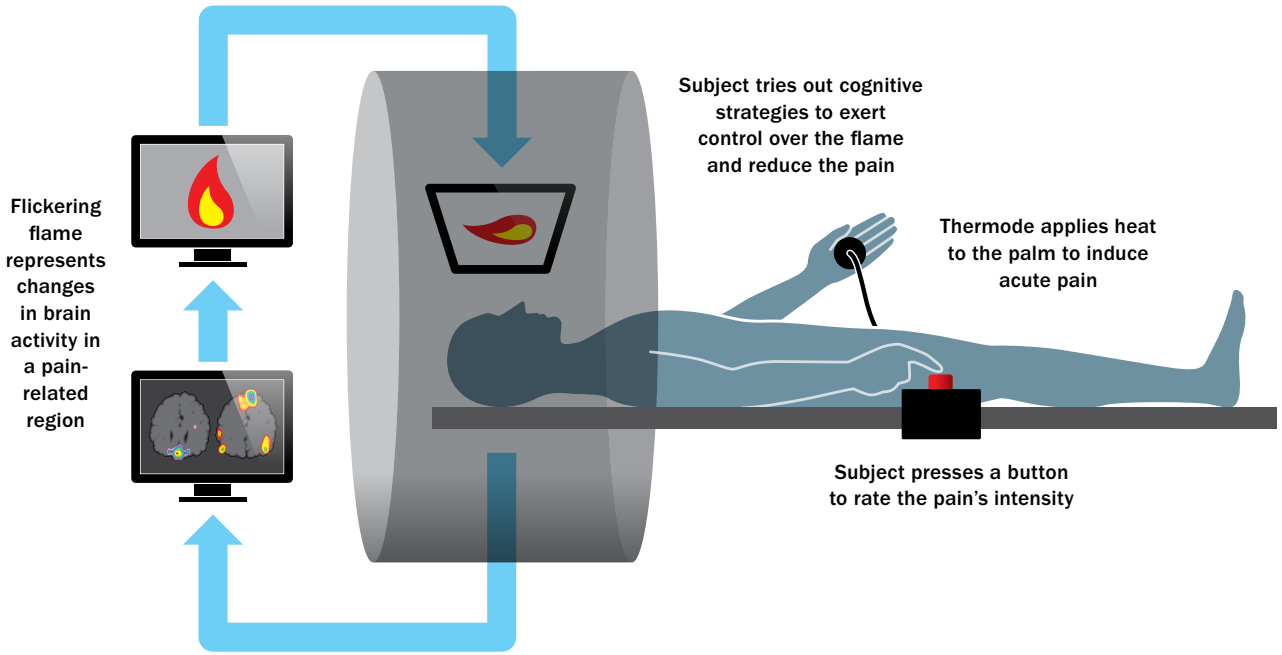
1» **A technique known as real-time functional MRI neurofeedback exposes people to their own brain activity as they lie in a scanner.**

2» **Seeing inside one's brain in real time opens up the possibility of targeted therapies that change the brain-activation patterns associated with pain, Parkinson's disease, depression and perhaps even addiction.**

3» **Eventually these techniques could also help healthy individuals to acquire knowledge and learn new behaviors more effectively.**

Eavesdropping on the Brain

In real-time functional MRI (rtfMRI) neurofeedback, a computer collects brain data from a person lying inside a scanner. Another computer analyzes the data to produce a representative image, which it sends to a screen in the scanner. This diagram shows a pain experiment.



ize the thought patterns associated with a creative mind-set. Brain imaging has revolutionized how neuroscientists and psychologists view the human experience. Now it is poised to help the rest of us alter that experience, from the inside out.

Seeing Inside the Mind

Researchers began exploring the use of neurofeedback in the early 1970s. At the time they focused on electroencephalography (EEG). An EEG reading uses electrodes placed on a person's scalp to pick up patterns of electrical activity near the surface. Typically a study participant might don the electrodes and perform some cognitive task, such as imagining moving an arm. Researchers would record the signals, translate them into a picture for the participant to see, and ask that subject to try to regulate their brain activity by mentally altering the picture in some way.

The clinical potential of neurofeedback soon caught researchers' attention. Among the disturbances that neuroscientists sought to alleviate were seizures, anxiety, depression, addiction and chronic pain. They saw some success using EEG neurofeedback to train patients suffering from epilepsy to normalize the neuronal rhythms underlying seizures. Yet the technology of the time had major limitations. Mapping the signals picked up by the EEG's electrodes to a specific brain area is exceedingly difficult and often impossible. The electrodes, which most clearly register neural activity near the surface of the brain, cannot listen in on the deep-brain structures implicated in many disorders.

In the 1990s fMRI revolutionized neuroimaging research. This now widespread technique works by measuring the oxygen content of blood. When the neurons in a certain region of the brain become highly active, they draw more oxygen as fuel from nearby blood vessels, thus triggering an increase in blood flow to that area. Blood that is rich in oxygen and blood that is oxygen-impoverished differ in their magnetism, and these distinctions serve as a proxy for levels of brain activation. So when the powerful magnet of an fMRI machine releases its bursts of radio waves, brain regions that are more

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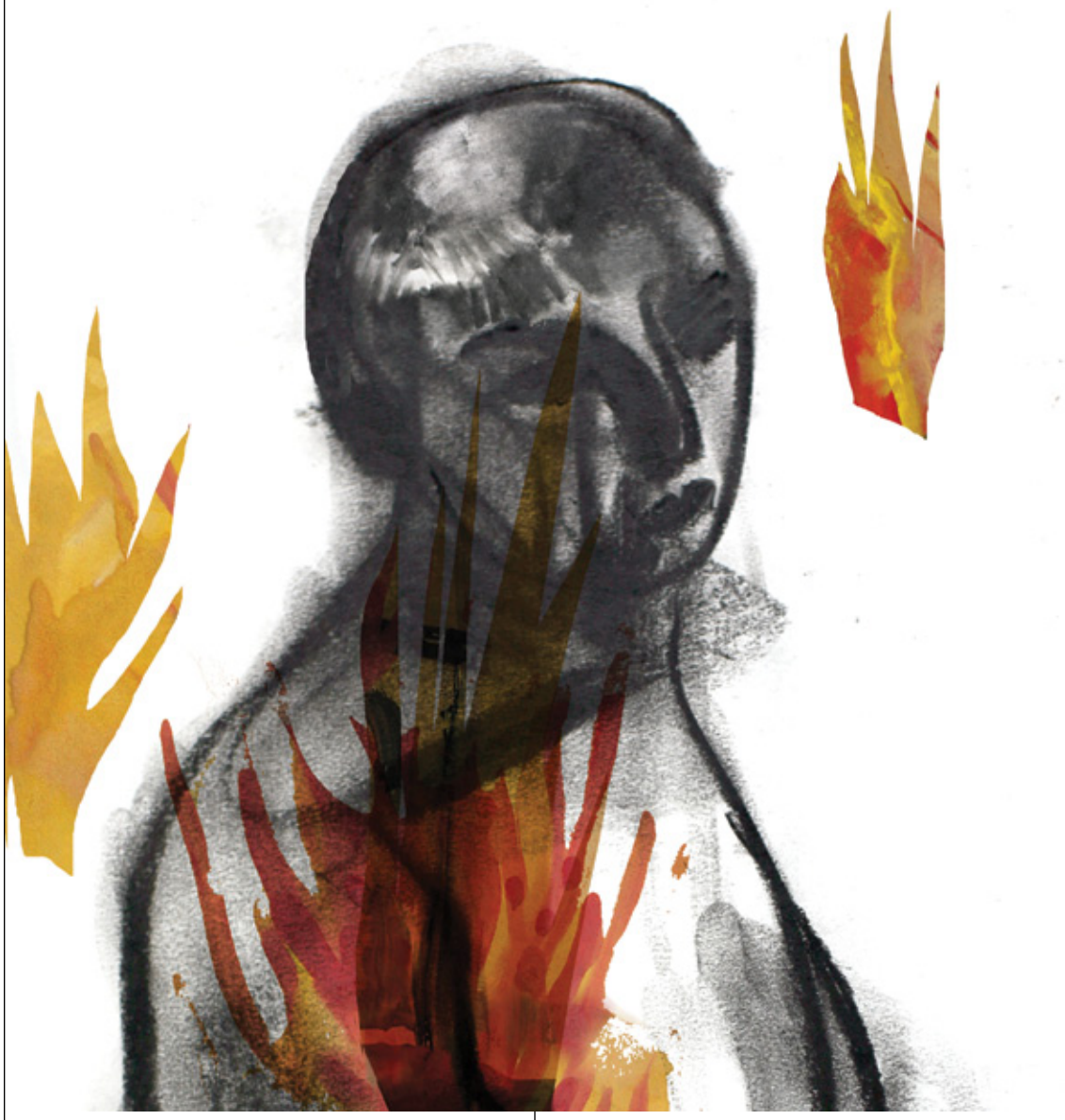
JASON LEE



or less engaged will produce a correspondingly strong or weak signal. By comparing the resulting maps of variations in the oxygen content of blood under different conditions, neuroscientists and psychologists can gain insight into how the brain carries out a given task.

The first serious efforts to adapt fMRI to neurofeedback occurred in 1995, when biophysicist Robert Cox, then at the Medical College of Wisconsin, and his colleagues found a way to process data from brain scans in real time, as opposed to after an experiment was already over—a crucial initial step. Seven years later several laboratories showed they could share that continuous stream of data with the person being scanned and coach that individual into altering brain activity in specific areas.

In subsequent years, our lab at Stanford, along with neuroscientist R. Christopher deCharms, turned its attention to training people with pain to use neurofeedback to alleviate their suffering. We asked eight healthy participants and eight people with chronic pain to undergo fMRI scanning. The healthy subjects held a heat probe in their left palm as their head lay inside the machine. The temperature of each probe was set to the maximum level that its holder could endure without squirming, equivalent to a seven out of 10 on a pain scale.

We then described some strategies to both the healthy participants and the chronic pain sufferers for either increasing or tamping down their hurt. To amplify pain, for example, we suggested to our subjects that they attend to their discomfort, consider

VIVIENNE FLESHER

the sensation a threat—perhaps by focusing on its frightening aspects—or allow the painful sensation to wash over them. To diminish pain, we offered techniques such as shifting focus away from the pain, interpreting the sensation as nothing special or attempting to gain control over the experience. Participants were also encouraged to come up with their own strategies. This freedom quickly became an important part of the treatment's success. None of the researchers could have guessed that Thernstrom imagining herself as a martyr being burned at the stake would have been most effective for her.

As our subjects tried out their cognitive strategies, software analyzed the fMRI signal corresponding to their ACC and presented it back to them as a growing or shrinking virtual flame. The participants adjusted their thought patterns until they found one that drove the flame in the desired direction. Afterward, they all rated their pain.

We found that both groups could change their experience of pain; in fact, the chronic pain sufferers cut their pain ratings by half. The greater the participant's ability to control ACC function, the more that person's pain diminished. Both groups were also able to maintain control over their ACC activity and their experience of pain even when they were no longer receiving visual feedback. Our control groups—composed of subjects receiving no feedback, sham feedback, or biometrics such as their heart rate and perspiration—did not show the same degree of control over their pain and ACC activation after practicing their cognitive strategies.

Other scientists have applied this neurofeedback approach to combating the symptoms of Parkinson's. In 2011 neuroscientist Leena Subramanian of Cardiff University in Wales and her colleagues tested rtfMRI methods on 10 individuals with early-stage Parkinson's by scanning them twice in sessions spanning two to six months. During the first visit, half the participants observed the activity in their supplementary motor area (SMA), a motion-control region that is hypoactive in Parkinson's patients, while lying in a scanner. These individuals were given free rein to imagine any kind of movement in an effort to engage more of the SMA. The other five subjects made up the control group. They also imagined moving while in the scanner but did not see their brain activity. In the intervening months, all 10 participants devoted time at home to picturing themselves executing complex movements, such as playing a sport.

When the researchers scanned the participants' the second time, the patients who had received neurofeedback showed more activation in their SMA, performed faster on a finger-tapping task and improved on clinical symptoms of Parkinson's 37 percent more than the control subjects. Neurofeedback appears to have helped these patients develop a more effective mental imagery strategy than those who lacked that information, which gave the former group an advantage in their home practice.

None of the researchers could have guessed that Thernstrom imagining herself as a martyr being burned at the stake would have been the most effective strategy for her.

Focusing on single brain areas, as these two studies did, has produced exciting results, but this approach has its limits. Any thought or feeling invokes complex networks in the brain. Even simple acts, such as bending down to sniff a flower or contemplating shapes in a cloud, emerge from a precise choreography of chemical and neuronal ensembles. As our grasp of the dynamics underlying our mental states improves, we can unlock the true potential of rtfMRI.

A Tune-up for Brain Networks

A big step forward for this technology will come from matching specific mental states to activation patterns that encompass the entire brain, so that people learn how to alter broad patterns rather than particular regions. Already scientists have been able to map the complex activation patterns seen in fMRI images to subjective reports of what a person is thinking, allowing neuroscientists to pull off a rudimentary form of mind reading.

To intrude so deeply into a person's thoughts, that individual first must look at thousands of images while lying in a scanner. After building up a database of pairs of activation patterns and the images that triggered them, a computer can decode what a person might be picturing at a given time [see "Movies in the Cortical Theater," by Christof Koch; Scientific American Mind, January/February 2012]. We can gain further resolution, too, by having a computer learn to distinguish between

At times, we are either more or less prepared to pick up new information and skills, and neuroimaging has revealed the underlying brain states that correlate with this readiness.

different brain states associated with a certain stimulus or experience—say, a happy thought versus a sad reaction in response to a picture of a pony.

One way to improve rtfMRI is to conduct this type of pattern matching along with neurofeedback. We would need to assemble the pairs of brain states and stimuli anew for each participant, as the encodings of thoughts and memories differ from person to person. Part of the challenge here is that the software can err when classifying a volunteer's activation information as a particular brain state. With brain activity shifting subtly in fractions of a second, the desired state can end up labeled incorrectly or muddied by overlapping cognitive states. Sharing with a volunteer how his or her brain states are classified could expose errors and encourage that person to conjure up clearer brain states that are more representative of a certain thought or feeling. Ideally, this collaborative process would yield perfect accuracy so that our software could always tell if you are, say, happy versus sad.

Preliminary work by Stephen LaConte, now at the Virginia Tech Carilion Research Institute, and his colleagues suggests that this new technique may be useful for training brain states related to reducing cravings in addicts. In 2009 the researchers found that they could predict, based on brain-wide patterns of data, whether a chronic smoker was in a state of craving. Therapies targeted at diminishing the intensity of that brain pattern could help substance abusers overcome their harmful urges. More recently, our lab has used this pattern-matching method to detect the presence or absence of acute or chronic pain.

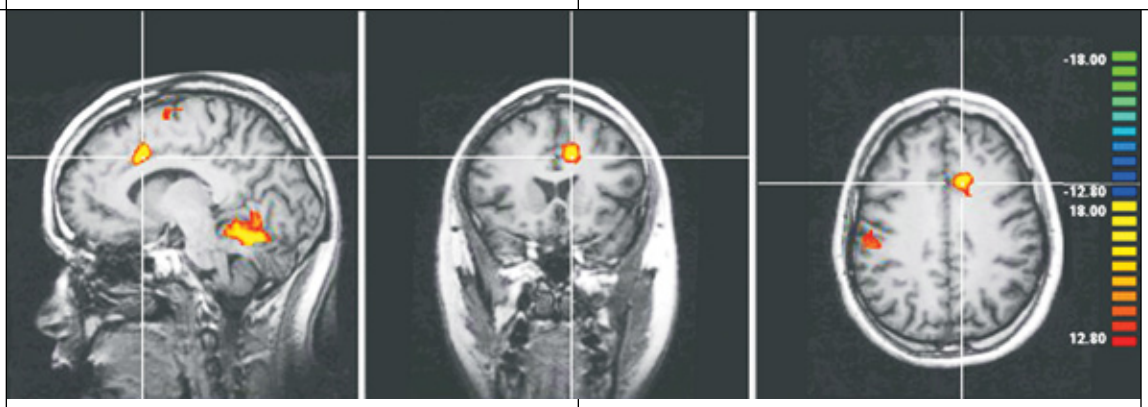
This electrode cap is performing near-infrared spectroscopy and electroencephalography. The imaging tool could make rtfMRI more widely accessible.

YOSHIKAZU TSUNO *Getty Images*

Even the therapies themselves could become tailored to individual use. As we learn more about what brain processes support specific cognitive techniques, rtfMRI neurofeedback could strengthen the relevant networks. A broader range of people could end up benefiting from strategies such as mindfulness meditation or cognitive-behavior therapy, which are already used to improve emotional, cognitive and physiological dysfunction.

The potential of rtfMRI is not limited to disease. Neurofeedback could be used to train people to develop subtle mental strategies that alter their neural function to promote creativity, for example. Once they have learned the techniques for inducing a more creative brain state, they can rehearse this frame of mind in their day-to-day activities, similar to the approach used in the Parkinson's study mentioned earlier. Practitioners would likely return to the scanner for an occasional mental tune-up to update their strategies as their brains adapt.

Neuroscientists have made initial strides toward applying rtfMRI to enhancing learning, perception, performance and wellness. Our ability to pick up new information and skills fluctuates—at times, we are either more or less prepared to learn, and neuroimaging has revealed the underlying brain states that correlate with this readiness. In one experiment published in 2012, for example, a team led by John Gabrieli of the Massachusetts Institute of Technology showed its subjects pictures of scenes and parsed their brain data in real time to monitor the performance of the parahippocampal place area (PPA), a region involved in remembering and recognizing scenes. The scientists discovered that their subjects formed more accurate memories of the pictures they viewed when the PPA was in a prepared state than when it was in a less optimal condition. Such studies



These brain scans reveal the average change in activation in the anterior cingulate cortex (*shown at crosshairs*) between the first and last times study subjects used rtfMRI neurofeedback to modulate their pain.

FROM "CONTROL OVER BRAIN ACTIVATION AND PAIN LEARNED BY USING REAL-TIME FUNCTIONAL MRI," BY R. CHRISTOPHER DECHARMS ET AL., IN *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES USA*, VOL. 102, NO. 51; DECEMBER 20, 2005

suggest that we can accelerate learning by adapting a training program to the brain's present condition.

More generally, rtfMRI neurofeedback can also be used as a novel tool for probing brain function. Traditional fMRI research involves asking participants to engage in a task and measuring the effect on the brain. The results give us associations, but we cannot know definitively whether the task caused the brain changes. With rtfMRI, we are able to test our assumptions about how the brain works by selectively manipulating specific brain areas or networks and observing the outcome. Neuroscientist Mitsuo Kawato, director of the ATR Computational Brain Information Communication Research Group in Japan, has coined the term "manipulative neuroscience" for this burgeoning field.

In work published in 2012 Kawato and his colleagues used rtfMRI techniques to test whether they could improve one small aspect of their subjects' visual perception without them ever becoming consciously aware of what they were learning. First, they had a computer learn the activation patterns in the visual cortex associated with specific orientations of lines—30, 70 or 120 degrees. They then gave their subjects feedback on how closely the activation in their visual cortex resembled one of these patterns and tried to coax them into matching their brain activity to that associated with seeing a particular diagonal line. The experimenters did so without showing their subjects any lines, explaining the meaning of the neural patterns they were pursuing or revealing the intention of the experiment.

Afterward, the participants were significantly better at detecting the diagonal line they had just been trained on than they had been at the beginning of the experiment. This study revealed an elegant way to test that the activation patterns we suspect are associated with a given stimulus or behavior—in this case, observing a particular diagonal line—are indeed linked. The vague relations hinted at by traditional brain scanning are finally giving way to more concrete results.

Before rtfMRI neurofeedback can become a widely used therapeutic tool, however, we will have to address the exorbitant cost of an fMRI scanner. Its initial adoption, then, will likely be in assuaging conditions that are notoriously difficult or expensive to treat long term, such as chronic pain and addiction. Other opportunities lie in blending rtfMRI with less expensive, more mobile imaging technologies, such as EEG or near-infrared spectroscopy (NIRS). NIRS is similar to fMRI, but it uses light rather than a magnet to measure brain function. Although EEG and NIRS do not offer the same whole-brain access as fMRI, researchers might be able to translate the portrait of brain activity achieved through rtfMRI neurofeedback into an EEG or NIRS signature.

With rtfMRI neurofeedback, we have the opportunity to peek under the hood—to access the origins of our conscious and unconscious thought processes. It allows therapists to offer treatment and simultaneously monitor the brain's response to that treatment. And it opens up the possibility of having therapies and training regimens evolve in step with an adapting brain. In exploring this new landscape, both to aid research and to accelerate healing, we are only beginning to learn of our own capacity for self-directed growth. M

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Big City Blues

Mounting evidence shows how city living can harm our mental health

By Andreas Meyer-Lindenberg

Our protagonist moves to the big city, seeking a better life. It's a classic—and increasingly common—tale. More than half the world's population now lives in a metropolis, and by 2050 that figure will very likely jump to two thirds. China's megacities in particular are fueling the trend, with more than 10 million new residents every year. Historically, urbanization has brought about stupendous changes—the Renaissance, the industrial revolution, globalization. Yet this urban migration represents one of the most dramatic environmental shifts human beings have ever undertaken. So one might be tempted to ask: How are we adapting to our new digs?

At first glance, trading green fields for gray grids would seem to be a trade up. City slickers have, on average, more money, better food and greater access to health care than country folk. On the flip side, though, recent studies indicate that memory and attention can suffer in urban environments, and psychologists have long known that city life takes an emotional toll. Urbanites are more likely to suffer from anxiety and depression, and the risk of schizophrenia increases dramatically among people raised in a city. Some researchers have calculated that children born in cities face twice, if not three times, the risk of developing a serious emotional disorder as compared with their rural and suburban peers.

These statistics may not surprise harried rush-hour commuters, but they are also not easily explained. Epidemiologists have ruled out the most obvious answers—namely, that people at risk for developing emotional disorders are more drawn to urban areas. Instead certain aspects of metropolitan life appear to incline the brain toward mental illness. A number of possible culprits are now under investigation, among them noise, pollution and social pressure, in both the form of greater competition and weaker community ties.

Several inquiries suggest that this last factor, social stress, is especially harmful. Our work at the Central Institute of Mental Health in Mannheim,

GONI MONTES

FAST FACTS

Hidden Costs of City Living

1» **Metropolitan populations are significantly more likely than rural ones to suffer from mental illnesses such as depression and schizophrenia.**

2» **Among urban dwellers, social stress leads to hyperactivity in the amygdala and anterior cingulate cortex, brain regions that play an important role in equilibrating our emotions.**

3» **The pressures of city life can change brain physiology, thereby increasing the risk of emotional disorders.**

Country living appears to produce neural changes that reduce the impact of stressful situations.

Germany, corroborates this view and provides the first neurobiological mechanism to explain it. In a series of studies, my colleagues and I have found evidence that the social strain of urban living engages specific stress circuits in the brain—circuits known to go awry in mood disorders and other mental illnesses. Perhaps by understanding this mechanism and its role in the etiology of psychiatric conditions, we can find ways to intervene and make cities more livable.

Stress in the City

Many studies have confirmed the link between social strain and mental illness. In 2010 Stanley Zammit and his colleagues at Cardiff University in Wales traced the origins of schizophrenia in 200,000 individuals in Sweden. They found an array of contributing factors, all of which were increasingly potent in more urban environments. In general, though, people who perceived themselves as isolated—immigrants, for example—were at significantly greater risk. Such research is invaluable but relies on a coarse metric: the frequency of clinically diagnosed psychiatric patients. To look for more subtle connections between the pressure of city life and emotional instability, my colleagues and I turned to functional magnetic resonance tomography, a means of monitoring brain activity by way of blood oxygenation levels.

In 2011 we recorded the brain activity of 32 German college students, who hailed from big cities, towns or countryside. As our recruits performed a series of brainteasers, we deliberately stressed them out. For example, while inside the scanner, each volunteer saw a phony performance meter, which indicated that they were doing poorly compared with everyone else. At the same time, one of us admonished them to try harder lest they ruin the experiment. Our ruse worked. Not only did we detect an elevated heart rate, blood pressure and level of stress hormones in our participants, but after the test—when we told them what we were up to—they confirmed that they had indeed felt pressured.

As expected, this stressful experience activated many areas in the brain. Astonishingly, though, we discovered one particular region, the amygdala, whose activity under pressure exactly matched the subjects' address: the more urban their home environment, the more engaged their amygdala became. This cherry-size structure, deep within the temporal lobe, serves as a danger sensor of sorts, prompting the "fight or flight" response. It also modulates emotions such as fear. In our study, the amygdala seemed almost impervious to stress among villagers and was only moderately active among those from small towns. For big city residents, stress kicked it into overdrive.

We had not expected such a strong correlation, and so we repeated the experiment, placing 70 additional test subjects under slightly different stress conditions. Again, we saw the same pattern. In each experiment, we could readily identify city residents by brain scan alone: urban life had marked all of them with telltale hyperactivity in the amygdala. This finding revealed at least one way in which city stress can lead to mental illness. An amygdala in high gear is also observed in patients suffering from depression and anxiety. Not all urbanites succumb to mood disorders, of course, but we surmise that chronic overstimulation of this brain region puts some people at a higher risk.

The very same mechanism may play at least a small role in prompting violent behavior. Violence is not a psychiatric diagnosis per se; it results from

SKIP NALL *Aurora Photos*

(The Author)

ANDREAS MEYER-LINDENBERG is a mathematician and psychiatrist. He is director of the Central Institute for Mental Health in Mannheim, Germany.

an exceedingly complex interplay of factors. Even so, data from the U.S., Germany and elsewhere confirm that violence is a bigger problem in cities, and several lines of inquiry link violent behavior with overstimulation of the amygdala.

Urban Upbringing

We wanted to follow up on another important observation—namely, the increased risk for schizophrenia in people born and raised in cities. We analyzed the same subjects described above and quantified their early urban exposure using a simple score: we assigned three points for each year they resided in a city as a child, two for each year in a town and one for each year of country living. Again, we found one specific brain region—the perigenual anterior cingulate cortex (pACC)—whose activity levels under stress reflected the city score. Subjects who spent the most time growing up in cities showed the highest levels of pACC activity under pressure. Our second experimental group of 70 students showed the same correlation between pACC activation and urban upbringing.

This finding was not a total surprise. The pACC and the amygdala are closely interconnected. Studies indicate that the pACC serves to inhibit activity in the amygdala. If the pACC is damaged through chronic stimulation during a city upbringing, it might then fail to quell an overactive amygdala in an urban adult. If the same adult were sheltered from social strain, this deficit might never surface. Indeed, we gave brainteasers to a control group, without any pressure, and found no association between childhood environment and activity in the amygdala or pACC.

Additional research supports this idea. Various researchers—including Tsutomu Takahashi of Toyama University in Japan—have found structural changes in the pACC in patients with schizophrenia. Notably, these alterations also manifest among those who are at an increased genetic risk of the disease developing, before they exhibit any psychiatric symptoms. Similarly, working in conjunction with Daniel Weinberger and his colleagues at the National Institute of Mental Health, we have found dysfunctional feedback between the pACC and amygdala in people who are at an increased genetic risk for mood disorders but are not mentally ill.

Lean on Me

Our data reveal that the longer a person lives in a city, the less communication occurs between their amygdala and pACC. Genes and other factors then steer city dwellers closer to developing schizophrenia, anxiety, depression or violent tendencies. Fortunately, scientists have found mechanisms that strengthen feedback between these two brain regions. In 2011 Lisa Feldman Barrett and her colleagues at Massachusetts General Hospital reported that the volume of the amygdala increases with the size of a person's circle of friends. Our team has found that the hormone vasopressin—which, among other roles, is released during moments of bonding—reduces activity in areas of the cingulate cortex, including the pACC, and boosts feedback to the amygdala.

These studies highlight the well-documented fact that a close network of friends and family can insulate us from the most damaging effects of stress, but this is not the whole story. A lack of green space, noise and other environmental factors may also contribute to pACC and amygdala dysfunction, a possibility we plan to pursue in future imaging tests. Such research could have far-reaching consequences: Almost a third of schizophrenia cases might be avoided if more people were born in a rural setting. Herein lies a paradox: we cannot act on this insight without urbanizing the countryside. But we can try to design our cities so that they promote emotional well-being. In this way, we might take aim at the real goal of psychiatry, which is to prevent serious emotional disorders, not just treat them. M

We could identify city residents by brain scan alone. They had all been marked by telltale hyperactivity in the amygdala.

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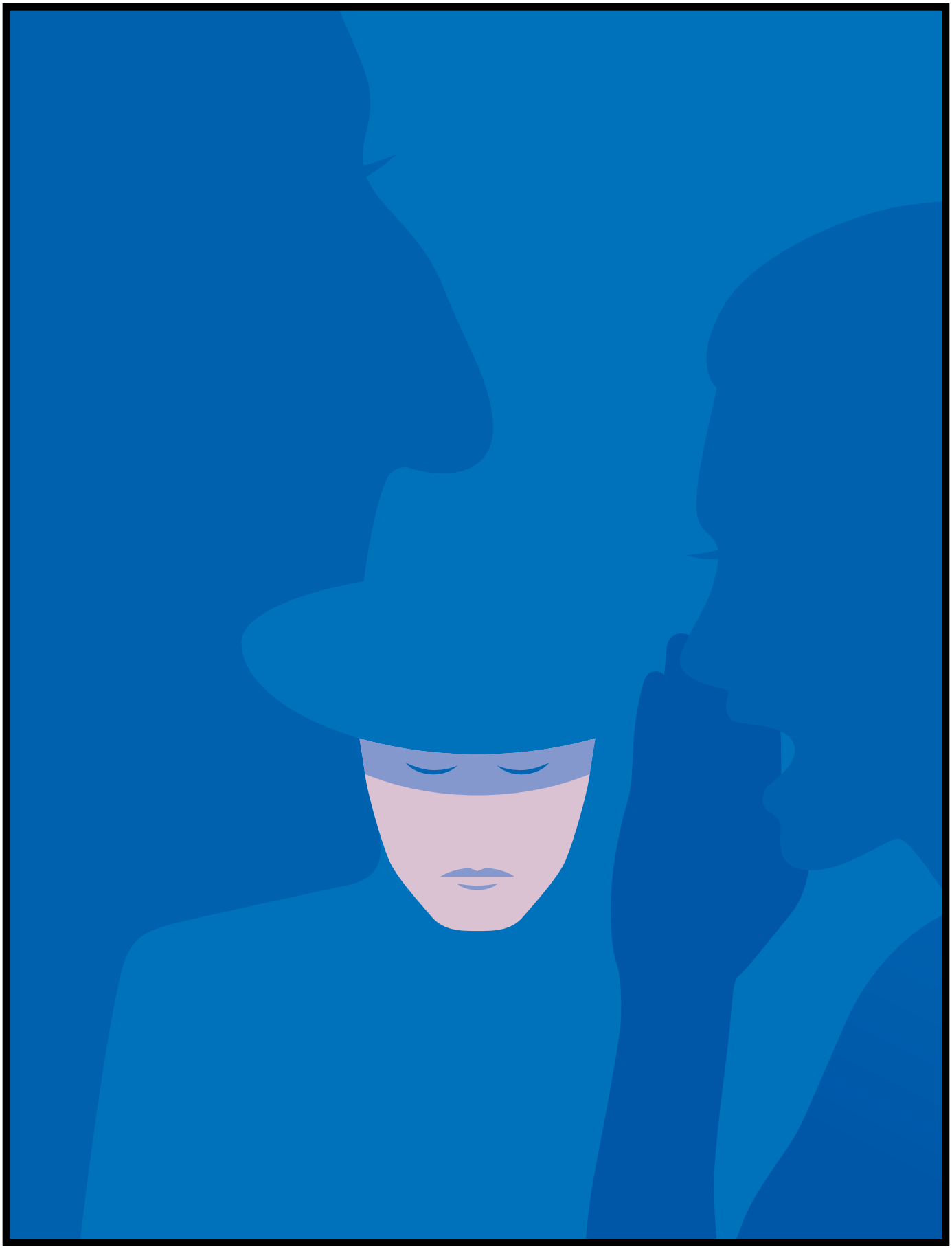


A Social Salve for Schizophrenia

Treating the less well-recognized social aspects of schizophrenia could help patients lead fuller, more productive lives

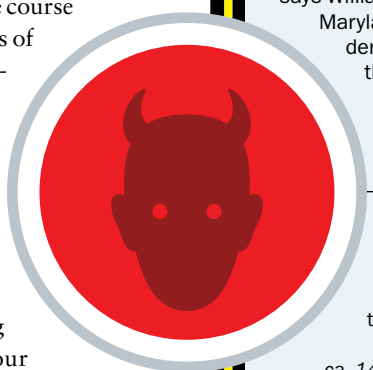
By Matthew M. Kurtz Illustrations by Patrick George

Emil Kraepelin, a German psychiatrist, wrote in 1913 that the causes of schizophrenia were "wrapped in impenetrable darkness." He outlined the symptoms that still characterize the disorder, including delusions, hallucinations and disorganized thinking. Kraepelin used a different term—"dementia praecox"—that reflected his belief in the disease's unremitting downward course (dementia) and its early onset (praecox).

Today we no longer embrace either dementia or praecox as components of schizophrenia, but the impenetrable darkness he described still lingers. Schizophrenia's causes and mechanisms remain poorly understood, and the most common treatments do little to restore patients to health. Between 70 and 80 percent of individuals who have schizophrenia are unemployed at any given time, and the vast majority of these sufferers will remain dependent on disability insurance throughout the course of life. The cost of the disorder to society, in terms of lost wages and lifelong medical care, is on the order of billions of dollars. And for the approximately 1 percent of the population that struggles with the disorder and their families, the effects can be devastating.

With drug development proceeding gradually, a suite of cognitive interventions has emerged with the potential to significantly upgrade patients' quality of life. These training programs target the core skills that support our ability to navigate social encounters and keep track of the day's demands. Although most of us take these capabilities for granted, they are all too often lacking in schizophrenia sufferers. With heightened awareness of these psychological techniques, more individuals with schizophrenia should be able to lead full and productive lives.

ISTOCKPHOTO (*road*)



Evolution of Schizophrenia

By Daisy Yuhas

Less than 200 years ago schizophrenia emerged from a tangle of mental disorders known simply as madness. In the upcoming fifth edition of psychiatry's primary guidebook, the *Diagnostic and Statistical Manual of Mental Disorders,* or *DSM-5,* schizophrenia will finally shed the outdated, 19th-century descriptions that have characterized it to this day. Yet the disorder remains poorly understood. "There is substantial dissatisfaction with schizophrenia treated as a disease entity; its symptoms are like a fever—something is wrong, but we don't know what," says William Carpenter, a psychiatrist at the University of Maryland and chair of the manual's Psychotic Disorders Work Group. Psychiatrists may discover that this disorder is not a single syndrome after all but a bundle of related conditions.

Madness, Demons and Delusions

circa 1550 B.C.
The Book of Hearts from ancient Egypt records how poison, demons, fecal matter or blood trouble may be at the root of madness.

ca. 1400 B.C.
The ancient Hindu Vedas describe illnesses characterized by bizarre behavior, lack of self-control, filth and nudity brought on by devils.

ca. 400 B.C.
Another early text, *The Yellow Emperor's Classic of Internal Medicine* from China, describes how insanity, dementia and seizures arose from demonic possession and other supernatural forces.

> Most of us in the field of schizophrenia have met people who function just fine in social settings as long as no one mentions the CIA.

Social Solutions

In May the American Psychiatric Association is expected to release a new edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM*), the psychiatric bible for classifying mental disorders. The book represents the first major update in how clinicians approach diseases of the mind in almost two decades. For schizophrenia, the revisions met with general approval. Until now, psychiatrists had to choose among a number of subtypes, such as paranoid, disorganized or catatonic, that held little diagnostic value. The new version will do away with all those labels.

Less prominent in the manual and in most discussions of schizophrenia are the social symptoms: persistent difficulties associated with living independently and maintaining meaningful relationships. Clinicians typically rely on drugs to treat the most prominent features of the disease, namely, the visions and false beliefs outlined by Kraepelin, whereas these equally debilitating lifestyle factors are often neglected. Antipsychotic medications, first discovered in France in the early 1950s, have severe limitations. Major side effects, such as weight gain and rigid limbs, often accompany their use, and in some cases the medication does not restore patients' sense of reality. More to the point, no studies link a drug-induced reduction in symptoms with the ability to hold down a job, live independently and sustain interpersonal bonds. None.

For patients to regain health and independence, psychiatrists also need to address the common deficits in attention, memory, planning and social awareness. For example, most if not all people with the disorder struggle with impaired cognitive skills, such as the ability to pay attention to directions or to remember which items to purchase at the store. Also quite common are difficulties with social skills. These include, for example, trouble reading your boss's angry expression when you inform her you will miss an important deadline or understanding why a friend is upset when you arrive half an hour late to dinner. When in a predicament, these individuals also tend to blame others, rather than themselves or the situation.

The development of methods for enhancing schizophrenia patients' social and cognitive skills has traditionally lagged be-

FAST FACTS

Better Than Drugs

1» Schizophrenia is best known for the delusions, hallucinations and disordered thinking that characterize the disease, but difficulties maintaining social ties and living independently are equally debilitating.

2» New therapies that aim to shore up basic social and cognitive skills have been shown to help people with schizophrenia build meaningful relationships, hold down jobs and cope with the disorder.

3» These techniques have helped rehabilitate schizophrenia sufferers more than any drug treatment, yet they are not widely practiced.

hind pharmacotherapy in the U.S. In part, the legacy of Sigmund Freud is to blame. He believed that people with schizophrenia were not amenable to psychoanalysis, and the idea stuck. Recent research, however, has found that certain psychological training regimens can ameliorate deficits in people with schizophrenia.

A review of several dozen studies on patient outcomes, published in 2011, suggests that allaying these challenges has a closer relation with many measures of successful coping—such as holding down a job, maintaining a strong social network and participating in community activities—than does addressing with drugs the disease's more prominent symptoms. False beliefs of persecution and illusory voices are not the biggest obstacle to normal interactions for most schizophrenia sufferers; instead problems following what others say to them or anticipating what another person is thinking tend to cause more disruption. Most of us working in this area have met people with the disorder with good cognitive and social skills who function just fine in professional and community settings as long as no one mentions the CIA. Helping less fortunate schizophrenia sufferers achieve this level of social functioning would go a long way toward easing the burden for all.

The good news is that a rapidly growing set of psychological interventions aim to shore up such elementary cognitive skills. One therapy is called cognitive remediation. First developed to treat traumatic brain injury, this approach is geared to improving patients' ability to concentrate, remember, plan and solve problems, either by restoring skills through repetitive practice or by acquiring strategies for bypassing those deficits.

Cognitive Boot Camp

Cognitive remediation therapies typically use computer software or paper-and-pencil exercises. They can occur individually or in groups, at home or in the clinic, and they always include high doses of positive reinforcement. Computerized exercises might involve distinguishing between brief sounds, for example, teasing apart "bah" and "boh." Visual training might focus on improving scanning abilities, perhaps by detecting a small yellow box amid distractions. An attention-shifting task might include identifying items of a particular color in several rows of streaming objects.

(The Author)

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1334 A.D.
Opicinus de Canistris, an Italian scribe, is struck by a strange illness in which he believes he sees the Virgin Mary. Afterward, he becomes socially withdrawn and devotes his time to creating fantastical maps. The case may describe either a stroke or an early example of schizophrenia.

Early Dementia

1809
French and English physicians Philippe Pinel and John Haslam independently describe young patients who show signs of "premature dementia." These cases are commonly referred to as the first thorough portraits of schizophrenia.

1834
Ukrainian writer Nikolay Gogol's *Diary of a Madman* follows Poprishchin, whose delusions of grandeur accompany his slide into insanity. The story is considered one of the earliest descriptions of schizophrenia in literature.

1871
German psychiatrists Karl Ludwig Kahlbaum and Ewald Hecker are among the first to categorize forms of "madness." Kahlbaum describes catatonia—characterized by alternating immobility and frenzy—and paranoia, in which an individual is overwhelmed by fear. Hecker identifies hebephrenia, which involves erratic behavior and incoherent speech.

1896
Emil Kraepelin, a German psychiatrist, describes dementia praecox as a lifelong disease that worsens with time. He later incorporates Hecker and Kahlbaum's disorders as syndromes of dementia praecox.

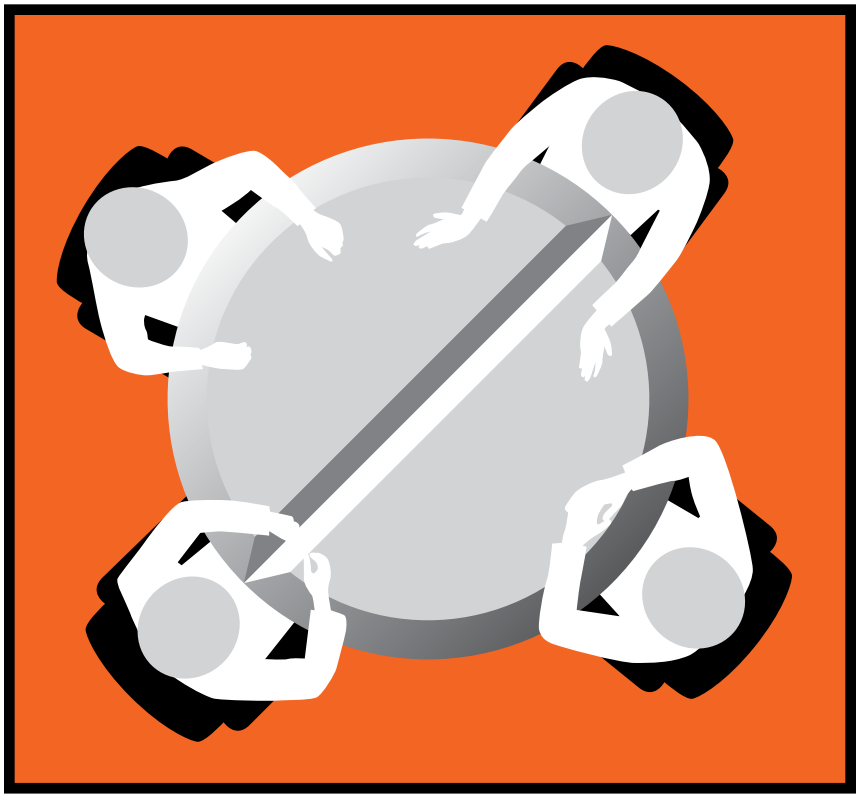
1906
Swiss psychiatrist Adolf Meyer rejects Kraepelin's concept of dementia praecox as a biological disease. Instead he favors a psychoanalytic approach, in which mental illness is triggered by life experiences, such as stress or a difficult childhood. Meyer's ideas will influence the *DSM-I* and *DSM-II* descriptions of schizophrenia.

"Schizophrenia"

1908
Swiss psychiatrist Eugen Bleuler, who did not believe that the disorder known as dementia praecox always involved deterioration and only struck adolescents, coins the term "schizophrenia," referring to a split mind.

1914
First use of term "schizophrenic" in a *Scientific American* publication, in an article entitled "The Psychanalytic Movement."

1930
Roaring 20s icon Zelda Fitzgerald is diagnosed with schizophrenia. She spends the rest of her life in mental hospitals. Her husband, F. Scott Fitzgerald, is inspired to write the novel *Tender Is the Night* about a woman's mental illness.



My colleagues and I decided to test whether such exercises can improve concentration skills in schizophrenia patients. In a study published in 2007 we divided our recruits into two groups. Half our participants performed these exercises, and the other half—our control group—learned basic computer skills, namely, how to use Microsoft Office programs. At the end of the study, all the patients were asked to keep in mind a list of numbers and mentally manipulate those figures. Compared with their peers who had learned generic computer tasks, the subjects who had practiced cognitive remediation performed much better, demonstrating a strengthened working memory. This study suggests that the effects are not caused by mere exposure to a computer or to general cognitive stimulation but arise from reinforcing the building-block sensory and cognitive skills that support many thought processes.

> These therapies might help protect people from developing full-blown schizophrenia or at least slow the disease's progression.

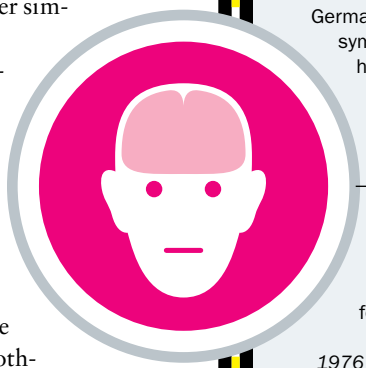
Other cognitive remediation programs focus on more complex activities. For example, a patient might see a computer screen with an array of numbers and letters and be asked to count how many numbers appeared. At the flash of a red light, the patient was to start alphabetizing the letters in the array instead. At the next flash, the person was to return to tallying numbers. In a 2007 paper psychologist Til Wykes of King's College London and her research group compared how patients fared when practicing these kinds of interventions as opposed to when they received only typical support services. The subjects who performed these exercises, but not the control group, saw substantial gains in their working memory and cognitive flexibility. They also improved on several measures of social function, such as maintaining hygiene, initiating appropriate interactions with others and avoiding confrontational situations.

Remarkably, these therapies appear to create demonstrable changes in the brain. Recent work has shown that cognitive remediation can increase activation in the medial prefrontal cortex, an area involved in decision making that sits right behind the forehead. In a 2012 study, for example, neuroscientist Karuna Subramaniam of the University of California, San Francisco, and her colleagues found that this heightened brain activity is linked with schizophrenia patients' improved performance during "reality monitoring," which is the ability to differentiate between internal experiences and the outside world. When people begin receiving cognitive training at the time of diagnosis, during the earliest stages of the disease's progression, they can also stave off the loss of brain volume in key parts of the temporal lobe. Abnormalities in these areas of the brain, which deal with processing sensory information and language, are often associated with schizophrenia.

Newer treatments, called social cognitive training programs, are also aimed at assisting people with the disorder become better social detectives: among other skills, by helping them to decipher emotional cues and take another person's perspective. These interventions include practice recognizing the aspects of facial expressions that signal certain emotions, for example, that raised eyebrows indicate surprise. A social cognitive training regimen might also help schizophrenia sufferers avoid jumping to conclusions by prompting them to compose alternative explanations for an unpleasant interaction. Consider a schizophrenia sufferer who is cut off on a highway exit ramp by another driver. That individual

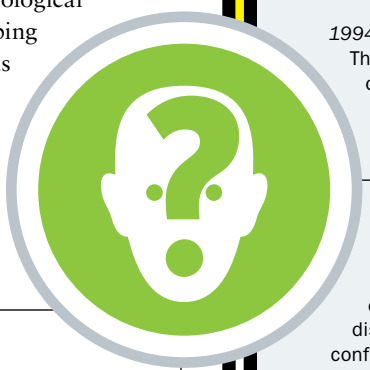
might first assume that the offending driver is a member of the CIA conducting surveillance on him and trying to force him into an accident so he lands in the hospital. These therapies encourage the patient to consider other interpretations, such as by noting that it is nearly 9 A.M. and the other driver simply might be late for work.

Initial studies have produced promising support for social cognitive interventions, which involve, among other tasks, conducting repeated, detailed analyses of facial expressions or scenarios. A 2012 meta-analysis by my colleague Christi L. Richardson and me showed that rehearsing these skills two to three times a week for several months helped practitioners learn such skills as appropriate language and tone of voice, which improved their interactions with others. These individuals participated more often in their community, developed more meaningful friendships and performed better at their jobs. They also demonstrated fewer symptoms of anxiety and depression, which often accompany the disease, as compared with patients in the control group, who were given typical community treatment.



Sadly, few treatment centers offer these psychological interventions. Although change is always gradual, greater emphasis on providing access to the rich array of psychological treatment technologies developed for schizophrenia could have a profound influence on the way we view outcomes for this devastating disorder. The evidence suggests that we can protect people from developing full-blown versions of schizophrenia using these therapies or at least slow the disease's progression.

We might even be able to assist people before the first symptoms manifest. New studies are applying psychological therapies to people at an elevated risk of developing psychosis, with promising early results. Much as practicing scales and arpeggios can help a pianist maintain good form, reinforcing fundamental cognitive skills could let schizophrenia patients stay connected with society. Drugs may help stitch together a broken sense of reality, but that is just half the battle. M



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- **Computerized Cognitive Training Restores Neural Activity within the Reality Monitoring Network in Schizophrenia.** Karuna Subramaniam et al. in *Neuron,* Vol. 73, No. 4, pages 842–853; February 23, 2012.
- **Social Cognitive Training for Schizophrenia: A Meta-analytic Investigation of Controlled Research.** Matthew M. Kurtz and Christi L. Richardson in *Schizophrenia Bulletin,* Vol. 38, No. 5, pages 1092–1104; September 2012.

1958
Premiere of *Suddenly Last Summer,* by Tennessee Williams. Williams is said to have based his troubled heroine, Catharine Holly, on his sister, Rose Williams, who was diagnosed with schizophrenia and underwent a lobotomy.

1959
German psychiatrist Kurt Schneider identifies core symptoms of schizophrenia, such as auditory hallucinations and delusions, that distinguish it from other forms of psychosis. His criteria end up informing the *DSM-III*.

Biological Mystery

1972
Neurologist Fred Plum calls the disorder a "graveyard of neuropathologists," a reference to the apparent lack of a brain-based explanation for schizophrenia.

1976
A study of CT scans suggests differences in the size of cerebral ventricles in patients with schizophrenia. This is the first of many studies to identify brain anomalies associated with schizophrenia.

1980
Building on Kraepelin's definition, the *DSM-III* recognizes five subtypes of schizophrenia: disorganized (hebephrenic), catatonic, paranoid, residual and undifferentiated.

1986
German psychiatrist Karl Leonhard suggests schizophrenia is a group of psychoses—including hallucinations and cognitive dysfunction—rather than a single disorder.

1994
Mathematician John Forbes Nash, Jr., receives a Nobel Prize. His struggles with schizophrenia are the subject of *A Beautiful Mind,* a biography by Sylvia Nasar and an eponymous Oscar-winning film.

1994
The *DSM-IV* is published. It includes subtypes of schizophrenia but notes their limited utility in diagnosis.

Contemporary Questions

2002
The Japanese Society of Psychiatry and Neurology changed the name of schizophrenia from *seishin bunretsu byo,* or "mind-split disease," to *togo shitcho sho,* or "integration disorder." The change has reduced stigma and confusion about the nature of the disease.

2009
In what *New York Times* reporter Nicholas Wade dubs "a Pearl Harbor of schizophrenia research," three studies in *Nature* journals implicate between tens and thousands of possible gene variants.

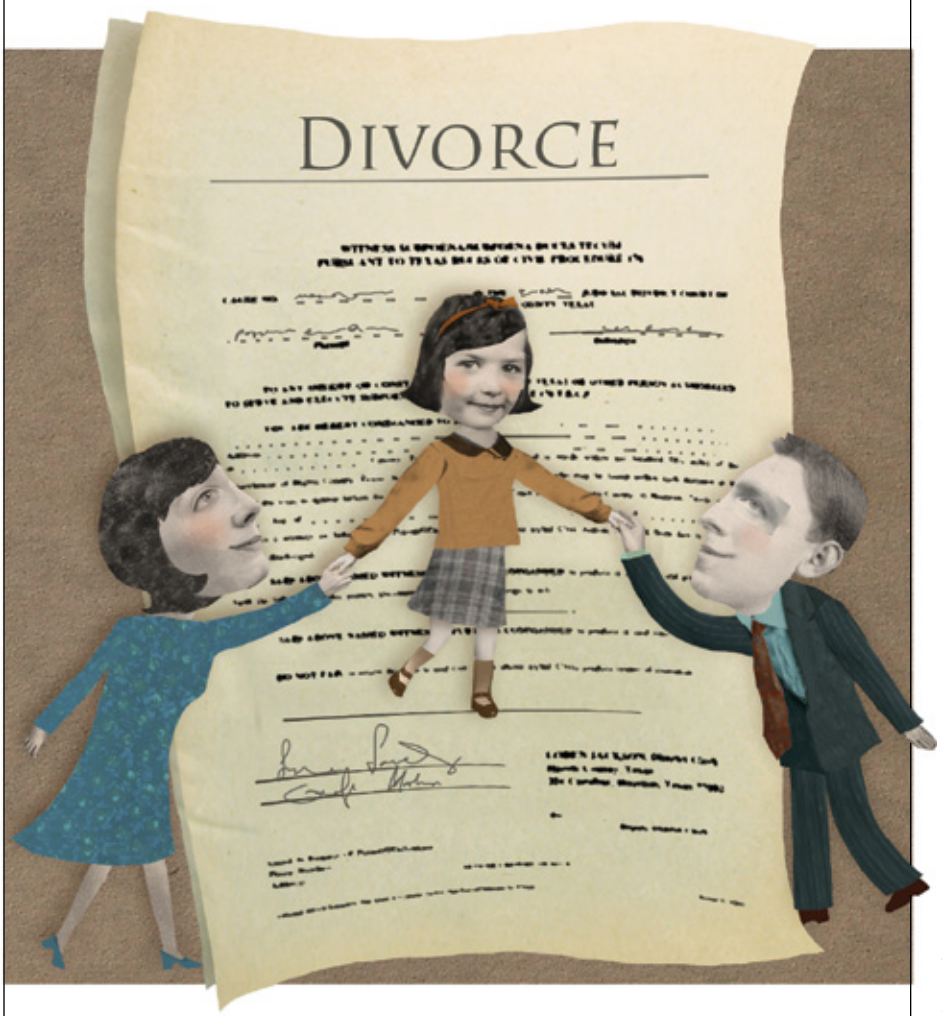
2013
The *DSM-5* will remove the subtypes of schizophrenia. To receive a diagnosis of schizophrenia, patients must now exhibit delusions, hallucinations or disorganized speech. They may also experience motor difficulties, such as catatonia, and negative symptoms, such as social withdrawal or lack of emotional responsiveness.

DAISY YUHAS is a freelance science writer in New York City.

Is Divorce Bad for Children?

The break-up may be painful, but most kids adjust well over time

BY HAL ARKOWITZ AND SCOTT O. LILIENFELD



COURTESY OF HAL ARKOWITZ (*Arkowitz*); COURTESY OF SCOTT O. LILIENFELD (*Lilienfeld*); ISABELLE CARDINAL (*illustration*)

MANY of the 1.5 million children in the U.S. whose parents divorce every year feel as if their worlds are falling apart. Divorcing parents are usually very concerned about the welfare of their children during this troublesome process. Some parents are so worried that they remain in unhappy marriages, believing it will protect their offspring from the trauma of divorce.

Yet parents who split have reasons for hope. Researchers have found that only a relatively small percentage of children experience serious problems in the wake of divorce or, later, as adults. In this column, we discuss these findings as well as factors that may protect children from the potentially harmful effects of divorce.

Rapid Recovery

Divorce affects most children in the short run, but research suggests that kids recover rapidly after the initial blow. In a 2002 study psychologist E. Mavis Hetherington of the University of Virginia and her then graduate student Anne Mitchell Elmore found that many children experience short-term negative effects from divorce, especially anxiety, anger, shock and disbelief. These reactions typically diminish or disappear by the end of the second year. Only a minority of kids suffer longer.

Most children of divorce also do well in the longer term. In a quantitative review of the literature in 2001, sociologist Paul R. Amato, then at Pennsylvania State University, examined the possible effects on children several years after a divorce. The studies compared children of married parents with those who experienced divorce at different ages. The investigators followed these kids into later childhood, adolescence or the teenage years, assessing their academic achievement, emotional and behavior problems, delinquency, self-concept and social relationships. On average, the studies found only very small differences on all these measures between children of divorced parents and those from intact families, suggesting that the vast majority of children endure divorce well.

Researchers have consistently found that high levels of parental conflict during and after a divorce are associated with poorer adjustment in children. The effects of conflict before the separation, however, may be the reverse in some cases. In a 1985 study Hetherington and her associates reported that some children who are exposed to high levels of marital discord prior to divorce adjust better than children who experience low levels. Apparently when marital conflict is muted, children are often unprepared when told about the upcoming divorce. They are surprised, perhaps even terrified, by the news. In addition, children from high-discord families may experience the divorce as a welcome relief from their parents' fighting.

Taken together, the findings suggest

that only a small percentage of young people experience divorce-related problems. Even here the causes of these lingering difficulties remain uncertain. Some troubles may arise from conflict between Mom and Dad associated with the divorce. The stress of the situation can also cause the quality of parenting to suffer. Divorce frequently contributes to depression, anxiety or substance abuse in one or both parents and may bring about difficulties in balancing work and child rearing. These problems can impair a parent's ability to offer children stability and love when they are most in need.

Grown-up Concerns

The experience of divorce can also create problems that do not appear until the late teenage years or adulthood. In 2000 in a book entitled *The Unexpected Legacy of Divorce: A 25 Year Landmark Study,* Judith Wallerstein, then at the University of California, Berkeley, and her colleagues present detailed case studies suggesting that most adults who were children of divorce experience serious problems such as depression and relationship issues.

Yet scientific research does not support the view that problems in adulthood are prevalent; it instead demonstrates that most children of divorce become well-adjusted adults. For example, in a 2002 book, *For Better or For Worse: Divorce Reconsidered,* Hetherington and her co-author, journalist John Kelly, describe a 25-year study in which Hetherington followed children of divorce and children of parents who stayed together. She found that 25 percent of the adults whose parents had divorced experienced serious social, emotional or psychological troubles compared with 10 percent of those whose parents remained together. These findings suggest that only 15 percent of adult children of divorce experience problems over and above those from stable families. No one knows whether this difference is caused by the divorce itself or by variables, such as poorer parenting, that often accompany a marriage's dissolution.

In a review article in 2003, psychologists Joan B. Kelly of Corte Madera, Calif., and Robert E. Emery of the University of Virginia concluded that the relationships of adults whose parents' marriages failed do tend to be somewhat more problematic than those of children from stable homes. For instance, people whose parents split when they were young experience more difficulty forming and sustaining intimate relationships as young adults, greater dissatisfaction with their marriages, a higher divorce rate and poorer relationships with the noncustodial father compared with adults from sustained marriages. On all other measures, differences between the two groups were small.

Bouncing Back

Even though children of divorce generally do well, a number of factors can reduce the problems they might experience. Children fare better if parents can limit conflict associated with the divorce process or minimize the child's exposure to it. Further, children who live in the custody of at least one well-functioning parent do better than those whose primary parent is doing poorly. In the latter situation, the maladjusted parent should seek professional help or consider limiting his or her time with the child. Parents can also support their children during this difficult time by talking to them clearly about the divorce and its implications and answering their questions fully.

Other, more general facets of good parenting can also buffer against divorce-related difficulties in children. Parents should provide warmth and emotional support, and they should closely monitor their children's activities. They should also deliver discipline that is neither overly permissive nor overly strict. Other factors contributing to children's adjustment include postdivorce economic stability and social support from peers and other adults, such as teachers.

In addition, certain characteristics of the child can influence his or her resilience. Children with an easygoing temperament tend to fare better. Coping styles also make a difference. For example, children who are good problem solvers and who seek social support are more resilient than those who rely on distraction and avoidance.

The good news is that although divorce is hard and often extremely painful for children, long-term harm is not inevitable. Most children bounce back and get through this difficult situation with few if any battle scars. M

Children who are problem solvers and seek support are more resilient than those **who rely on distraction and avoidance**.

HAL ARKOWITZ and SCOTT O. LILIENFELD serve on the board of advisers for *Scientific American Mind.* Arkowitz is an associate professor of psychology 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)

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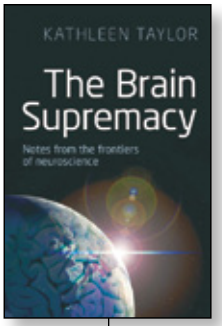
- **Reconciling Divergent Perspectives: Judith Wallerstein, Quantitative Family Research, and Children of Divorce.** Paul R. Amato in *Family Relations,* Vol. 52, No. 4, pages 332–339; October 2003.

books

BRAIN NEW WORLD

The Brain Supremacy: Notes from the Frontiers of Neuroscience

by Kathleen Taylor. Oxford University Press, 2012 ($29.95)



What if our thoughts could be plumbed by a brain scanner and memories manipulated with the flip of a genetic switch? Neuroscientist Taylor believes these science fiction–like scenarios could become reality because new technologies may soon allow unprecedented access to our brains.

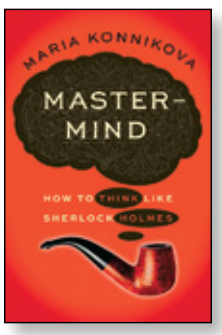
Taylor begins *The Brain Supremacy* by contemplating a future in which we can decipher others' private emotions and ideas as well as sculpt designer minds. Scientists can already decode single words and reconstruct mental images using functional MRI. We also tinker with brain activity on a daily basis by consuming mood-altering chemicals, such as caffeine and alcohol. More targeted neural enhancements, which might involve inserting new genes or modifying existing ones, could improve not only our cognition but also our personality, fashioning more law-abiding citizens or devoted spouses.

The intended appeal of *The Brain Supremacy* may be its future-focused musings, but this is the weakest part of the book. Though compelling in theory, Taylor's predictions fall flat because, as she admits, we are nowhere close to creating the tools or understanding the brain sufficiently to probe it in such depth. For instance, her critiques of fMRI make it clear that the technology is not equipped for full-fledged mind reading; it is too slow to catch moment-to-moment neural activity, and its data are often too crude to interpret.

Taylor's richest material lies in her explanations of what neuroscience can do now. She crafts an elegant guidebook on current technologies and methods for studying the brain, comparing the capabilities of different approaches and conveying the tedium of most day-to-day science. She describes her early research using rats to model activity in a part of the brain that processes touch. Her team inserted electrodes into the rats' brains and injected chemicals to observe how sensory receptors responded, then extracted the brains for analysis. The ability to probe and tinker with a brain in this way is invaluable in our search for knowledge.

Taylor does touch on research that could lay the foundation for more invasive and comprehensive cognitive enhancements. For instance, she reveals how investigators engineered mice to have a specific number of serotonin receptors, which are located in various brain regions and have been shown to affect the success of antidepressants. Mice with fewer receptors responded to Prozac, whereas those with many did not, supporting the hypothesis that simple genetic differences might explain why a drug works in some people and fails in others. This research showcases our potential to tailor drugs to an individual or tweak genes to make treatments more effective.

This comprehensive guide to the powers and limitations of neuroscience has much to offer, whether one agrees or disagrees with Taylor's predictions. Her goal is to intrigue and motivate further investigation, and she succeeds on that front. —*Daisy Yuhas*



ELEMENTARY MIND-SET

Mastermind: How to Think Like Sherlock Holmes

by Maria Konnikova. Viking Adult, 2013 ($26.95)

Long before science revealed that synapses fire in patterns, literature endeavored to map the cognitive landscape. From Odysseus restraining himself against the Sirens' song to Tom Sawyer conning his way out of painting fences, fictional characters have captured many nuances of human psychology. Perhaps no character has articulated the science of thinking as directly as Sherlock Holmes, the great consulting detective created by Sir Arthur Conan Doyle. Holmes's prescient insights into the human mind form the basis of *Mastermind: How to Think Like Sherlock Holmes,* by science writer Konnikova.

Holmes's ability to solve the most confounding mysteries armed only with the ordinary human senses makes him a credible self-improvement role model. Konnikova, who writes the Literally Psyched blog for ScientificAmerican.com, examines Holmes's uncanny skills of deduction through the lens of modern psychology and neuroscience. In the process, Holmes emerges not only as a proponent of the scientific method but also, more surprisingly, as a practitioner of mindfulness. To think like Holmes is to be unfailingly objective and always present in the moment.

Konnikova mines Holmes's adventures for examples of the detective explicating psychological concepts established long after his time. Here is Holmes scolding Watson, when charmed by a comely female client, for succumbing to correspondence bias, the tendency to interpret behavior through someone's personality. There is Holmes explaining omission neglect, the tendency to ignore missing information, when he notes that a dog's silence can be as telling as its bark (for Holmes, this meant the dog knew the intruder). Amid tough cases, Holmes's pipe smoking, violin playing and trips to the symphony are not just quirks—they are his way of stimulating the creative process through mental and physical distance.

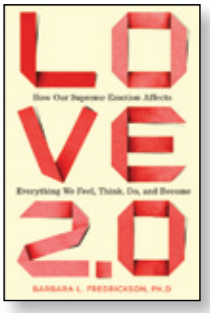
Scientifically, Konnikova does not cover any ground not already canvassed by other pop psychology books, which often do so in more depth. The novelty of *Mastermind*—a book that barely rises above its origins as blog posts—is in introducing these same ideas through the language and allegory of Conan Doyle's stories. Fast, impulsive thinking becomes the "Watson system"; slower, rational thinking the "Holmes system"; and the human mind is dubbed the "brain attic," a phrase coined by Holmes. These devices might tickle the Holmes fan but can be frustrating for a reader more interested in the science behind the extended metaphors.

Holmes's genius lies not only in an awareness of the common pitfalls in human thinking but also in his ability to overcome these weaknesses in himself. He achieved the latter through a lifetime of practice, Konnikova says—and that is the summation of her book's advice. Although *Mastermind* promises to teach you how to think like Holmes, it succeeds mostly in enumerating the many ways we behave like Watson. It's too hard, even inhuman, to go through life thinking like Holmes. —*Nina Bai*

MORE THAN A FEELING

Love 2.0: How Our Supreme Emotion Affects Everything We Feel, Think, Do, and Become

by Barbara L. Fredrickson. Hudson Street Press, 2013 ($25.95)



Emotion researcher Fredrickson wants to revamp our view of love. In *Love 2.0.,* she has us reimagine love as a series of micromoments in which any two people, even strangers, can click with each other. This feeling might pop up multiple times a day, perhaps when smiling at a stranger or striking up a conversation while waiting in line for coffee.

Fredrickson builds her case by expanding on research that shows how sharing a strong bond with another person alters our brain chemistry. She describes a study in which best friends' brains nearly synchronize when exchanging stories, even to the point where the listener can anticipate what the storyteller will say next. Fredrickson takes the findings a step further, concluding that having positive feelings toward someone, even a stranger, can elicit similar neural bonding.

This leap, however, is not supported by the study and fails to bolster her argument. In fact, most of the evidence she uses to support her theory of love falls flat. She leans heavily on subjective reports of people who feel more connected with others after engaging in mental exercises such as meditation, rather than on more objective studies that measure brain activity associated with love.

Fredrickson's strongest section is her exploration of how we can turn her insights into practice. For instance, she argues that loving-kindness meditation, which focuses on directing good-hearted wishes to others, can enhance our ability to connect. In one study, she found that regular use of this practice strengthens vagal tone, a measure of the vagus nerve, which relays sensory information between the brain and other areas. People with higher vagal tone are physically healthier, exhibiting less inflammation associated with cancer, and are more adept at bonding with others.

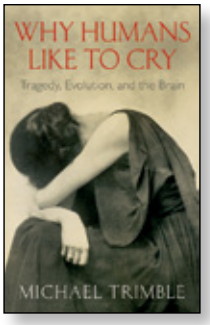
Love 2.0 offers a new perspective on a well-worn topic. Despite the book's flaws, Fredrickson's aim in broadening our view of the emotion is to spread the love. A worthy goal. —*Samantha Murphy*

ADRIAN NIEDERHÄUSER *iStockphoto*

COMPLEX TEARS

Why Humans Like to Cry: Tragedy, Evolution, and the Brain

by Michael Trimble. Oxford University Press, 2012 ($29.95)



Mammals can all produce tears, yet humans are the only ones who cry. In his new book *Why Humans Like to Cry,* neurologist Trimble delves into how evolution and culture seemingly shaped the human brain to express emotion on a higher level than the rest of the animal kingdom.

Weeping may have been one of the earliest forms of hominid communication. Initially a method to keep the eye lubricated and a response to pain, Trimble argues that crying became a way for early humans to share feelings of sorrow, joy and compassion and to empathize with others long before we developed language.

Human emotions arise from a network of interconnected brain regions. Trimble discusses research findings that show our brain's emotionally driven limbic system is deeply connected with other areas of the nervous system, such as the sensory cortex, which helps us process our surroundings. As a result, our feelings are integrated with our environment and bodily responses, a different paradigm than occurs in other species. In fact, he suggests that one possible reason we feel better after crying is that weeping stimulates our cranial nerves, which in turn appears to soothe our overactive amygdala.

Trimble also describes how various art forms, especially music, carry the power to elicit tears. This phenomenon can be explained, in part, by brain-imaging studies that show music can tap into the limbic system of the brain. Simple chords can evoke memories, physical reactions, and feelings of joy and sadness. In one study, researchers found that of 83 people listening to poignant music, 90 percent experienced shivers and 85 percent shed tears. Another study showed that familiar songs triggered emotional memories in listeners.

Trimble ambitiously cracks the surface of a complex human process. Crying, then, does not indicate weakness; rather it highlights our advancement.

—*Brian Mossop*

ROUNDUP

Brain **Truths** Three books seek to improve our outlook on life

Feeling overly worked up over the slow traffic light or the car honking as you cross the intersection? In **Your Survival Instinct Is Killing You: Retrain Your Brain to Conquer Fear, Make Better Decisions, and Thrive in the 21st Century** (Hudson Street Press, 2013), psychologist Marc Schoen explains why. He reveals that our brain's limbic system, which processes emotions, has become overly sensitive to potential threats. It no longer reacts only to immediate dangers, which gave our ancestors a keen survival instinct. Now simple annoyances can rev it up. Our brain's tendency to be in overdrive explains why we might feel anxious or short-tempered over the little things. Schoen recommends several tactics to help calm our nerves, including hypnosis and healthier eating habits.

Pressure to marry, raise children and earn a fat paycheck may lead many to feel unsatisfied if they have not achieved these goals by a certain age. In **The Myths of Happiness: What Should Make You Happy, but Doesn't, What Shouldn't Make You Happy, but Does** (Penguin Press, 2013), psychologist Sonja Lyubomirsky argues that we have it all wrong. Happiness does not depend on attaining these markers of "success." Rather this narrow view of success often leads to disappointment. She points to studies that show our mind-set, not our situation, dictates our happiness and says staying open-minded will help us make better choices and craft a more fulfilling life.

Wonder why that girl in your econ class gets under your skin or why you don't trust politicians? Your unconscious might be talking. In **Subliminal: How Your Unconscious Mind Rules Your Behavior** (paperbound, Vintage, 2013), physicist Leonard Mlodinow explores how our unconscious mind dictates much about how we perceive and experience the world, influencing our relationships, our opinions and even our memories. By understanding the driving force that is our unconscious, we can become more aware of our underlying biases and misperceptions and work to rectify them.

—*Victoria Stern*

askthe**Brains**

Can we control our thoughts? Why do thoughts pop into my head as I'm trying to fall asleep?

*—**Esther Robison,** New York City*

Barry Gordon, *professor of neurology and cognitive science at the Johns Hopkins University School of Medicine, replies:*

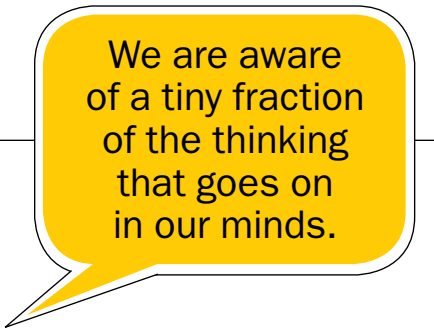
WE ARE AWARE of a tiny fraction of the thinking that goes on in our minds, and we can control only a tiny part of our conscious thoughts. The vast majority of our thinking efforts goes on subconsciously. Only one or two of these thoughts are likely to breach into consciousness at a time. Slips of the tongue and accidental actions offer glimpses of our unfiltered subconscious mental life.

The intrusive thoughts you may experience throughout the day or before bed illustrate the disconcerting fact that many of the functions of the mind are outside of conscious control. Whether we maintain true control over any mental functions is the central debate about free will. Perhaps this lack of autonomy is to be expected as the foundations for almost all the mind's labors were laid long before our ancestors evolved consciousness.

Even deliberate decisions are not completely under our power. Our awareness only sets the start and the end of a goal but leaves the implementation to unconscious mental processes. Thus, a batter can decide to swing at a ball that comes into the strike zone and can delineate the boundaries of that zone. But when the ball comes sailing through, unconscious mental functions take over. The actions required to send him to first base are too complex and unfold too quickly for our comparatively slow conscious control to handle.

We exert some power over our thoughts by directing our attention, like a spotlight, to focus on something specific. The consequences of doing so can be amusing, as in the famous experiments in which about one third of the people watching a basketball game failed to spot a man in a gorilla suit crossing the court. Or the consequences can be disastrous, as when a narrow focus prevents a driver from noticing a light turning red or an oncoming train.

Although thoughts appear to "pop" into awareness before bedtime, their cognitive precursors have probably been simmering for a while. Once those preconscious thoughts gather sufficient strength, the full spotlight of consciousness beams down on them. The mind's freewheeling friskiness is only partly under our control, so shutting our mind off before we sleep is not possible.



Can training to become ambidextrous improve brain function?

*—**Rachel Fallon,** via e-mail*

Michael Corballis, *professor of cognitive neuroscience and psychology at the University of Auckland in New Zealand, responds:*

ALTHOUGH TEACHING people to become ambidextrous has been popular for centuries, this practice does not appear to improve brain function, and it may even harm our neural development.

Calls for ambidexterity were especially prominent in the late 19th and early 20th centuries. For instance, in the early 20th century English propagandist John Jackson established the Ambidextral Culture Society in pursuit of universal ambidexterity and "two-brainedness" for the betterment of society.

This hype died down in the mid-20th century as benefits of being ambidextrous failed to materialize. Given that handedness is apparent early in life and the vast majority of people are right-handed, we are almost certainly dextral by nature. Recent evidence even associated being ambidextrous from birth with developmental problems, including reading disability and stuttering. A study of 11-year-olds in England showed that those who are naturally ambidextrous are slightly more prone to academic difficulties than either left- or right-handers. Research in Sweden found ambidextrous children to be at a greater risk for developmental conditions such as attention-deficit hyperactivity disorder. Another study, which my colleagues and I conducted, revealed that ambidextrous children and adults both performed worse than left- or right-handers on a range of skills, especially in math, memory retrieval and logical reasoning.

These effects are slight, but the risks of training to become ambidextrous may cause similar difficulties. The two hemispheres of the brain are not interchangeable. The left hemisphere, for example, is typically responsible for language processing, whereas the right hemisphere often handles nonverbal activities. These asymmetries probably evolved to allow the two sides of the brain to specialize. To attempt to undo or tamper with this efficient setup may invite psychological problems.

It is possible to train your nondominant hand to become more proficient. A concert pianist demonstrates superb skill with both hands, but this mastery is complementary rather than competitive. The visual arts may enhance right-brain function, though not at the expense of verbal specialization in the left hemisphere. A cooperative brain seems to work better than one in which the two sides compete. M

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

JAMIE CARROLL /iStockphoto

Head Games

Match wits with the Mensa puzzlers

1 NO ACCOUNTING FOR TASTE

Sylvia will walk alongside someone but not after him; she will eat grapefruit but not apples; she likes her friend Maryanne Johnson but not her neighbor Marilyn Smith; she will eat at a chophouse but not at a restaurant. Will she visit Ireland or Switzerland?

2 WORD PROBLEM

Each letter in the subtraction problem below stands for a number from 0 to 9. Find the right substitution to make the equation correct.

EMIT
−MITE
TIME

3 CALENDAR MATH

What's the number of days in a week less than the number of days in a long month less than 1/5 of 10 times the square root of the number that is four less than the number of days in a year?

4 WORD MORPH

Go from HAIR to COMB by changing one letter at a time, with a legitimate word at each step.

HAIR
_ _ _ _
_ _ _ _
_ _ _ _
_ _ _ _
_ _ _ _
_ _ _ _
COMB

5 CRYPTOGRAM

Solve the code to find out what happened when Old Mother Hubbard went to the cupboard to get her poor dog a bone. When she got there, the cupboard was bare,

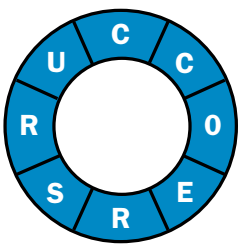
UQ UJG JCF VQ VCMG QWV C DCPM NQCP

6 TIMES TABLES

Dean was playing with his toy soldiers. He set them up in rows, trying to arrange a parade, but he had trouble. When he set them up by pairs, he had one soldier left. By threes, fours, fives and sixes, he had the same problem. At seven across, he had two left over; at eight across, one left over; at nine across, four left over. But at 11, the rows worked out with no soldiers left over. What was the least number of toy soldiers he could have had in his army?

7 WRITING IN CIRCLES

The following word circle contains a word. Find the right starting letter and move in one direction only, either clockwise or counterclockwise, to decipher the word.



8 SCRAMBLE

Which of the following groups of letters, when unscrambled, is least like the others?

PEEIRR TNROENT SAAOECRMTN OOLNDRA

9 BUDGET DESIGN

Clotheshorse Carl has $2,000 to spend on coats and shoes. Coats are $110 each, and each shoe (just one shoe) is $40 cheaper than a coat. How many coats and pairs of shoes could he buy to spend his $2,000 exactly?

10 MIRRORS

Fill in the blanks with a word that fits the left definition when read forward and the right definition when read backward.

a male deer	____	____	**gangster movie slang for pistols**
weapons	____	____	**cozy**
give out	____	____	**measure of continuous existence**
a mechanic's need	____	____	**a strip of leather or cloth**

Answers

1. Ireland. She only likes words that can be broken into two parts, each of which makes a word itself.
2. 9,108 − 1,089 = 8,019
3. Zero.
4. One possible route:
HAIR
HAIL
HALL
HALE
HOLE
HOME
COME
COMB
5. So she had to take out a bank loan. (A = C, B = D, and so on.)
6. 121.
7. RECCURS.
8. ORLANDO. The others are state capitals: PIERRE, TRENTON, SACRAMENTO.
9. Eight coats ($880) and eight pairs of shoes ($1,120).
10. STAG GATS
GUNS SNUG
EMIT TIME
PARTS STRAP

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BRIGHT HORIZONS™ 17

NORWEGIAN FJORDS, JULY 5–15, 2013

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Cruise prices vary from $2,169 for an Interior Stateroom to $7,499 for a Royal Suite, per person. For those attending our Program, there is a $1,575 fee. Port charges are $235. Government taxes and an Insight Cruises service fee are $215 per person. Gratuities are $150 per person. Program subject to change.

Neurobiology

Speaker: Robert Sapolsky, Ph.D.

The Biology of Memory

Consider the biology of memory. We'll start with the neurobiology of different types of memory, from the pertinent regions of the brain down to the pertinent molecules and genes. Learn about memory's impressive features, wild inaccuracies, and failings in neurological diseases. Examine individual differences in memory skills and find out how to improve your own memory capacities.

Sushi and Middle Age

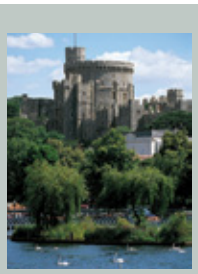
When was the last time you tried a really different, strange type of food, explored the work of a new composer, or made a substantial change in appearance? As we age, we get less interested in novelty and increasingly crave the familiar. Examine the neurobiology and psychology underlying this age-related effect.

Humans: Are We Just Another Primate? Are We Just a Bunch of Neurons?

Dr. Sapolsky both does neurobiology research in the lab and research on wild baboons in East Africa. He'll consider human nature from these two perspectives. Are we just another primate on a continuum with all the others, or are we intrinsically special? Find out a biologist's answer.

The Biology of Aggression and Violence

Examine the biology of violence, dealing with a single fact that makes this one of the most complicated subjects in behavioral biology — we don't hate violence, just violence in the wrong context. Looking at neurobiology, Us/Them dichotomies, hormones, evolutionary biology, and game theory, put the phenomenon of violence in a scientific context.



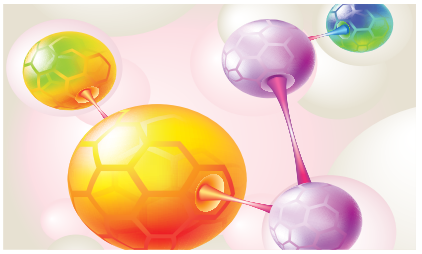
Hampton Court and Windsor Castle (July 2)

Join us visiting two timeless treasures in a day designed to bring British history to life. Enhance your knowledge of Britain's history with an idyllic day trip to Windsor Castle (left) and Hampton Court Palace. They are related yet differing demonstrations of British monarchy, nationhood, and domesticity.

It's good to be Queen, and the evidence is all about you at 1,000 year old Windsor Castle. Rubens, Rembrandt, and a remarkable collection of fine art envelope you in history. Go behind the scenes at the legendary seat of the House of Windsor.

Hampton Court (also known as King Henry VIII's summer palace) is a place of royal passions and competing interests. Pomp and consequence, subterfuge and service inform the history of the palace. Our visit will put the juxtaposed Tudor and Baroque architecture, larger than life personalities, exquisite Chapel Royal, and magnificent gardens in historical context for you.

For more info please call 650-787-5665 or log on to ScientificAmerican.com/Travel



Chemistry

Speaker: Robert Hazen, Ph.D.

Genesis: The Scientific Quest for Life's Origins — Is life's origin an inevitable process throughout the cosmos, or is it an improbable accident, restricted to a few planets (or only one)? How does a lifeless geochemical world of oceans, atmosphere, and rocks transform into a living planet? Find out how scientists use experimental and theoretical frameworks to deduce the origin of life.

The Diamond Makers

Diamond forms deep in Earth when carbon experiences searing heat and crushing pressure. Decades ago General Electric scientists learned how to mimic those extreme conditions of Earth's interior in the laboratory to make synthetic diamonds. Learn the human drama and technological advances involved in producing this coveted gem and industrial tool from carbon-rich substances.

The Story of Earth: How the Geosphere and Biosphere Co-evolved

Earth is a planet of frequent, extravagant change. Its near-surface environment has transformed over and over again across 4.5 billion years of history. Learn about the work of Dr. Hazen and colleagues that suggests that Earth's living and nonliving spheres have co-evolved over the past four billion years.

Chemical Bonding — The solid, liquid, and gaseous materials around us depend on the specific elements involved and the chemical bonds that hold those atoms together. By looking at the nature and significance of ionic, metallic, and covalent bonds you'll gain a new understanding of the workings of the world around you.

Quantum Physics

Speaker: Benjamin Schumacher, Ph.D.

Private Lives of Quantum Particles

Quantum systems can exhibit all sorts of bizarre behavior. But many of these phenomena can only be observed under conditions of the strictest privacy, where systems are "informationally isolated" from the world. These are not accidental features of quantum theory. They are inescapable facts about the microscopic world: Quantum physics is what happens when nobody is looking.

2π Is Not Zero (But 4π Is) — If you rotate any geometrical shape by 360 degrees (2π radians) about any axis, you will end up with exactly the same shape. But this fact, seemingly obvious, is not true for quantum particles with spin. Learn how a rotation by 2π makes a big difference, and how it all comes down to a simple minus sign — probably the most important minus sign in all of physics. Enjoy quantum fun, demystified by Dr. Schumacher.

The Physics of Impossible Things

Physicists find it surprising useful to ponder the impossible. Using the laws of nature, assess the possibility of science fiction's favorite phenomena and explore seemingly impossible things, which while odd, are possible. Venture into the study of impossible things and come away with an affirmation of the consistent logic of nature, and renewed wonder at real phenomena.

The Force That Isn't a Force — What makes a rubber band elastic? It's entropy, the microscopic disorder of its molecules. Now, entropy may provide a clue to the most familiar and mysterious of the basic forces of nature: gravity. Explore the link between entropy and gravity, and gain fascinating and unexpected insights of contemporary theoretical physics.

Archaeology

Speaker: Kenneth Harl, Ph.D.

From Old Europe to Roman Provinces

Explore the prehistoric foundations of Scandinavia and the Viking Age from ca. 3000 B.C. to 400 A.D. From Megalithic cultures to the arrival of Indo-Europeans, to Northern Bronze Age innovations and Celtic and Roman contributions, learn the unique environmental, cultural, and social factors that create a context for the Vikings.

Great Halls and Market Towns in Viking Age Scandinavia — Using archaeology and literary sources (especially saga and Eddas), learn how the "great halls" emerged as the main focus of Scandinavia civilization. Find out how the development of towns facilitated trade and were vital for the transformation and technological advance of Scandinavian society.

Ships and Ship Building in the Viking Age — European history records the effectiveness of the fearsome Viking longship; find out the features and technologies that made it so. Based on archaeological finds, learn about the multi-millennial evolution of the longship, from linden to oak, dugout to mast and sail. Gain an appreciation for the form and function, as well as the wider implications of Norse naval mastery for three hundred years.

Warfare in the Viking Age — The Viking's applied technologies led to three centuries of robust military and economic power for Scandinavia. Discover what factors made the Vikings accomplished warriors and learn what archaeological finds tell us about Viking exploration, settlement, and development of kingdoms.

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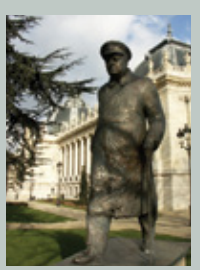
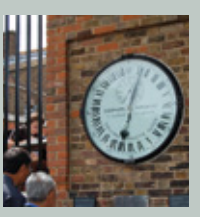


The Royal Observatory and the Churchill War Room/Museum (July 4)

Take the road less traveled in London, visiting two less well known gems of the City, both uniquely fascinating and inspiring.

Courage, duty, shared sacrifice, and conviction are the foundation of the Churchill Cabinet War Rooms. Hidden in plain sight in the heart of London, a scant 600 miles from Berlin. Step back in time and discover how Churchill and Britain's government functioned in secrecy in these quarters, from the Blitz to VE Day. The furnishings, maps, and ephemera are as they were on VE day, May 8, 1945. Hear the stories and imagine life under bombardment in the simple and inspiring environment of the Cabinet War Rooms.

Are you the precise type? Are you a fan of Google maps or GPS? Or Cutty Sark? Join us on a tour of maritime Greenwich, where our prime objective is visiting the Royal Observatory, Greenwich, home of the Prime Meridian of the World and Greenwich Mean Time. Stroll a deeply historic corner of London significant in local, national, and international culture. See the Royal Observatory, the National Maritime Museum, the tea clipper Cutty Sark, and the Royal Naval College. Master the lingo of time — UT0, UT1, UTC, and GMT. Stand astride two hemispheres on the Prime Meridian, a moment sure to be recorded on your timeline.



Stonehenge and Bath (July 3)

Pass a day on the Salisbury Plains and Somerset Hills, absorbing the history of two spots with ancient cultural roots.

Mute, mysterious, and megalithic, Stonehenge calls to us across the millennia. We'll respond, and walk the site in its details. Learn the significant geography, the archaeological and astronomical background, and the key stone names. But those are just the facts — the memories and true meaning of Stonehenge will be up to you.

Bath beckons the seasoned traveler. People are drawn to Bath to see its honey-colored Bath limestone buildings, and to explore its 2,000 year history as a place of relaxation and restoration. Plumb the details and nuances of Bath's fusion of architecture, culture, and history in a city with many echoes of and homages to the ancient world, while embodying the Georgian worldview.

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OF TWO MINDS

BY DWAYNE GODWIN AND JORGE CHAM

IN THE 1960S ROGER SPERRY AND MICHAEL GAZZANIGA STUDIED PATIENTS WHO HAD HAD THEIR CORPUS CALLOSUM CUT.

THE CORPUS CALLOSUM CONNECTS THE TWO HALVES OF YOUR BRAIN.

THIS SURGERY, STILL IN USE TODAY, IS PERFORMED TO HELP CERTAIN EPILEPTIC PATIENTS CONTROL SEVERE SEIZURES.

BECAUSE EACH HALF OF YOUR BRAIN CONTROLS AND RECEIVES INFORMATION FROM THE OPPOSITE SIDE OF THE BODY ...

... SPERRY AND GAZZANIGA WERE ABLE TO TRAIN TASKS AND IMAGES TO EACH HEMISPHERE SEPARATELY.

THEY FOUND THAT PICTURES THAT WERE SHOWN TO ONE SIDE WOULD BE PUZZLING TO THE OTHER SIDE, WHICH HADN'T SEEN THE IMAGES.

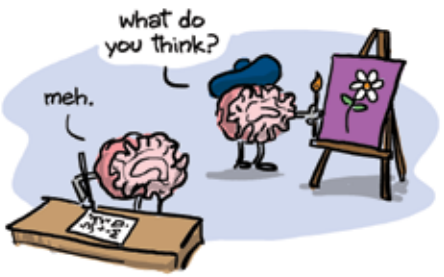
WHEN LEARNING A NEW TASK, THE HAND CONTROLLED BY THE TRAINED SIDE WOULD SOMETIMES CORRECT THE OPPOSITE HAND WHEN IT MADE A MISTAKE.

MIND THE GAP

ONE PATIENT CALLED "P.S." HAD THE RARE ABILITY TO ANSWER QUESTIONS DIFFERENTLY FROM EACH HEMISPHERE.

AS IF TWO CONSCIOUS MINDS EXISTED IN HIS BRAIN.

ALTHOUGH IT'S SAID THAT THE LEFT BRAIN IS "ANALYTIC" AND THE RIGHT BRAIN IS "ARTISTIC" ...

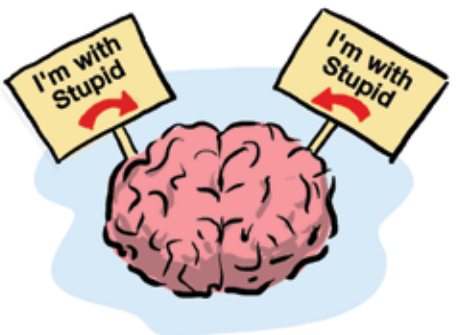


... FUNCTIONAL IMAGING HAS SHOWN THAT SUCH SPECIALIZED TASKS ACTUALLY ENGAGE NETWORKS ACROSS THE ENTIRE BRAIN.

EACH HALF CAN ALSO COMPENSATE FOR THE OTHER:

YOUNG PATIENTS WITH AN ENTIRE HALF BRAIN REMOVED CAN ADAPT AND GROW UP WITH AMAZINGLY FEW DEFICITS.

THE TWO HALVES OF YOUR BRAIN ARE LIKE A MARRIED COUPLE: THEY CAN ACT INDEPENDENTLY, BUT WITH GOOD COMMUNICATION THEY CAN WORK BEAUTIFULLY TOGETHER.



Dwayne Godwin is a neuroscientist at the Wake Forest University School of Medicine. Jorge Cham draws the comic strip Piled Higher and Deeper *at www.phdcomics.com.*

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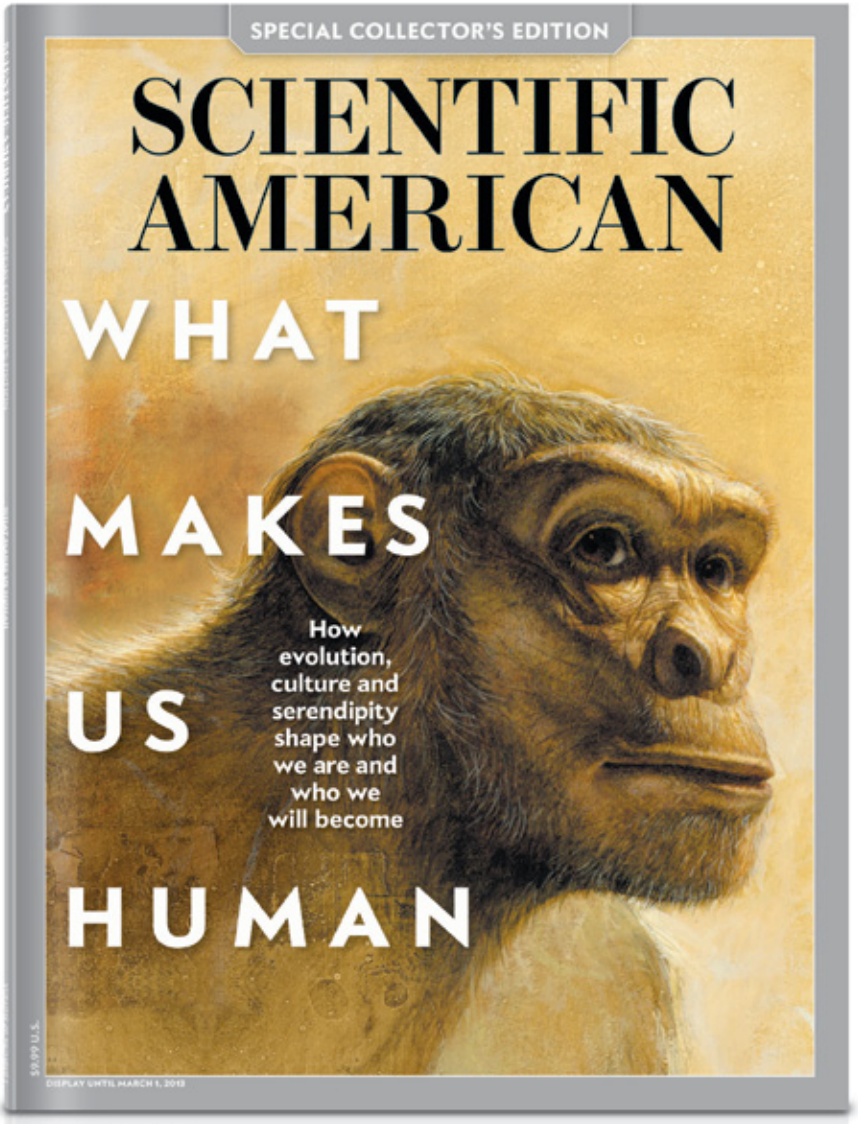

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