

SCIENTIFIC AMERICAN  
**MIND**

BEHAVIOR • BRAIN SCIENCE • INSIGHTS

May/June 2013

[www.ScientificAmerican.com/Mind](http://www.ScientificAmerican.com/Mind)

Brain-  
Training  
Games  
for Kids  
*page 38*



Why  
We  
Cheat

Deceit is part  
of what makes  
us human—  
but we can  
win over our  
flawed nature

**The Mental Toll  
of Violence**

**New Understanding  
of Multiple Sclerosis**

PROMOTION

# Creativity at your fingertips.



Get closer to the leading edge of science and technology: experience the SCIENTIFIC AMERICAN Tablet Edition - available for iPad®.



TO RENEW

[SCIENTIFICAMERICAN.COM/UPGRADE](http://SCIENTIFICAMERICAN.COM/UPGRADE)

TO SUBSCRIBE

[SCIENTIFICAMERICAN.COM/TABLET](http://SCIENTIFICAMERICAN.COM/TABLET)

Apple and iPad are trademarks of Apple Inc., registered in the U.S. and other countries. App Store is a service mark of Apple Inc.

SCIENTIFIC AMERICAN  
**MIND**<sup>TM</sup>  
BEHAVIOR • BRAIN SCIENCE • INSIGHTS

**EDITOR IN CHIEF AND SENIOR VICE PRESIDENT:**  
Mariette DiChristina  
**MANAGING EDITOR:** Sandra Upson  
**EDITOR:** Ingrid Wickelgren

**ART DIRECTOR:** Patricia Nemoto  
**ASSISTANT PHOTO EDITOR:** Ann Chin

**COPY DIRECTOR:** Maria-Christina Keller  
**SENIOR COPY EDITOR:** Daniel C. Schlenoff  
**COPY EDITOR:** Aaron Shattuck

**EDITORIAL ADMINISTRATOR:** Avonelle Wing  
**SENIOR SECRETARY:** Maya Harty

**CONTRIBUTING EDITORS:** Gareth Cook,  
David Dobbs, Robert Epstein, Emily Laber-  
Warren, Karen Schrock Simring, Victoria Stern

**MANAGING PRODUCTION EDITOR:** Richard Hunt  
**SENIOR PRODUCTION EDITOR:** Michelle Wright

**BOARD OF ADVISERS:**

**HAL ARKOWITZ:** Associate Professor  
of Psychology, University of Arizona

**STEPHEN J. CECI:** Professor of Developmental  
Psychology, Cornell University

**R. DOUGLAS FIELDS:** Chief, Nervous System  
Development and Plasticity Section, National  
Institutes of Health, National Institute of Child  
Health and Human Development

**S. ALEXANDER HASLAM:** Professor  
of Social and Organizational Psychology,  
University of Queensland

**CHRISTOF KOCH:** Chief Scientific Officer,  
Allen Institute for Brain Science, and  
Professor of Cognitive and Behavioral Biology,  
California Institute of Technology

**SCOTT O. LILIENTHAL:** Professor of Psychology,  
Emory University

**STEPHEN L. MACKNIK,** Director,  
Laboratory of Behavioral Neuropsychology,  
Barrow Neurological Institute

**SUSANA MARTINEZ-CONDE,** Director,  
Laboratory of Visual Neuroscience,  
Barrow Neurological Institute

**JOHN H. MORRISON:** Chairman, Department  
of Neuroscience, and Director, Neurobiology  
of Aging Laboratories, Mount Sinai School  
of Medicine

**VILAYANUR S. RAMACHANDRAN:** Director,  
Center for the Brain and Cognition, University  
of California, San Diego, and Adjunct Professor,  
Salk Institute for Biological Studies

**DIANE ROGERS-RAMACHANDRAN:** Research  
Associate, Center for the Brain and Cognition,  
University of California, San Diego

**STEPHEN D. REICHER:** Professor of Psychology,  
University of St. Andrews

*Some of the articles in Scientific American Mind  
are adapted from articles originally  
appearing in Gehirn & Geist.*

**SENIOR PRODUCTION MANAGER:**

Christina Hippeli

**ADVERTISING PRODUCTION MANAGER:**

Carl Cherebin

**PREPRESS AND QUALITY MANAGER:**

Silvia De Santis

**CUSTOM PUBLISHING MANAGER:**

Madelyn Keyes-Milch

**PRODUCTION COORDINATOR:**

Lisa Headley



# Your Inner Charlatan

I slunk into my social studies classroom with my head down. Graded homework assignments sat on the corner of my teacher’s desk. As my fellow seventh grade students chatted before class began, I casually slid my late homework into the middle of the pile. When our teacher later distributed the papers, he would see mine was not graded, assume he’d missed it, and I’d be off scot-free. Indeed, my ploy worked like a charm.

Decades later I still reflect on that episode with a twinge of guilt. Understanding the reasons behind our dishonest behavior and how to curb our nature are the subject of microbiologists Ferric C. Fang and Arturo Casadevall’s cover story, “Why We Cheat,” on page 30. One impetus they identified is fear—specifically, a dread of failure.

Extreme fear can override other moral intuitions, too. In a war zone, for example, a soldier’s intense emotions may trigger a so-called predator mode. A combatant in this state of mind is less likely to view bloodshed as reprehensible or to experience psychological trauma as a result of battle. On page 46, “An Appetite for Aggression” describes some surprising findings—and their implications.

As scientists plumb our dark side, they are also discovering ways to shore up our cognitive weaknesses. Research on ADHD has led to computer games aimed at strengthening working memory, a skill that undergirds intelligence. See “Calisthenics for a Child’s Mind,” by *Mind* editor Ingrid Wickelgren, on page 38.

We may also one day find ourselves buttressing our brain with therapies derived from two substances best known as illegal party drugs, psilocybin mushrooms and ketamine. In this issue’s two-part special report, starting on page 58, we explore these drugs’ unique effects on depression, addiction and other disorders.

*Scientific American Mind* has been growing and improving as well. Last month we launched a new home page—[mind.scientificamerican.com](http://mind.scientificamerican.com)—and unveiled a blog network. In print and online, we seek to bring you insights into the rich mental tapistry that makes up our inner world.

Sandra Upson  
Managing Editor  
[editors@SciAmMind.com](mailto:editors@SciAmMind.com)

COVER IMAGE BY AARON GOODMAN;  
SCIENTIFIC AMERICAN MIND IS A TRADEMARK OF SCIENTIFIC AMERICAN, INC., USED WITH PERMISSION

FEATURES

COVER STORY

30» **Why We Cheat**

Scientists are unraveling the causes of fraud and dishonesty and devising new strategies for rooting them out.

BY FERRIC C. FANG AND ARTURO CASADEVALL

38» **Calisthenics for a Child's Mind**

Scientists have concocted mental fitness regimens to strengthen weak thinking skills in students—in effect, making kids smarter.

BY INGRID WICKELGREN

46» **An Appetite for Aggression**

Humans may have evolved to experience bloodlust during combat. The peculiar psychology of war likely holds answers for avoiding future atrocities.

BY ROLAND WEIERSTALL, MAGGIE SCHAUER AND THOMAS ELBERT

50» **Solving the Mystery of MS**

New medicines for multiple sclerosis have made a big difference in patients' lives, but a breakthrough in therapy may require rethinking the origins of the disease.

BY JAMES D. BOWEN

SPECIAL REPORT  
HALLUCINOGENS AS THERAPY

58» **Calming a Turbulent Mind**

Psilocybin, the active ingredient in magic mushrooms, is being explored as a therapeutic tool to improve the lives of people with a life-threatening illness.

BY ERICA REX

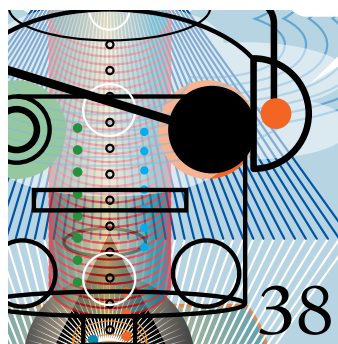
67» **A Trip Out of Depression**

Ketamine, an anesthetic and illicit party drug, is emerging as a fast-acting antidepressant.

BY SIMONE GRIMM AND MILAN SCHEIDEGGER



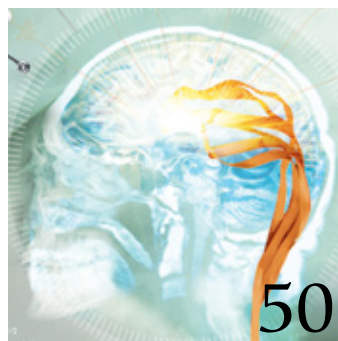
30



38



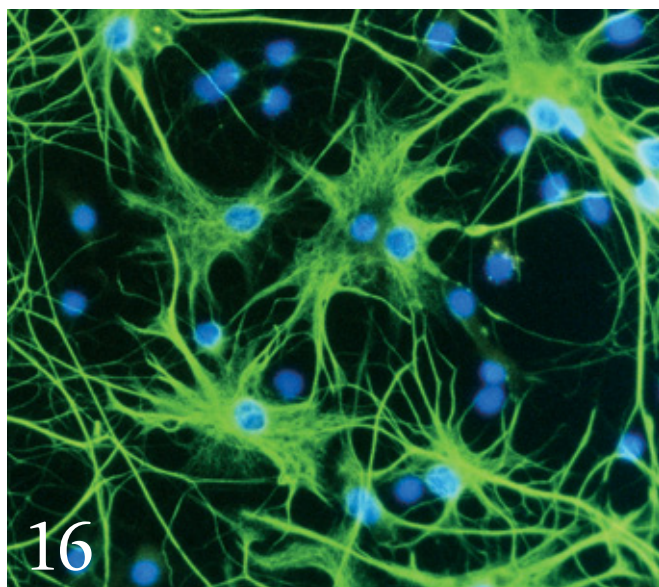
46



50



67



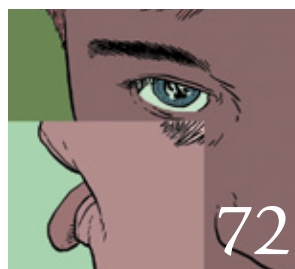
16



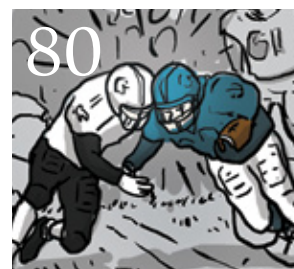
23



28



72



80

**1 » From the Editor**

**4 » Letters**

**7 » Head Lines**

- » Older adults: trusting and happy.
- » Healing the body with the mind.
- » Personality traits of China's only children.
- » Drugs with unapproved uses.
- » Why sleep deprivation elevates mood.
- » How kids think about identity.
- » Newly discovered itch cells.
- » Changes in psychiatry's diagnostic manual.

**23 » Illusions**

Advertisers exploit the intersection of time and illusion to sell their products.  
 BY STEPHEN L. MACKNIK, LEANDRO LUIGI DI STASI AND SUSANA MARTINEZ-CONDE

**26 » Perspectives**  
**Taking the Bad with the Good**

Surprise: negative emotions are essential for mental health.  
 BY TORI RODRIGUEZ

**28 » Perspectives**

**Inside the Dog Mind**

"Dognition" is about helping people find the genius in their dog, says Duke University neuroscientist Brian Hare.  
 INTERVIEW BY GARETH COOK

**72 » Facts and Fictions in Mental Health**

Is ADHD overdiagnosed but undertreated?  
 BY SCOTT O. LILIENTHAL AND HAL ARKOWITZ

**74 » Reviews and Recommendations**

Temple Grandin on autism. Bonobos have ethics, too. Drunk tank pink. A new science of memory.  
 Also: How outside forces influence our inner world.

**76 » Ask the Brains**

Why do top athletes choke? How does the brain react to a romantic breakup?

**78 » Head Games**

Match wits with the Mensa puzzlers.

**80 » Mind in Pictures**

Battered Brains.  
 BY DWAYNE GODWIN AND JORGE CHAM

Scientific American Mind (ISSN 1555-2284), Volume 24, Number 2, May/June 2013, published bimonthly by Scientific American, a trading name of Nature America, Inc., 75 Varick Street, 9th Floor, New York, N.Y. 10013-1917. Periodicals postage paid at New York, N.Y., and additional mailing offices. Canada Post International Publications Mail (Canadian Distribution) Sales Agreement No. 40012504. Canadian BN No. 127387652RT; TVQ1218059275 TQ0001. Publication Mail Agreement #40012504. Canada Post: Return undeliverables to 2835 Kew Dr., Windsor, ON N8T 3B7. Subscription rates: one year (six issues), \$19.95; elsewhere, \$30 USD. Postmaster: Send address changes to Scientific American Mind, P.O. Box 3187, Harlan, Iowa 51537. To purchase additional quantities: U.S., \$10.95 each; elsewhere, \$13.95 each. Send payment to SA Mind, P.O. Box 4002812, Des Moines, Iowa 50340. For subscription inquiries, call (888) 262-5144. To purchase back issues, call (800) 925-0788. Printed in U.S.A.



# SCIENTIFIC AMERICAN MIND

BEHAVIOR • BRAIN SCIENCE • INSIGHTS

PRESIDENT: Steven Inchcoombe  
EXECUTIVE VICE PRESIDENT: Michael Florek

VICE PRESIDENT AND ASSOCIATE PUBLISHER,  
MARKETING AND BUSINESS DEVELOPMENT:

Michael Voss

DIRECTOR, ADVERTISING:

Stan Schmidt

VICE PRESIDENT, DIGITAL SOLUTIONS:

Wendy Elman

DIRECTOR, GLOBAL MEDIA SOLUTIONS:

Jeremy A. Abbate

SALES DEVELOPMENT MANAGER: David Tirpack

PROMOTION MANAGER: Diane Schube

PROMOTION ART DIRECTOR: Maria Cruz-Lord

MARKETING RESEARCH DIRECTOR: Rick Simone

SALES REPRESENTATIVE: Chantel Arroyo

MANAGING DIRECTOR, CONSUMER MARKETING:

Christian Dorbandt

ASSOCIATE CONSUMER MARKETING DIRECTOR:

Catherine Bussey

E-COMMERCE MARKETING MANAGER:

Evelyn Veras

SENIOR MARKETING MANAGER/ACQUISITION:

Patricia Elliott

DIRECTOR, ANCILLARY PRODUCTS:

Diane McGarvey

## HOW TO CONTACT US

### FOR ADVERTISING INQUIRIES:

Scientific American Mind  
75 Varick Street, 9th Floor  
New York, NY 10013  
212-451-8893  
fax: 212-754-1138

### FOR SUBSCRIPTION INQUIRIES:

U.S. and Canada: 888-262-5144  
Outside North America:  
Scientific American Mind  
PO Box 5715, Harlan, IA 51593  
515-248-7684  
www.ScientificAmerican.com/Mind

### TO ORDER REPRINTS:

Reprint Department  
Scientific American Mind  
75 Varick Street, 9th Floor  
New York, NY 10013  
212-451-8877  
fax: 212-451-8252  
reprints@SciAm.com

### FOR PERMISSION TO COPY OR REUSE MATERIAL FROM SCIAMMIND:

Permissions Department  
Scientific American Mind  
75 Varick Street, 9th Floor  
New York, NY 10013  
212-451-8546  
www.ScientificAmerican.com/permissions  
Please allow three to six weeks for processing.



## NO MIND BOOST FROM MUSIC?

In “Brain-Changing Games,” writer Lydia Denworth stated, “With practice, a violinist can play a Mozart string concerto beautifully, but that will not make her better at much else.” Is she not aware that there are more studies on the benefits of learning musical instruments and art on the mind than on the benefits of video games?

Gabriel Newman  
via e-mail

**DENWORTH RESPONDS:** *Although there have been studies showing transfer from music, nearly all of them have been called into question in recent years. Much of the literature makes the mistake of inferring causation from correlation and fails to control for confounding variables. A forthcoming study from Glenn Schellenberg, a psychologist at the University of Toronto Mississauga, who studies transfer from music specifically, shows that the association between music lessons and cognition disappeared when demographics and personality are held constant. In addition, studies of adult professional musicians show no cognitive benefits over comparable professional nonmusicians.*

*For more information, please see the recent ScientificAmerican.com blog post at <http://tinyurl.com/music-smarts>.*

## EYE MOVEMENTS FOR ANXIETY

In “Can Eye Movements Treat Trauma?” [Head Lines], Tori Rodriguez cites new evidence that eye movements are an effective ingredient in eye movement desensitization and reprocessing (EMDR). In our column “Taking a Closer Look” [Facts and Fictions in Mental Health, December 2006/January 2007], however, we cited a large body of other evidence that contradicts that claim. At best, we can conclude from the mixed results only that further research is needed to resolve the issue. People seeking treatment for anxiety should not feel compelled to seek out EMDR if a competent therapist is available to deliver standard exposure therapy.

Hal Arkowitz and Scott O. Lilienfeld  
via e-mail

## YOUNG ADULT BEHAVIOR

The title alone of “Yet Another Stage of Life?” [Perspectives] suggests that author Robert Epstein is disgruntled at the plight of the members of this “emerging adulthood,” who just can’t seem to “launch” themselves into the rarefied class of grown-ups. I was far from convinced by his hypothesis: that the presence of the term will inevitably be detrimental to the individuals it describes by providing a socially acceptable condition for uncertainty and inaction.

Epstein seems to be frustrated that the label “emerging adulthood” is being used to validate the languor of young people and annoyed that what was once deemed failure to grow up is now integrated into the accepted path to adulthood. He says it’s “imprudent . . . to suggest that most or all individuals that age are inherently unstable and unfocused.”

I was not aware that such a severe suggestion was so widespread. Although there are plenty of young individuals in their twenties whose lives are marked by “identity explorations,” “instability” and “self-focus” (and by the way, who is to say these are bad things?), there are plenty whose lives are not, who would probably claim that the negative stereotypes Epstein associates with emerging adulthood don’t apply to their situation.

# Think Clearly.

Your brain. It makes up only 2% of your body weight, yet it consumes roughly 20% of your body's energy when at rest. That means the human brain needs a whole lot of nutrition to stay alert and focused throughout the day. Citicoline is nature's way of keeping the brain's energy-producing centers firing. Clinically tested for efficacy, Cognizin® delivers a patented form of Citicoline that supplies your brain with the energy it needs to stay sharp.\* Cognizin is also pure, vegetarian and allergen-free. So look for Cognizin brand Citicoline on the ingredient panel of your favorite supplements to help keep your mental edge.\*



## Cognizin®

For the evolution of your mind®

To learn more about Cognizin®  
visit [www.cognizin.com](http://www.cognizin.com)



Follow Cognizin®

\*These statements have not been evaluated by the Food and Drug Administration.  
This product is not intended to diagnose, treat, cure, or prevent any disease.

Cognizin® is a registered trademark  
of KYOWA HAKKO BIO CO., LTD.  
Copyright ©2013 KYOWA HAKKO U.S.A., INC.  
All Rights Reserved.

Look for Cognizin®  
Citicoline in these  
fine brands.



**GUNGHO**

**Healthy Origins**  
*Healthy Value from Reliable Origins*

**HempNaturals**  
EVOLVE.

**Jarrow**  
FORMULAS

Balance **JoMar**  
Your Life Labs

**LifeExtension**



**nawgan**

**PATHWAY**  
*To Healing*

**PipingRock**  
HEALTH PRODUCTS



**SWANSON**  
Health Products

**TIANCHI**  
BRIGHTEN YOUR MIND

Whether they do or do not does not matter: it is important to remember that young people shouldn't let stereotypes dictate how they progress through life and that the emerging adults of today are faced with a myriad of inhibiting circumstances that the author's generation did not have to face.

**Matthew Didisheim (age 24)**  
Missoula, Mont.

**EPSTEIN REPLIES:** *The problem with stage-of-life concepts such as "emerging adulthood" is that they sometimes become self-fulfilling prophecies, creating expectations that generate and perpetuate the stereotypes that they describe. This has certainly happened with adolescence, a stage of life many Westerners now mistakenly believe has always existed everywhere, even though it is still almost entirely absent in more than 100 cultures around the world. In the U.S., teens, parents and even many therapists believe that it is normal for teens to be*

*in turmoil or in conflict with parents, and everyone behaves accordingly.*

*When our young people finally escape the culture-driven chains of adolescence, do we really want to trap them for another decade in a new "stage" in which they are again expected to perform badly?*

Epstein addresses the recent "discovery" of emerging adulthood. Has any research been done on emerging adulthood (and adolescence, for that matter) in the two million to four million American children being homeschooled? It seems to me that here is a ready-made population with a single common factor—these children are not sitting with a roomful of age-graded peers for up to 12 years—that could be studied discretely. As a veteran home educator

who has experienced firsthand the maturity of most homeschooled children, my prediction is that the labels "adolescence" and "emerging adulthood" would not stand.

**Susan Gibbs de San Martin**  
Ossining, N.Y.

**EPSTEIN REPLIES:** *The writer's instincts appear to be correct. Studies show that young people who spend most of their time with responsible adults rather than with peers—one of the hallmarks of homeschooling—seem to be able to*

a leap of faith. Forensic evidence can answer critical questions, but it can never prove a person's guilt or innocence on its own.

Second, the authors fail to state that postconviction exonerations are as much the result of a subjective interpretation of evidence as the original convictions. Oftentimes exonerations are an effort by the courts to pick the lesser of two possible evils, the worse being wrongful incarceration.

**John M. Collins, Jr.**  
Chief Managing Editor  
*Crime Lab Report*  
via e-mail



Do exonerations lack scientific rigor just as initial verdicts often do?

*avoid the turmoil that is so typical of American adolescence and, in turn, the immaturity and uncertainty of the post-teen years here.*

**SCIENCE IN THE COURTROOM**

"Your Brain on Trial," by Scott O. Lilienfeld and Robert Byron, was an outstanding exploration of our courts' disconnect from the powers of modern science. But the authors made two errors. First, in describing the exoneration of Ronald Cotton and the subsequent DNA match to another man, Bobby Poole, Lilienfeld and Byron state that Poole "was identified definitively by DNA evidence as the rapist." To opine that the semen was the result of a rape and that Poole acted alone requires

*Because the demonstration of innocence after conviction must be airtight in almost all circumstances, most such efforts fail. The fact that petitions that are based on DNA succeed is a testament to the strength of the scientific evidence.*

**ERRATA**

In "Stolen Memory," by Dwayne Godwin and Jorge Cham [Mind in Pictures], January/February 2013, the top sentence in the first panel of the cartoon should read, "One in eight *older* Americans has Alzheimer's disease."

"Is Cocoa the Brain Drug of the Future?" by Daisy Yuhas [Head Lines], March/April 2013, misstated Catherine Kwik-Uribe's profession. She is a nutrition scientist.

**HOW TO CONTACT US**

For general inquiries or to send a letter to the editor:  
**Scientific American Mind**  
75 Varick Street, 9th Floor  
New York, NY 10013  
212-451-8200  
editors@SciAmMind.com



# Head Lines

FROM THE LABS TO YOUR LIFE



## The Aging Brain

Trusting, content and chock-full of information

KURT DRUBBEL/ISTOCK/PHOTO



News from our Web site Prions, the proteins behind mad cow disease, also help us learn by strengthening the connections between neurons.

## » Aging Brains How perception, mood and memory shift

### Forgetting Is Harder for Older Brains

Adults hang on to useless information, which impedes learning

Kids are wildly better than adults at most types of learning—most famously, new languages. One reason may be that adults’ brains are “full,” in a way. Creating memories relies in part on the destruction of old memories, and recent research finds that adults have high levels of a protein that prevents such forgetting.

Whenever we learn something, brain cells become wired together with new synapses, the connections between neurons that enable communication. When a memory fades, those synapses weaken. Researchers led by Joe Tsien, a neuroscientist at the Medical College of Georgia, genetically engineered mice to have high levels of NR2A, part of a receptor on the surface of some neurons that regulates the flow of chemicals such as magnesium and calcium in and out of a cell. NR2A is known to be more prevalent in the brains of mammals as they age. The engineered mice, though young, had adult levels of NR2A, and they showed some difficulty forming long-term memories. More dramatically, their brains could barely weaken their synapses, a process that allows the loss of useless information in favor of more recent data.

A similar process may govern short-term memories as well. When you hear a friend ask for coffee, the details of her order don’t just slip away in your mind—your brain must produce a protein that



actively destroys the synapses encoding that short-term memory, according to a 2010 paper in *Cell*.

Much psychological research supports the idea that forgetting is essential to memory and emotional health [see “Trying to Forget,” by Ingrid Wickelgren; *SCIENTIFIC AMERICAN MIND*, January/

February 2012]. Tsien’s new work, published January 8 in *Scientific Reports*, suggests that older brains hold on to their connections more dearly—which helps to explain why learning is more laborious as we age and why memory trouble later in life so often involves the accidental recall of outdated information. —Ian Chant

#### How to Intentionally Forget a Memory

##### Direct Suppression

Try to block out all thoughts of a certain memory.

- Increases activity in the **right dorsolateral prefrontal cortex**, which mediates working memory and cognitive control.
- Reduces activity in the **hippocampus**, an area important for conscious recollection.



##### Thought Substitution

Try to forget by substituting the unwanted memory with a more desired one.

- Increases activity in the **left caudal prefrontal cortex**, thought to decrease saliency of intrusive memories, and the **midventrolateral prefrontal cortex**, which helps to retrieve a specific memory.

ISTOCKPHOTO (top): JAMIE CARROLL /ISTOCKPHOTO (bottom)

**M** Happiness may come from hitting a time-management sweet spot of not feeling rushed yet having little excess time, according to a recent survey.

## Auto-Correct for Your Brain

Most people make good decisions most of the time. But when drug addiction, disease or brain injury enters the picture, rational thinking can go awry. What if the damaged brain just needed a little reminder of how it feels to choose wisely?

Enter the MIMO neural prosthesis, an array of electrodes implanted in the brain that make contact with eight neuron circuits in the prefrontal cortex, the brain's command center for decision making. The device can both record the brain activity associated with good choices and stimulate the relevant neurons to get the brain back on track. Although the implant can listen in only on a tiny subset of the neurons in this region, the scientists who developed it, based at Wake Forest Baptist Medical Center, were surprised to discover that they could still pick up signature patterns associated with correct choices, at least in the context of a simple task.

The researchers tested the neural prosthesis on monkeys that were trained to move a cursor over a picture on a computer screen to get a food reward. The implant first recorded the brain activity associated with choosing the correct picture. Then the monkeys were given cocaine, and their performance plummeted. But when the implant was switched on to send electric current to the neurons that had earlier been associated with the correct answers, the monkeys immediately started selecting the right pictures again. Some of them did an even better job than they had before receiving cocaine.

Decisions we humans face, of course, are more complicated than identifying which picture will give us a treat. And surgically inserting implants in a healthy person's brain—just in case that brain gets damaged later—is not likely to happen any time soon. Yet the researchers hope that their work could one day lead to implants or perhaps a noninvasive stimulator that would help people suffering from brain damage make the right call—with nothing more than a gentle reminder of what that call is.

—Ian Chant



## Age Brings Happiness

Exactly how much joy, however, depends on when you were born

**Do people get happier or crankier as they age? Stereotypes of crotchety neighbors aside, scientists have been trying to answer this question for decades, and the results have been conflicting. Now a study of several thousand Americans born between 1885 and 1980 reveals that well-being indeed increases with age—but overall happiness depends on when a person was born.**

Previous studies that have compared older adults with the middle-aged and young have sometimes found that older adults are not as happy. But these studies could not discern whether their discontent was because of their age or because of their different life experience. The new study, published online January 24 in *Psychological Science*, teased out the answer by examining 30 years of data on thousands of Americans, including psychological measures of mood and well-being, reports of job and relationship success, and objective measures of health.

The researchers found, after controlling for variables such as health, wealth, gender, ethnicity and education, that well-being increases over everyone's lifetime. But people who have lived through extreme hardship, such as the Great Depression, start off much less happy than those who have had more comfortable lives. This finding helps to explain why past studies have found conflicting results—experience matters, and tough times can influence an entire generation's happiness for the rest of their lives. The good news is, no matter what we've lived through, we can all look forward to feeling more content as we age.

—Karen Schrock Simring

## Why Older Adults Are Too Trusting

Activity in a key brain area drops with age

The older people get, the more trusting they become—a tendency that can be dangerous because it puts elders at risk for exploitation and abuse. But why does it happen? A new study suggests that older people have trouble identifying untrustworthy faces because of an age-related drop in activity in the anterior insula, a brain region that may play a role in assessing trust and risk.

Researchers at the University of California, Los Angeles, asked 119 adults who were at least 55 years old and 24 younger adults to look at pictures of faces that exhibited either trustworthy, neutral or untrustworthy qualities (according to previous analysis). Compared with the younger subjects, the older participants were much more likely to label the suspicious faces as credible and approachable. When the researchers asked a subset of the subjects to perform a similar task while undergoing a functional MRI scan, the older subjects exhibited lower activity in the anterior insula, a small region inside the cerebral cortex (below), than did the younger ones. Although the difference in activity was most pronounced when the groups looked at the untrustworthy faces, the younger subjects exhibited higher activity in the anterior insula than did their older counterparts when they looked at the trustworthy faces, too.

The findings suggest that “the anterior insula is important for assessing trust, period,” explains U.C.L.A. doctoral student Elizabeth Castle, lead author of the study published last December in the *Proceedings of the National Academy of Sciences USA*. The region may be responsible for the positive and negative “vibes” we get about people when we meet them, which may, unfortunately, dissipate with age.

—Melinda Wenner Moyer



**Older adults' brains do not respond as strongly to cues such as a false smile or an unusual pattern of eye contact.**



### Profile of the Anterior Insula

The anterior insula is implicated in reactions of disgust and has been shown to support general bodily awareness. The region senses our visceral states, which form the basis of gut feelings that inform decision making. Previous research has also shown that neural activation in the anterior insula is important for assessing risks, responding to breaches in trust, representing expected financial risks and predicting the safety of choice outcomes, according to the *PNAS* paper.

—M.W.M.

## » Healing the Body with the Mind

Guided imagination exercises help the body repair itself after surgery

**M**ental imagery might help you “find a happy place” in more ways than one: it can actually hasten recovery from surgery, according to two recent studies.

In the first study, people who had undergone surgery to repair the anterior cruciate ligament of the knee (ACL) were randomly assigned to one of two groups. All participants received standard rehabilitation during the six months after surgery, but one group also practiced guided imagery while recovering. The imagery, which was conducted in sessions with a therapist and recorded for later listening, included mentally rehearsing physical therapy exercises and visualizing the physiological healing process specific to ACL surgery, such as scar tissue becoming flexible with gentle stretching. According to the results published in the December 2012 issue of the *Scandinavian Journal of Medicine and Science in Sports*, the group that practiced imagery showed greater im-

provements in knee stability and reduced levels of stress hormones. The study authors speculate that imagery may speed recovery by reducing stress, which has been shown to interfere with healing.

The other experiment focused on patients scheduled for gallbladder removal and was published in the February 2012 issue of *Brain, Behavior, and Immunity*. The patients were randomly assigned to either a group receiving only standard care or to one that also involved relaxation and guided imagery for three days before and seven days after surgery. “We used a relaxation intervention to try to reduce stress and therefore get a better inflammatory response to surgery and improve healing,” says Elizabeth Broadbent, professor of medicine at the University of Auckland in New Zealand and co-author of the study. The first set of imagery exercises focused on being relaxed and ready for surgery, whereas the postsurgery imagery



concentrated on the body’s healing process.

For example, participants imagined oxygen and nutrients traveling to the surgical wound and helping the body knit the skin back together, easing discomfort and bringing soothing relief.

Compared with the control group, participants who practiced imagery reported a larger reduction in stress, and their wounds showed signs of greater collagen deposition and faster healing. Although it is not possible to determine how much the effects result from the imagery versus simply being relaxed, Broadbent says both factors probably worked together and that the imagery most likely enhanced the stress-reducing effects of the relaxation.

—Tori Rodriguez

## » Profile of a Little Emperor

China’s one-child policy has affected the personalities of a generation of only children

**I**n 1979 China instituted the one-child policy, which limited every family to just one offspring in a controversial attempt to reduce the country’s burgeoning population. The strictly enforced law had the desired effects: in 2011 researchers estimated that the policy prevented 400 million births. In a new study in *Science*, researchers find that it has also caused China’s so-called little emperors to be more pessimistic, neurotic and selfish than their peers who have siblings.

Psychologist Xin Meng of the Australian National University in Canberra and her colleagues recruited 421 Chinese young adults born between 1975 and 1983 from around Beijing for a series of surveys and tests that evaluated a variety of psychological traits, such as trustworthiness and optimism. Almost all the participants born after 1979 were only children compared with about one fifth of those born before 1979. The study participants born after the policy went into effect were found to be both less trusting and less trustworthy, less inclined to take risks, less conscientious and optimistic, and less competitive than those born a few years earlier.

“Because of the one-child policy, parents are less likely to teach their child to be imaginative, trusting and unselfish,” Meng says. Without siblings, she notes, the need to share may not be emphasized, which could help explain these findings.

Only children in other parts of the world, however, do not show such striking differences from their peers. Toni Falbo, a social psychologist at the University of Texas at Austin, who was not involved in the study, suggests that larger social forces in China also probably contributed to these results. “There’s a lot of pressure being placed on [Chinese] parents to make their kid the best possible because they only had one,” Falbo says. These types of pressures could harm anyone, even if they had siblings, she says.

Whatever its cause, the personality profile of China’s little emperors may be troubling to a nation hoping to continue its ascent in economic prosperity. The traits marred by the one-child policy, the study authors point out, are exactly those needed in leaders and entrepreneurs.

—Carrie Arnold



GETTY IMAGES AND PETEK ARICI /iStockphoto (top); ISTOCKPHOTO (bottom)



( PHARMA WATCH )

## THE UNADVERTISED USES OF DRUGS

Why your doctor might give you an antidepressant to treat your migraines

Every prescription drug available in the U.S. has been approved by the Food and Drug Administration via a lengthy, expensive process of clinical trials. These trials show that the drug is safe and effective at treating a particular condition. But doctors often prescribe drugs off-label, for conditions they are not approved to treat. Here's why.

—Luciana Gravotta

	Example Drug	Approved Use	Off-Label Use	Strength of the Evidence	Side Effects	Notes
<p><b>1. Evidence is good and consistent</b></p> <p>Studies may consistently support the use of a drug in treating a specific condition, but the large trials required for FDA approval may not materialize. Some medical groups, such as the American Academy of Neurology (AAN), offer their members guides to off-label prescribing, with grades that rate the evidence.</p>	Amitriptyline (Elavil): Tricyclic antidepressant	Depression	Migraine prevention	AAN's grade is A (many large clinical trials)	Drowsiness	One of the first drugs found to work against migraines, before approved drugs were available. Many people still prefer it to other options
	Topiramate (Topamax): Anti-convulsant	Epilepsy	Alcohol addiction	In two trials it outperformed naltrexone, the approved drug for treating alcohol dependence	Tingling, burning or numbing sensations on the skin; more rarely, anorexia	
<p><b>2. FDA-approved options are lacking</b></p> <p>About 88 percent of the disorders outlined in psychiatry's diagnostic manual (the DSM) do not have an FDA-sanctioned treatment drug, so psychiatrists often try drugs approved for other conditions. Sometimes the evidence supports off-label use, but not always.</p>	Olanzapine (Zyprexa): Atypical antipsychotic	Schizophrenia, bipolar disorder	Dementia	Many clinical trials show robust efficacy	Increased mortality in older adults	About one quarter of the people living in nursing homes are given antipsychotics because no other treatment is available for severe dementia
	Quetiapine (Seroquel): Atypical antipsychotic	Schizophrenia, bipolar disorder	Anxiety disorders, PTSD, insomnia	Strong for anxiety, weak for PTSD, extremely weak for insomnia	Suicidal thoughts	Highly prescribed in the military for insomnia and PTSD. Some experts believe recent suicide spikes in the military may be linked to an increase in antipsychotic drug prescriptions
<p><b>3. No drug is 100 percent effective</b></p> <p>Brain drugs are notoriously hit and miss—even those that are FDA-approved don't work for everyone, nor do they work all the time. Doctors may look for treatments that can help those who don't respond.</p>	Phenelzine (Nardil): MOAI antidepressant	Depression with phobias or hypochondria	Social anxiety disorder	Many clinical trials show it is highly effective	Sudden and possibly fatal rise in blood pressure if people stray from a strict diet	Approved drugs for social anxiety disorder tap into the brain's serotonin system, but many patients fail to respond. Phenelzine offers an alternative
	Ketamine: Anesthetic	Surgery	Major depression	[see page 67]	Hallucinations, addiction	Unlike other antidepressants, which take weeks to kick in, ketamine starts working in a few hours
<p><b>4. Most drugs are not approved for children</b></p> <p>The FDA offers companies a one-year extension on their drug patent if they invest in clinical trials with children, but many have ignored the carrot. As doctors diagnose more kids with bipolar disorder and depression, they are turning to drugs tested on adults, with mixed results.</p>	Lamotrigine (Lamictal): Anti-convulsant	Epilepsy, bipolar disorder	Bipolar disorder in children	Strong; studies show that in kids both the depressive and manic symptoms of the disorder improve	Dangerous skin reactions; more common in children than in adults	Childhood bipolar disorder is a controversial diagnosis. The new edition of the DSM will replace it with a disorder called disruptive mood regulation [see page 21]
	Citalopram (Celexa): SSRI antidepressant	Major depression	Depression in children	Fair; a handful of studies consistently show efficacy	Suicidal thoughts	Only one antidepressant is FDA-approved to treat minors with depression: fluoxetine (Prozac) for age 8 and up.

ISTOCKPHOTO

people in the U.S. suffer from compulsive hoarding, at least double the number of people diagnosed with obsessive-compulsive disorder.

SCIENTIFIC  
AMERICAN™

Travel

BRIGHT  
HORIZONS™ 18

RHONE RIVER, NOV. 29 – DEC. 6, 2013



For information on more trips like this, please log onto [www.ScientificAmerican.com/Travel](http://www.ScientificAmerican.com/Travel)

In November, the tourists are gone from Provence. The harvest's been gathered. The south of France exhales, resuming her essential rhythms, manifesting her ancient uniqueness, effortlessly. It's the perfect time to relax, recharge, and revel in the latest with Scientific American Bright Horizons 18 on a Rhone River cruise from November 29 to December 6, 2013. We'll explore developments in cosmology, cancer, and wine science, and plumb Roman engineering.

Experience river cruising's panoramic charms on Bright Horizon 18's voyage on AmaWaterway's AmaDagio, sailing from Lyon to Arles, France. The light, colors, and flavors of France await.

Make your reservation at <http://www.insightcruises.com/SciAm-18>, call us at 650-787-5665 or email us at [Concierge@InsightCruises.com](mailto:Concierge@InsightCruises.com).

The cruise fares start at \$2,799 for a Category E. French Balcony cabins start at \$3,378. A Junior Suite is available for \$4,498. Cruise fares include six half-day excursions. For those attending our educational Program, there is a \$1,395 fee. Additional per-person fees include: government taxes and fees (\$147) and gratuities are €15 per day. The Program, Cruise pricing, and options are subject to change. For more info please call 650-787-5665 or email us at [concierge@insightcruises.com](mailto:concierge@insightcruises.com).



## Quantum Physics

Speaker: Frank Linde, Ph.D.

### The Wild World of Subatomic Particles

Explore the realm of electrons, protons, quarks, and Higgs bosons — a world where the normal rules don't apply. Dr. Linde will lead a tour of the smallest constituents of matter, illuminating the theories of quantum mechanics and relativity that govern the subatomic universe. You'll also learn about the mysteries of dark matter, missing antimatter, and the origin of mass.

### The Story of the Higgs

A tiny particle called the Higgs boson was predicted 50 years ago to explain the quandary of why particles have mass. After decades of searching, physicists finally tracked down the Higgs in 2012, inside the world's largest particle accelerator. Learn why this one particle is so important, and how its discovery will shape the future of physics.

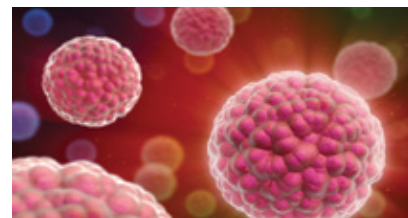


## The Mystery of Dark Matter

Dark matter is thought to make up about a quarter of the universe, yet scientists don't know what it is. Learn the history of this mysterious stuff, as well as the best guesses for what it might be made of. Dr. Linde will explain how researchers study something that can't be seen, and the ongoing searches aiming to detect dark matter for the first time.

### Particle Physics and You

Subatomic particle experiments deep underground and inside giant accelerators can seem far removed from everyday life. But the knowledge gained about the universe's smallest building blocks has real-world consequences. Dr. Linde will stir your curiosity about particle physics and answer the common question: What use is it?



## Targeting Cancer

Speaker: David Sadava, Ph.D.

### Know the Enemy: A Biography of the Target

Set the stage for understanding the attack on cancer by looking at its cellular biography. In most cases, cancer starts off as perfectly normal cells. And then something happens. Find out what those "somethings" may be, and how they transform the cell.

### The War on Cancer: Then and Nowadays

In 1972, the U.S. declared war on cancer. Learn the scientific background that led to this bold declaration, and why victory has been elusive.

We see progress in extending the lives of cancer patients, and even cures. But the result is not victory but a long war of attrition. Find out why.

### Targeting the Cancer Genome

Knowing the cancer genome in detail leads to precise targeting of potential cancer triggers in the cell. Two spectacular recent successes in targeting certain types of leukemia and breast cancer led to a proliferation of very expensive drugs similarly targeted to specific cancers. Are these drugs worth it? Explore the scientific accomplishments and ethical issues involved in medical progress.

### Natural Medicine and the War on Cancer

Faced with a dreadful diagnosis, many cancer patients supplement or substitute their doctor's recommendations by "going alternative." Turns out that some common cancer-fighting drugs originated in traditional medicines. Learn about the process of transforming a traditional treatment to a mainstream therapy. How are alternative medicines evaluated? Are they effective? Join Dr. Sadava and make some surprising discoveries.



### Archaeology

Speaker: Lynne Lancaster, Ph.D.

### Introduction to Culture and Technology in Gaul

Gaul was influenced by the Iberians, Celts, Greeks, and Romans. Each culture brought skills and technologies such as town planning, architecture and construction, mining of salt and metals, and the adoption of coinage. Get an overview of the technology, culture, and politics of the Greek and Roman colonization of France.

### Fire-Based Technologies in Gaul: Terracotta Production and Metal-Working

Terra cotta and metal artisans had to master techniques of balancing chemical interaction to achieve the desired results. Find out how the Romans adopted Greek methods to mass produce pottery. In contrast to this imported knowledge, learn about Celtic metal-working skills, which the Romans assimilated and put to military use.

### Building an Amphitheater

Along with bath buildings, the construction of an amphitheater was one of the greatest investments a community could take on. Dig into the engineering and construction process: site preparation for enormous loads, quarrying and transporting great numbers of stone blocks, erecting the structure and distributing loads. Enrich your appreciation of ancient architecture in the Roman world and beyond.

### Aqueducts, Baths and Water Mills

The Romans exploited water technology much earlier and on a greater scale than has been realized. This was all possible due to

the mastery of aqueducts. We will explore the principles behind the laying out and functioning of Roman aqueducts, including the use of inverted siphons, tunnel cutting, and arch construction.



### Cosmology

Speaker: Mark Whittle, Ph.D.

### The Birth of Our Universe: Evidence for the Big Bang

Is the current evidence for the Big Bang strong enough to consider it a fact? Survey the contents of the Universe and scrutinize the six key pieces of evidence for its birth in a "Hot Big Bang."

### Billion Years of History: the Birth and Maturation of Galaxies

Study the natural history and structure of galaxies directly, from infancy to maturity. Orient yourself to our own Milky Way, and the types of galaxies that form a web of galaxies filling the Universe. Contemplate dark matter and black holes, and get the latest thought in cosmology.

### The Universe's First Million Years: Primordial Light and Sound

Take a trip back in time to explore the incandescent fireball of the infant Universe, just ½ million years after the Big Bang. Learn the astounding qualities of its light and how cosmologists use the primordial sound of this period to measure a number of the Universe's properties. Listen, think, and wonder at the cosmological Dark Age before the first stars.

### Cosmic Inflation: Making Universe(s) from Nothing!

How was our expanding Universe created? We'll look to cosmic inflation theory for answers and food for thought. Using the astonishing fact that the total mass/energy of the Universe is zero, and its implications, we can begin to understand how cosmic inflation both creates

and launches our expanding Universe — out of nothing! Examine cosmic puzzles, possibilities, and intriguing speculation.



### Oenology

Speaker: James Kennedy, Ph.D.

### Climate Change and Impact on the Wine World

Wine's chemical composition varies widely across different areas of the world. Much of a wine's uniqueness stems from the impact of place on wine composition. Discover how the climates in the wine regions of the world are changing, and what this means for wine as we know it. In a lab session, we'll taste wine from warm regions.

### The Rhone and Its Wines

The Rhone River region produces some of the finest wines in the world. As the Rhone River flows south to the Mediterranean, the grapes and the wines produced from them change considerably. Combining a lecture with a wine tasting, Dr. Kennedy will discuss this amazing wine-growing region and the wines it produces.

### Wine and Health

From the French Paradox to resveratrol and beyond, Dr. Kennedy investigates the composition of wine and the role that wine plays in human health. Is wine the wonder beverage as often portrayed in popular media, or is the fascination just a means to feel good about alcohol consumption?

### Advances in Grape and Wine Production

Wine labels often evoke the tradition, romance, and history of winemaking. The flowery language and imagery obscures the technological progress made over the past century in viticultural and winemaking practices. Discover how some of the finest wines in the world are produced using sophisticated, state-of-the-art technology and science.

SCIENTIFIC AMERICAN

Travel

HIGHLIGHTS RHONE RIVER  
NOV. 29 – DEC. 6, 2013



### INSIDER'S TOUR OF CERN

Pre-cruise: November 28, 2013—From the tiniest constituents of matter to the immensity of the cosmos, discover the wonders of science and technology at CERN. Join Bright Horizons for

a private pre-cruise, custom, full-day tour of this iconic facility. (If the LHC is still undergoing its scheduled maintenance it is anticipated we will go into the LHC Cavern.)

Whether you lean toward concept or application there's much to pique your curiosity. Discover the excitement of fundamental research and get a behind-the-scenes, insider's look at the world's largest particle physics laboratory.

We'll have an orientation, visit an experiment, get a sense of the mechanics of the Large Hadron Collider (LHC). If at all possible, we'll go down inside the LHC tunnel (picture left), then make a refueling stop for lunch, and have time to peruse the grounds and exhibits on the history of CERN and the nature of its work. And if you're so inclined, you can visit the CERN gift shop.

The price is \$899 per person (based on double occupancy). This trip is limited to 50 people. NOTE: CERN charges no entrance fee to visitors.

For more info please call 650-787-5665 or log on to [ScientificAmerican.com/Travel](http://ScientificAmerican.com/Travel)

SCIENTIFIC  
AMERICAN™

Travel

BRIGHT  
HORIZONS™ 19

SOUTHEAST ASIA, FEB. 3RD – 17TH, 2014



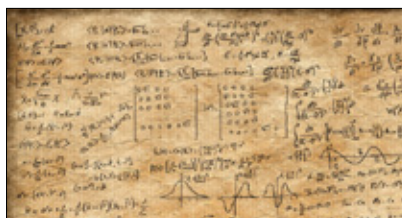
For information on more trips like this, please visit [www.scientificamerican.com/travel](http://www.scientificamerican.com/travel)

Look forward and backward, inward and outward on a science adventure in southeast Asia. Poised between vast continent and vast ocean, our cruise conference will explore the latest in science. Join Bright Horizons 19 in a landscape of fabled kingdoms, rich biodiversity, and poignant place names as we sail from Hong Kong to Singapore February 3–17, 2014 on Holland America Line's Volendam.

Realize the hope of seeing Angkor Wat, or of visiting Xian's Terracotta Warriors and Beijing's cultural treasures on Bright Horizon's custom optional pre- and post-cruise explorations.

Gain the experts' insights into contemporary science while enjoying Southeast Asia's lush scenic beauty, legendary hospitality, tempting cuisine, and rich history. Connect with Bright Horizons' thoughtful community. Reserve now to join the fun. For full details, visit [InsightCruises.com/SciAm-19](http://InsightCruises.com/SciAm-19) or call us at (650) 787-5665.

Cruise prices vary from \$1,999 for an Interior State-room to \$7,199 for a Neptune Suite, per person. For those attending our Program, there is a \$1,675 fee. Port Charges are \$299 per person; gratuities are \$11.50 per person per day; taxes and fees are \$100 per person. The Program, cruise pricing, and options are subject to change. For more info please call 650-787-5665 or email us at [concierge@insightcruises.com](mailto:concierge@insightcruises.com).



## THEORETICAL PHYSICS

Speaker: Sean Carroll, Ph.D.

### The Hunt for the Higgs Boson

For decades, particle physicists have searched for the elusive Higgs boson, the missing piece of the "Standard Model" that explains the world we see. Last year, scientists at the Large Hadron Collider announced that they'd found it. Learn why the Higgs boson is so important, and what the future of particle physics might hold.

### Our Preposterous Universe

In the last century scientists learned that the universe is over 10 billion years old, that it is expanding, and that ordinary stars, planets, and people represent less than five percent of the universe. We'll discuss the rest, which is in the form of mysterious substances called "dark matter" and "dark energy."

### The Arrow of Time

We can turn an egg into an omelet, but not an omelet into an egg. That's the arrow of time, which can be explained by assuming that the universe has been increasing in disorder since it began. We'll discuss the nature of time, the origin of entropy, and what happened before the Big Bang.



## The Many Worlds of Quantum Mechanics

Despite the success of quantum mechanics, most physicists would agree that we still don't understand what it means. Learn about the source of this puzzlement, and why an increasing number of scientists think the world we experience is constantly branching into different versions, representing the many possible outcomes of quantum measurements.



## MINDFULNESS

Speaker: Ronald Siegel, Psy.D.

### Introduction to Mindfulness

Mindfulness has been practiced for thousands of years, and holds promise for alleviating anxiety, depression, stress and addiction. This workshop will draw upon ancient wisdom and the discoveries of modern science to help you cultivate mindfulness — both to deal with everyday difficulties and to live a richer, happier, more fulfilling life.

### The Science of Happiness

Though most human beings want to be happy, few of us know how to achieve happiness. Learn why popular pathways to happiness don't work, and how mindfulness can lead toward wisdom, compassion, meaning and connection. We'll look to modern science, as well as ancient Buddhist insight, to explore pathways to happiness.

### Mindfulness for Relationships

Ancient Eastern meditative techniques, originally solitary practices refined by hermits, monks, and nuns, are remarkably useful for facing interpersonal challenges. Learn how mindfulness meditation can help you develop the emotional intelligence, self-regulation, and empathy necessary for successful relationships, and how to use mindfulness to react less defensively to the inevitable ups and downs of interpersonal life.

For more info please call 650-787-5665 or visit [scientificamerican.com/travel](http://scientificamerican.com/travel)



## The Neurobiology of Mindfulness

As psychotherapists adapt ancient contemplative practices to the challenges of treating modern psychopathology, researchers are using fMRI, EEG, and other brain imaging techniques to investigate the neurobiological mechanisms by which mindfulness practices work. This presentation will explore the implications of these investigations for learning how to change our brains.



## ARCHAEOLOGY

Speaker: John R. Hale, Ph.D.

### A Land of Natural Wonders

Learn about the spectacular natural wonders of Southeast Asia, from ancient rainforests to stunning coral reefs. We'll cover the wealth of unique plant and animal species native to this region, as well as the history of the first domestication of rice, chicken, and pigs here. It's a trove of geology, biology, and natural history.

### Cradle of Human Evolution

Find out why Southeast Asia is at the forefront of evolutionary research, and why 19th century scientists believed the human species originated here. We'll cover some of the most game-changing fossils found in the region, from "Java Man" to "Peking Man" to Gigantopithecus and "Flores Man."

### Land of Lost Kingdoms

Fascinating kingdoms, from the Khmer rulers who built Angkor Wat to the Siamese kings who defied European colonialists, once reigned in Southeast Asia. Though always living under the threat of Chinese takeover, these powers nonetheless created unique cultures and artistic traditions. We'll discuss this rich history and the monuments they left behind.

### Faiths in Collision

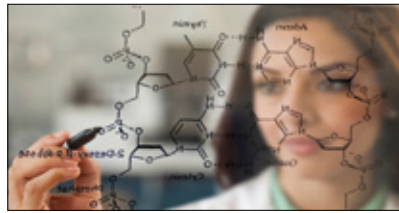
Learn how three of the world's major religions — Hinduism, Buddhism, and Islam — gained firm footholds in Southeast Asia, eventually overcoming the region's native animistic religious cults. We'll discuss the remarkable architecture — temples, monasteries, mosques — of these religions, as well as the ways their beliefs continue to permeate everyday life.

### The Story of the Spice Trade

The spices of Southeast Asia — pepper, cinnamon, cloves, nutmeg, cardamom, and others — led Europeans to forge sea-routes seeking out these treasures, and even motivated Columbus' search for a shortcut to Asia (which led him to stumble on America). Learn how the global trade that we take for granted today had its origins in the spice trade.

### Shipwrecks of Southeast Asia

Beneath the seas of Southeast Asia lies a museum of Arab dhows, Chinese junks, European trading ships, and World War II warships that were lured by commerce or war. Learn how ancient coins, woodcarvings, bronzes, and the wooden hulls of ships themselves helped archaeologists reconstruct the trade routes that linked East and West.



## GENETICS & EVOLUTION

Speaker: John Mattick, Ph.D.

### The Story of the Molecular Biology Revolution

Learn about the heady days when enzyme chemists joined physicists to decipher the genetic code, and later joined the bacterial geneticists to develop the tools that launched the gene cloning and genomic revolutions that are laying bare the programming of life. It's a story of great characters, rivalries and debates, pioneering vision and crippling hubris.

### The Origin of Life

The story of life is a dramatic, mysterious tale, originating in a primordial soup of organic molecules, and ultimately resulting in species that can remember, learn, sing, think, and write. Learn how evolution navigated cellular biology, and probe the complex innovations that must have occurred along the way.

### Junk DNA: Challenging the Dogma

Non-coding sequences of DNA were dismissed as junk when discovered, but scientists now are realizing that these segments are copied into RNA in precise patterns that orchestrate gene expression during development. Learn how what once was thought to be junk actually holds the secret to understanding human evolution, development, diversity, and cognition.

### Evolving Evolution

We'll contrast two early views of evolution by Charles Darwin and Jean-Baptiste Lamarck, and discuss how scientists' understanding of evolution has itself evolved over time. The traditional picture, that mutation is random and selection acts only on the progeny, may be incorrect. Evolution, it seems, has learned how to learn, and we're the result.

### Your Genome and You

Gene sequencing, once a costly and difficult process, is set to become routine in the near future. Medicine is evolving from the art of

crisis management to the science of good health, increasingly tailored to individuals' genetic and environmental circumstances. Learn what we stand to gain, and what surprises may be in store.



## HISTORY OF SCIENCE

Speaker: Steven Goldman, Ph.D.

### The Global Roots of Modern Science

Learn how modern science emerged in Western Europe in the 17th century, and grew to maturity in the 19th century. We'll also discuss how the development of modern science is deeply indebted to important contributions from China, the Arabic-speaking lands, and India, as well as from ancient Greece and Rome.

### Order Out of Chaos

We'll discuss the profound change the natural sciences underwent in the late 1900s, when scientists in multiple disciplines simultaneously discovered the power of top-down systems thinking, as opposed to bottom-up world building. In this session, become familiar with systems thinking and investigate the possibilities it offers.

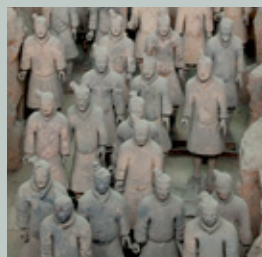
### The Mind, the Brain, and You

Learn how theories of the mind have evolved throughout time, from the 19th century, when philosophical speculation gave way to the sciences of psychology and physiology, to the late 20th century, when psychology and physiology converged with cognitive neuroscience and computer-based artificial intelligence technologies.

### Innovation, Globalization and the Future of America

The steam power-based Industrial Revolution of the mid-19th century quickly gave way to economies that critically depend on continuous technological innovation and access to global markets for growth and sustained prosperity. We'll discuss what America's people, institutions, and policy need to compete in global markets.

## SCIENTIFIC AMERICAN Travel HIGHLIGHTS SOUTHEAST ASIA FEB. 3 - 17, 2014

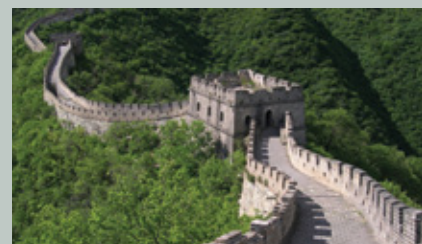


Great Wall; Xi'an and its Terracotta warriors; Guilin and a look at rural village life.

### CHINA TOUR

PRE-CRUISE — Sunday, January 26 to February 3, 2014: A fabulous, definitive, high-end eight-day excursion through China taking in Tian'anmen Square, the Summer Palace, and the Forbidden City in Beijing; the

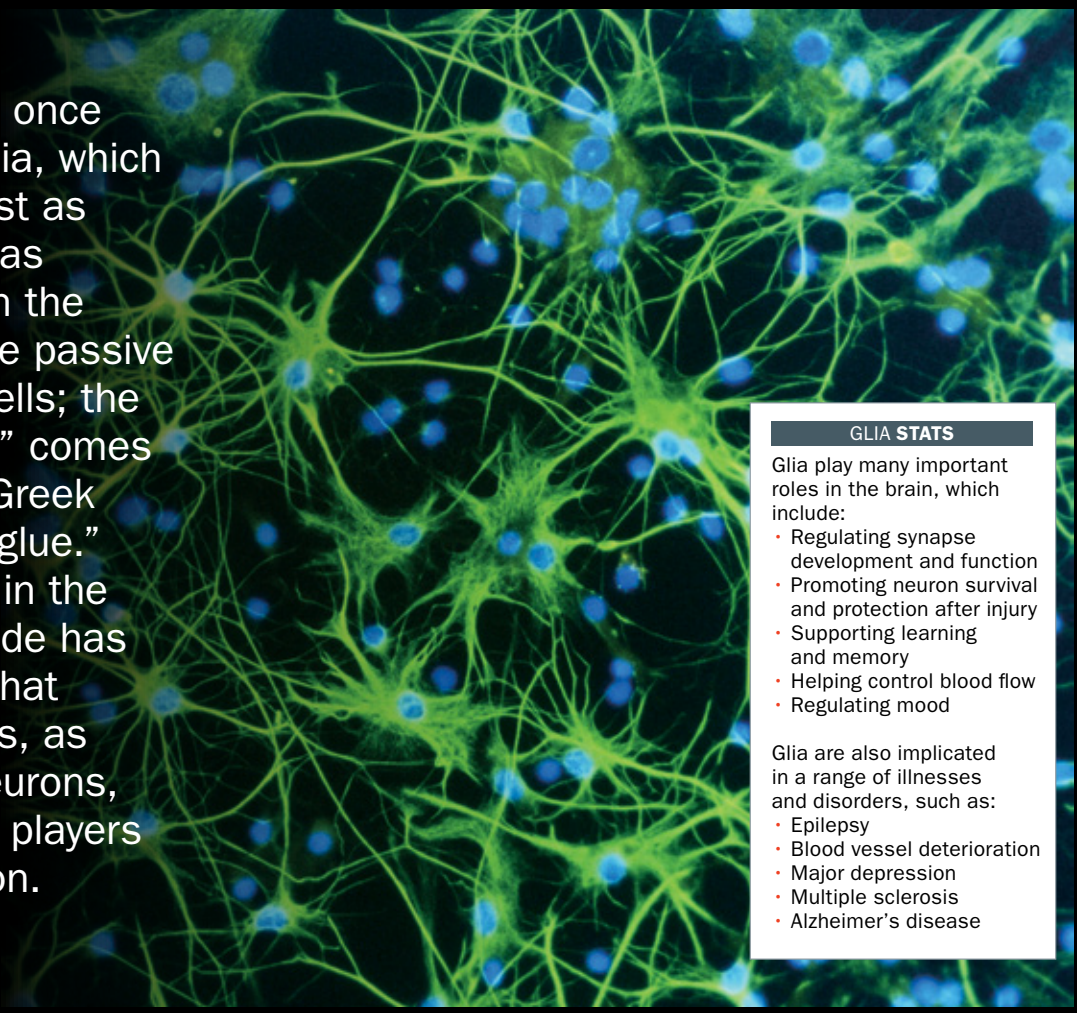
This tour was designed specifically for the Bright Horizons guests and is provided by our colleagues at Imperial Tours.



For more info please call 650-787-5665 or visit [scientificamerican.com/travel](http://scientificamerican.com/travel)

## » Glia New roles for the “other” brain cells

Scientists once thought glia, which are at least as prevalent as neurons in the brain, were passive support cells; the word “glia” comes from the Greek word for “glue.” Research in the past decade has revealed that these cells, as well as neurons, are active players in cognition.



### GLIA STATS

Glia play many important roles in the brain, which include:

- Regulating synapse development and function
- Promoting neuron survival and protection after injury
- Supporting learning and memory
- Helping control blood flow
- Regulating mood

Glia are also implicated in a range of illnesses and disorders, such as:

- Epilepsy
- Blood vessel deterioration
- Major depression
- Multiple sclerosis
- Alzheimer's disease

## Glia Spark Seizures

The brain's electrical storms may originate in nonelectrical cells

**W**hen neurons fire together uncontrollably, epileptic seizures ensue. Yet what sparks the cells to go haywire in the first place? In January scientists found an unexpected answer. When glial cells in the cortex of fruit flies cannot properly control their calcium levels, they leave neighboring neurons vulnerable to seizures.

Researchers at the Massachusetts Institute of Technology identified a genetic mutation that causes fruit flies to seize when they are exposed to heat or vibration. On studying the mutation, they found that it affects a gene called *zydeco* that controls calcium exchange inside glial cells—a surprise considering that most research about seizures has focused on neurons. And

logically so: neurons fire electrical impulses, whereas most glial cells do not. “It threw us for a loop at first,” explains lead author and M.I.T. graduate student Jan Melom.

The mutation identified in the study prevents tiny calcium fluctuations from occurring in glia, which Melom believes results in a buildup of calcium inside the cells. Because stress such as heat usually further boosts calcium levels, the combination could trigger “some sort of glial reaction that spirals into a seizure,” she says. One major question is how the glia communicate with neurons, prodding them to overexcite. Because a version of *zydeco* exists in mammals, the answer could help explain the genesis of epileptic seizures in humans, too. —Melinda Wenner Moyer

N. KEDERSHA Science Source



Perch living in rivers contaminated by common anti-anxiety drugs, such as Xanax and Valium, were found to behave more boldly and



## A Fast-Acting Antidepressant

Glial activity reveals how sleep deprivation elevates mood

Sleep deprivation is a quick and efficient way to treat depression. It works 60 to 70 percent of the time—far better than existing drugs—but the mood boost usually lasts only until the patient falls asleep. As an ongoing treatment, sleep deprivation is impractical, but researchers have been studying the phenomenon in an effort to uncover the cellular mechanisms behind depression and remission. Now a team at Tufts University has pinpointed glia as the key players.

The researchers previously found that astrocytes, a star-shaped type of glial cell, regulate the brain chemicals involved in sleepiness. During our waking hours, astrocytes continuously release the neurotransmitter adenosine, which builds up in the brain and causes “sleep pressure,” the feeling of sleepiness and its related memory and attention impairments. The neurotransmitter causes this pressure by binding to adenosine receptors on the outside of neurons like a key fitting into a lock. As more adenosine builds up, more receptors are triggered, and the urge to sleep gets stronger.

In the new study, published online January 15 in the journal *Translational Psychiatry*, the scientists investigated whether this process is responsible for the antidepressant effects of sleep deprivation. Mice with depressivelike symptoms were administered three doses of a compound that triggers adenosine receptors, thus mimicking sleep deprivation. Although the mice continued to sleep normally, after 12 hours they showed a rapid improvement in mood and behavior, which lasted for 48 hours.

The results confirm that the adenosine buildup is responsible for the antidepressant effects of a lack of sleep. This finding points to a promising target for new drug development because it suggests that mimicking sleep deprivation chemically may offer the antidepressant benefits without the unwanted side effects of actually skipping sleep. Such an intervention could offer immediate relief from depression, in stark contrast with traditional antidepressants, which take six to eight weeks to kick in.

The study may also have implications beyond depression and sleep regulation, according to Dustin Hines, lead author and a postdoctoral fellow at Tufts. “For many years neuroscientists focused almost exclusively on neurons, whereas the role of glia was neglected,” Hines says. “We now know that glia play an important role in the control of brain function and have the potential to aid in the development of new treatments for many illnesses, including depression and sleep disorders.”

—David Levine

SHARON DOMINICK/ISTOCKPHOTO (left); FROM “NEUROSCIENCE: GLIA—MORE THAN JUST BRAIN GLUE,” BY NICOLA J. ALLEN AND BEN A. BARRÉS, IN NATURE, VOL. 457, FEBRUARY 5, 2009 (right)

## Without Glia, the Brain Would Starve

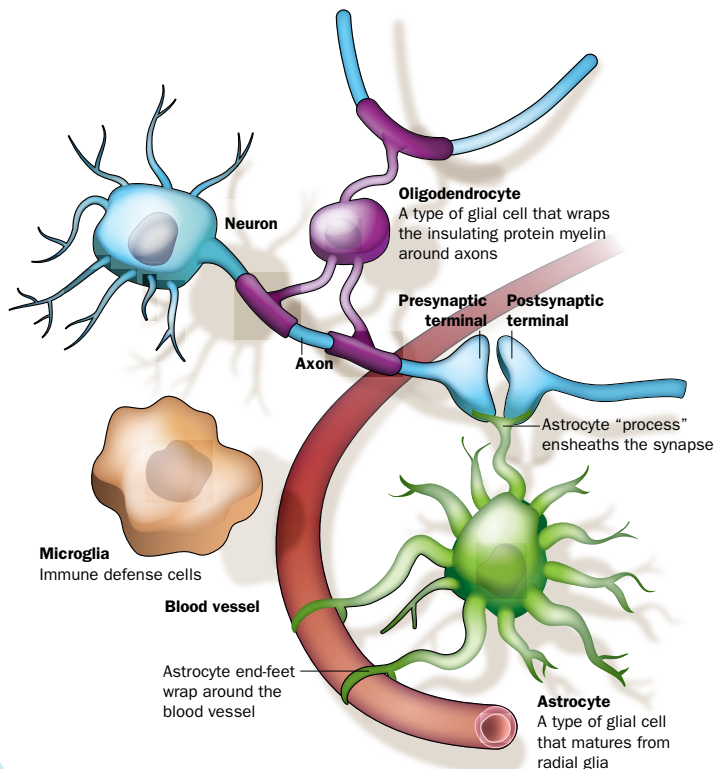
Blood vessels break down if certain glial cells are not present

The brain is voracious: compared with other organs, it consumes 10 times more oxygen and nutrients, receiving them by way of dense networks of blood vessels. Scientists know how these networks initially grow, but a surprising new study suggests that they are stabilized in early life by stem cells in the brain called radial glia. The finding could have significant implications for our understanding of Alzheimer’s disease, a condition characterized in part by brainwide vascular problems.

Radial glia are stem cells that have been shown to help neurons grow and migrate throughout the brain. So when Zhen Huang, a neuroscientist at the University of Wisconsin–Madison, eliminated a gene in mice and thereby prevented radial glia from regenerating, he was “surprised to find [blood] vessels regress,” he says. The mice lacking this gene not only developed fewer radial glia, blood vessel density in their cortex also dropped by 83 percent.

Huang found that the loss of glial cells caused activity in a biochemical pathway called Wnt to increase. In additional experiments, he showed that ramping up Wnt in healthy mouse embryos caused their vascular brain networks to collapse, whereas turning Wnt down preserved them. Given that the brains of people with Alzheimer’s are also plagued by blood vessel problems, the findings suggest that radial glia—and their careful control over Wnt—could be important for ensuring healthy brain energy metabolism and preventing neurodegeneration.

—Melinda Wenner Moyer



antisocially. | The first retinal implant was approved for use in the U.S. It required 20 years of development and more than \$200 million in funding.

## » A Push to Map All the Brain's Neurons

In February, President Barack Obama hinted that the White House would soon announce a large-scale initiative aimed at mapping the activity in the brain at the cellular level. Several scientists con-

firmed the project would probably be based on the Brain Activity Map proposal outlined in *Neuron* in June 2012. SCIENTIFIC AMERICAN MIND asked a few top neuroscientists what they think.



**RAFAEL YUSTE,**  
a neuroscientist  
at Columbia Uni-  
versity and an  
adviser for the  
White House's  
initiative:

The Brain Activity

Map could advance our knowledge by providing an unprecedented view into the large-scale activity of different parts of the brain of experimental animals—and hopefully also humans. These data could reveal how the brain works at the level of small- and large-scale circuits, something we currently cannot see. Just as it is very difficult to see an image on a television screen if you can see only one or a few pixels at a time, current neuroscience tools that can record the activity of only one or a few neurons at a time make it difficult to see the bigger picture. The Brain Activity Map could provide the tools to enable researchers and clinicians to “see the whole screen.”



**PARTHA MITRA,**  
a neuroscientist  
and theoretical  
biologist at Cold  
Spring Harbor  
Laboratory:

We do need tools  
to record from

many neurons. But simply increasing the number of neurons that are providing the recording won't solve the problems neuroscience faces today: a broader approach is needed. Anatomical network structure and neuronal physiology together determine the laws that underlie the many ways neurons communicate and influence one another, so these areas need to be pursued with equal emphasis, despite the proposal's recommendation to focus solely on brain activity. Arguably, a map of neuronal network architecture—not an activity map—is the closest analogue of the human genome for the brain.



**R. DOUGLAS FIELDS,**  
a neuroscientist  
and senior investi-  
gator at the Na-  
tional Institutes  
of Health:

Mapping out the  
anatomy of neuronal

connections in the brain is an important and necessary step. Schizophrenia, autism and drug abuse probably involve neurons that work fine but are operating in suboptimal or dysfunctional networks. But there is one major oversight, apparently, in this initiative. From what I have heard, the project will not map glia. Glia regulate neuronal network communication in many ways, yet we have only the most rudimentary understanding of glia in comparison with what is known about neurons. If the goal of this funding initiative is to map the connections in the brain, I think we should connect all the parts into the map, not just one cell type.

## » Love That Knows Bounds

A hormone that promotes social attraction also helps men keep their distance

Oxytocin, the so-called love hormone, activates feelings of trust and attraction between people when it is released in the brain, and it rises in the early stages of romantic love. Yet it is not just a Cupid's arrow that spurs you to fall in love with the nearest person, according to a recent study published in the *Journal of Neuroscience*. Instead oxytocin's social magic depends on whether or not a person is in a monogamous relationship.

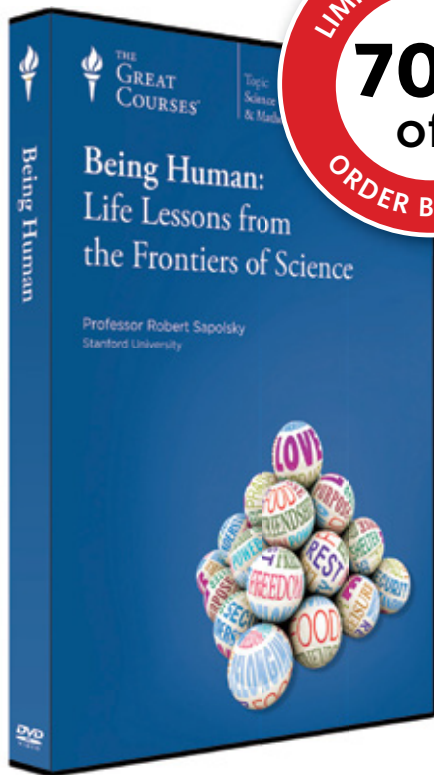
A team of researchers from the University of Bonn in Germany and elsewhere monitored a first encounter between straight male study participants and an attractive woman in a laboratory setting. When given oxytocin via an intranasal spray before the meeting, men who had indicated they were currently in a stable relationship kept a greater physical distance from the woman in the lab compared with single guys given oxytocin and with



single and “taken” guys given a placebo. Although they stayed only 10 to 15 centimeters farther away, the extra distance left the woman outside of what most people consider “personal space,” a zone reserved for loved ones. Moreover, it was not because they did not find her attractive: the monogamous men who received oxytocin rated the woman just as good-looking as the other men did.

The results suggest that oxytocin has a role in maintaining relationships after they are sparked and add to growing evidence for differences in how the hormone acts to modulate social interactions—for example, promoting bonds with familiar people but provoking aggression with strangers. “It's not all positive with oxytocin,” says Dirk Scheele, a psychologist involved with the study. “And what you call prosocial or antisocial depends on your perspective.” —Michele Solis

**M** Couples who used an oxytocin nasal spray became better communicators and experienced less stress than couples given a placebo spray.



## What Makes You *You*?

Why do we have bad moods? Why do we long for the foods, fashions, and music of our youths? Why are we capable of having such strange and vivid dreams? Understanding our humanity—the very essence of who we are—is one of the deepest mysteries in modern science. But fields including evolutionary biology, neuroscience, anthropology, psychology, and sociology are starting to reveal more about the mechanisms of human behavior—and just how intriguing the human species truly is.

In the 12 riveting lectures of **Being Human**, acclaimed neurobiologist and award-winning Professor Robert Sapolsky of Stanford University takes you to the front lines of this research as he shares the surprising, amusing, and undeniably fascinating study of humanity. Thought-provoking, witty, and sometimes myth-shattering, this course is sure to have you thinking about, observing, and appreciating your own life in new and novel ways.

**Offer expires 06/25/13**

**1-800-832-2412**

**WWW.THEGREATCOURSES.COM/6MIND**

## Being Human: Life Lessons from the Frontiers of Science

Taught by Professor Robert Sapolsky  
STANFORD UNIVERSITY

### LECTURE TITLES

1. What's So Special about Being Human?
2. Junk-Food Monkeys
3. The Burden of Being Burden-Free
4. Bugs in the Brain
5. Poverty's Remains
6. Why Are Dreams Dreamlike?
7. The Pleasures and Pains of "Maybe"
8. How the Other Half Heals
9. Why We Want the Bodies Back
10. Anatomy of a Bad Mood
11. This Is Your Brain on Metaphors
12. Sushi and Middle Age

**Being Human: Life Lessons from the Frontiers of Science**  
Course no. 1686 | 12 lectures (30 minutes/lecture)

**SAVE UP TO \$160**

DVD ~~\$199.95~~ **NOW \$39.95**

CD ~~\$134.95~~ **NOW \$24.95**

+\$5 Shipping, Processing, and Lifetime Satisfaction Guarantee  
Priority Code: 77857

Designed to meet the demand for lifelong learning, The Great Courses is a highly popular series of audio and video lectures led by top professors and experts. Each of our more than 400 courses is an intellectually engaging experience that will change how you think about the world. Since 1990, over 10 million courses have been sold.

## » Cells That Make You ...



### ... Itch

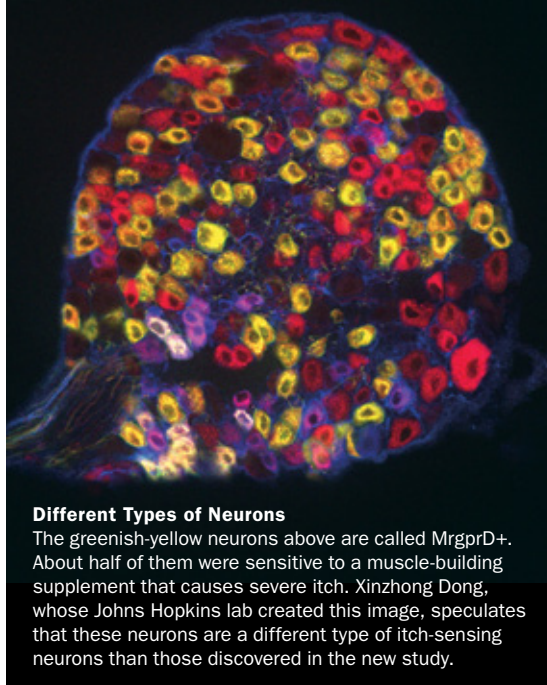
What is an itch? Scientists have speculated that it is a mild manifestation of pain or perhaps a malfunction of overly sensitive nerve endings stuck in a feedback loop. They have even wondered whether itching is mostly psychological (just think about bed bugs for a minute). Now a study rules out these possibilities by succeeding where past attempts have failed: a group of neuroscientists have finally isolated a unique type of nerve cell that makes us itch and only itch.

In previous research, neuroscientists Liang Han and Xinzhong Dong of Johns Hopkins University and their colleagues determined that some sensory neurons with nerve endings in the skin have a unique protein receptor on them called MrgprA3. They observed under a microscope that chemicals known to create itching caused these neurons to generate electrical signals but that painful stimuli such as hot water or capsaicin, the potent substance in hot peppers, did not.

In the new study published in *Nature Neuroscience*, the researchers used genetic engineering to selectively kill the entire population of MrgprA3 neurons in mice while leaving all the other sensory neurons intact. These mice no longer scratched themselves when exposed to itchy substances or allergens, but they showed no changes at all in responding to touch or pain-producing stimulation.

The mice's behavior confirms that MrgprA3-containing neurons are essential for itch, but it does not rule out the possibility that these cells might respond to other sensations as well. To find out, the neuroscientists engineered a receptor that responds to capsaicin injected into the MrgprA3 neurons, in a type of mouse that lacks the capsaicin receptor in all its other cells. Now the only neurons that would be stimulated by capsaicin were the MrgprA3 neurons. If these cells are indeed itch-specific, injecting capsaicin into a tiny spot on the mouse's skin should make the rodent scratch instead of wincing in pain—which is exactly what happened.

"Our current study has shown experimentally for the first time the existence of itch-specific nerves," Dong says. The discovery that itching is distinct from pain, touch or temperature sense should allow for the development of new drugs that block MrgprA3 receptors, which will silence the raging itch of poison ivy or eczema without affecting any other senses. —R. Douglas Fields



### Different Types of Neurons

The greenish-yellow neurons above are called MrgprD+. About half of them were sensitive to a muscle-building supplement that causes severe itch. Xinzhong Dong, whose Johns Hopkins lab created this image, speculates that these neurons are a different type of itch-sensing neurons than those discovered in the new study.



### ... Purr

Itching is not the only sensation to arise from unique neurons. A team at the California Institute of Technology has identified neurons that transmit the pleasurable sensations of massage, at least in mice. The cells responded to gentle rubbing but not to pinching or poking. Activation of the cells requires "a pressure component," says lead investigator David Anderson, a neuroscientist at Caltech, "much like you would apply if you were stroking your cat."

The team first identified the mysterious cells several years ago by an unusual protein on their surface called MrgprB4—closely related to the receptor expressed by the newly identified itch cells. The rare sensory cells make up only about 2 percent of the body's peripheral neurons that respond to external stimuli, but they seem to cover about half the skin's surface with large, branching nerve endings. Whereas sensory neurons that transmit pain have been intensely studied, this is the first demonstration in live animals of a sensory cell that gives pleasure. After the scientists activated those neurons with a designer drug, the mice came to favor the place where they received the drug, according to the paper published January 31 in *Nature*.

—Stephani Sutherland

#### ITCH FACTS

**1660** The year the meaning of itch was first defined. Samuel Hafener, a German physician, called it an unpleasant sensation that compels people to scratch.

#### Social Itching

**64** Percentage of people who scratched when watching others do so, according to a recent study.

#### Excessive Itchiness is a symptom of:

- Obsessive-compulsive disorder
- Depression
- Eating disorders
- Delusional thinking

COURTESY KEATING (stockphoto) (left); COURTESY OF XINZHONG DONG AND QIN LIU Johns Hopkins University (center); GETTY IMAGES (right)



Warm weather impairs our ability to make complex decisions and may instill a distaste for making decisions at all. ↑ Rats outfitted with a

# Psychiatry's New Bible

## As our understanding of mental illness grows, the diagnostic manual gets an update

The month of May marks the release of the *DSM-5*, the fifth edition of the American Psychiatric Association's best-selling *Diagnostic and Statistical Manual of Mental Disorders*. Because most insurance providers require a *DSM* diagnosis as a prerequisite for paying for treatment, the changes in the manual will affect health care for millions of Americans. Here are a few of the major revisions.

### NEW ADDITIONS

**Hoarding.** No longer just a symptom of obsessive-compulsive disorder, research has revealed that the inability to throw away useless items is a malady in its own right.

**Gambling disorder.** The newest and most controversial member of the "Substance-Related and Addictive Disorders" chapter, compulsive gambling is now officially treatable as an addiction.

**Disruptive mood regulation.** Until now, kids who are regularly hostile or aggressive were often given the controversial diagnosis of bipolar disorder. Critics worry that giving the symptoms a new name will not solve the real problem: medicating children with drugs never meant for developing brains.

### OUT WITH THE OLD

**Asperger's syndrome.** The diagnosis and its popular perception—intelligent, single-minded, socially awkward—are a mark of pride for some self-titled Aspies. Now their symptom profile has been folded into the much broader "autism spectrum disorder."

**Sex addiction.** Although the term "sex addiction" has not been in the manual since 2000, hypersexuality still warranted a diagnosis of "sexual disorder not otherwise specified." Now the idea that excessive sex is an illness is gone from the book completely.

### PROPOSED AND REJECTED

**Attenuated psychosis risk syndrome.** This proposed disorder was meant to identify children and teens at risk of psychotic disorders, but the model faced criticism over its mediocre ability to predict who will actually develop full-blown psychosis. The syndrome has been relegated to a chapter on conditions that require further research [see "At Risk for Psychosis?" by Carrie Arnold; *SCIENTIFIC AMERICAN MIND*, September/October 2011].

Adapted from "The Newest Edition of Psychiatry's 'Bible,' the DSM-V, Is Complete," by Ferris Jabr; published online January 28, 2013. [www.scientificamerican.com/article.cfm?id=dsm-5-update](http://www.scientificamerican.com/article.cfm?id=dsm-5-update)

## ➤ Sneaky Health Saboteurs

### Avoid these pitfalls to reach your goals

Plans for working out and eating well often go awry, and the reasons for those lapses are not always obvious. Three new papers highlight unconscious influences that affect our choices.

#### Watch Out for Uncertainty

A job search or medical testing can breed doubts about the future, which in turn can interfere with our food choices. In one recent paper, being made to feel uncertain led people to select brownies over fruit. "Uncertainty appears to affect people by sapping the same kind of attention resources required to exert self-control," says Katherine L. Milkman of the University of Pennsylvania and an author of the study in *Organizational Behavior and Human Decision Processes*. To counteract this effect, be mindful of situations that cause uncertainty and be aware that uncertainty can feel like fear, worry or anxiety. Accepting a lack of insight into the future as a part of life can help you spend less energy thinking about it, saving up self-control for decision making.

#### Think of Your Mind and Body as One

In several related studies published last fall in *Psychological Science*, researchers at the University of Cologne in Germany investigated the link between health behaviors and the belief in mind-body dualism—the concept that mind and body are two separate entities. Participants who were primed to embrace dualism made less healthy choices than participants encouraged to think of the mind and body as interrelated. The link goes both ways: when participants were primed with health-related concepts, they were less likely to subscribe to dualism. Study author Matthias Forstmann says people with a dualistic view may be more likely to neglect the body's health because they see the body as "a mere vessel for the mind." This view is contradicted by research showing that thoughts can influence physiological markers such as heart rate and hormones [see "Healing the Body with the Mind," on page 10] and that exercise has a significant effect on mood and cognitive abilities.



#### Beware Weak Temptations

It is easy to overestimate the healthiness of foods you find less tempting than your top vices, a paper in *Appetite* finds. Subjects judged the healthiness of different foods without realizing their nutritional profiles were identical. They were more likely to judge the less tasty and less attractive foods as healthier, and they also indicated they were more likely to consume those foods. Researchers say less desirable foods may not trigger our self-regulatory defenses the way our favorites do. If chocolate is your vice, don't underestimate that cookie just because you like it less. Look up nutritional information or just go ahead and have a reasonable portion of what you really want. —Tori Rodriguez

AXEL KORES / Stockphoto (top); CORBIS (bottom)

brain prosthesis learned to perceive infrared light, revealing the brain's flexibility and pointing the way to sensory enhancement for humans.



## How to Be a Better Friend



I've had the same best friend since the first grade, although we haven't lived in the same state since the Clinton administration, and we almost never call when we say we will. Without the obvious trappings of a good friendship, such as face time and basic thoughtfulness, how can we possibly feel so close? As I learned from talking to experts, those conventional friendly actions have much less to do with how satisfying a friendship is than with what you give each other on a more nuanced, psychological level. Here are some ways to strengthen your bonds—no sentimental cards required.

**#1 Share a secret.** It's no surprise that telling a friend something sensitive would make her feel like you trust and value her. But that's not the only reason it brings you closer. It also makes your friend feel as if you value her more than someone else, says Peter DeScioli, a postdoctoral fellow in psychology at Harvard University, who has done extensive research on the "alliance" theory of friendship. He has found that even if you don't score someone very highly on likable traits such as intelligence or kindness, you are more likely to rank her high up in your friend group if you know she counts you among her closest friends. This ranking idea sounds petty, but DeScioli explains that "we want our friends to take our side, even if it's a minor disagreement about where we all want to go out to dinner tonight." So dish out that gossip—and your friend will know you've got her back.

**#2 Treat him like a grown-up.** When a pal is struggling, it can be awfully tempting to grab him by the scruff of his neck and just tell him exactly what he should do. After all, isn't giving good advice part of being a good friend? Perhaps not, according to researchers who study self-determination. Edward Deci, a psychology professor at the University of Rochester, has found that

supporting a friend's autonomy—that is, making him feel as if he can make his own choices—creates a better relationship and may even improve his mental health. In one study, Deci and his colleagues did in-depth interviews with pairs of friends and found that the more of this type of support there was from a friend, the more satisfied the partner was with the friendship and the higher self-esteem the person had. "When people are relating to you and acknowledging your sense of importance, your sense of competence, you feel better about yourself," Deci adds. In other words, treating a friend like he's got his act together could actually help him get there.

**#3 Accept that no friendship is perfect.** Everyone readily admits that fights are a normal part of marriage and family relationships. But when it comes to friendships, people are much less comfortable accepting imperfections. This tendency can cause friends to give up too fast on their relationship when trouble arises, according to Jan Yager, a sociologist and author of the book *Friendships: The Power of Friendship and How It Shapes Our Lives* (Hannacroix Creek Press, 1999). "People have this mistaken notion that a friendship is supposed to be the respite from all the other

challenges in one's life," Yager says. "You have to deal with the co-worker or the boss, you have to deal with your relatives, but you choose your friends." Don't be afraid of the occasional tiff or misunderstanding. Once you make it through, the bonds are likely to be stronger than ever.

**#4 Be there—physically—during hard times.** This summer I'll fly down to California to spend a few days helping my best friend after her third child is born. It might be the only time I see her in 2013, but in terms of keeping our friendship strong, it'll probably be worth more than a dozen just-for-fun visits. Having a friend standing by can actually blunt the body's stress response during a trying experience, according to a study by William Bukowski, a psychologist at Concordia University. He and his colleagues asked schoolchildren to keep a journal of personal interactions for four days, and they took several saliva samples daily to measure levels of the stress hormone cortisol. They found that cortisol levels were significantly lower in kids who said a close friend was with them during a negative event, such as getting in trouble with a teacher. "Our bodies recognize that they don't have to respond so much to danger if someone is there to help," Bukowski says. —Sunny Sea Gold



## ▶▶ The Mind-Body Problem, Hamster Edition

Minds are less replicable than physical traits, according to young kids

Does the brain create the mind? Many neuroscientists would say yes, but most of us—suggests University of Bristol neuroscientist Bruce Hood—carry a conviction that the mind is a special entity, distinct from our physical body. In other words, if it were possible to make an exact copy of someone's body, including the brain, most people's gut feeling is that the duplicate's consciousness would differ in some way from the original. Hood, with colleagues at Bristol and at Yale University, decided to investigate this question with young children to see whether we hold views on this subject early in life.

The researchers introduced five- and six-year-old kids to a hamster. The hamster had special physical traits—a broken tooth, for example—and each child interacted with the hamster to create a few memories. Then the investigators placed the animal in an elaborate box they call the duplicator

and revealed a second, seemingly identical hamster. The children were asked a series of questions to reveal the degree to which they believed this new hamster was like the original.

Most children believed that physical traits, such as the broken tooth, were the same in both hamsters. About half of them, however, believed that the hamsters would not share memories. The findings, reported in the journal *Cognition* last December, suggest that we may develop our beliefs about the uniqueness of identity and mind at a very young age. The distinction between mental and physical replication was even greater when the original hamster was introduced with a name, "Dax." In this case, about 70 percent of the children doubted that mental traits had duplicated along with physical ones. What's in the name? Hood suspects that naming primes kids to see the hamster as more human and unique. —Daisy Yuhas



# Perfectly Timed Advertising

Marketing illusions that make time fly

BY STEPHEN L. MACKNIK, LEANDRO LUIGI DI STASI AND SUSANA MARTINEZ-CONDE

*Time is the most valuable thing a man can spend.*

—Theophrastus (371–287 B.C.)

ANCIENT philosophers were far from alone in their musings about time. Playwright Tennessee Williams wrote in 1944 that time is the longest distance between two places. And the years since have proved him right. Fast travel, instant communications and express deliveries between opposite ends of the world mean, more than ever, that time is not only relative but also an illusion.

But time is also money, or so the axiom goes. Certainly both time and money are precious, exist in limited quantities and can be intimately intertwined. Have you ever longed to get away but lacked the money or time to take your ideal vacation? In our travels we have noticed that airports, surprisingly, are a favorite location for high-end watch displays. It is as if travelers commonly must decide before imminent takeoff whether to pop into the newsstand to grab some gum and a copy of *Scientific American* or stop by the adjoining jewelry counter for a \$10,000 Rolex. Who chooses the latter? We can't, unfortunately, although we do like to window shop. Next time you do, pay special attention to the watch displays and see if you notice anything unusual. You may see how advertisers exploit the intersection of time and illusion to sell their products.

## Accurate Twice Each Day

Search for the term “watch images” on your favorite Internet browser, and you’ll find something bizarre. Almost every watch is set to 10:10. What belief,



A seemingly everyday tableau of colorful watches arrayed here are all set to a time of 10:10. Why that time? Therein lies an intriguing mental mystery.

what powerful insight, what shared brain mechanism could cause salespeople to hock their clocks with that setting? Is it that shoppers preferentially like to make purchases just after morning tea? Or, as conspiracy theorists have suggested, because 10:10 is the hour when John F. Kennedy, Martin Luther King, Abraham Lincoln or John Lennon was assassinated? Or when Fat Man and Little Boy burned the sky above Nagasaki and Hiroshima? Nope. All such proposals are factually incorrect.

According to the *New York Times*, the Hamilton Watch Company was among the first to set its products to 10:10—in the 1920s. The previous standard setting was 8:20. Some advertising executives now assume that the switch

occurred to turn the watches’ 8:20 “frown” upside down, into a “smile.”

But to visual neuroscientists like us, all this speculation begs the question as to why clock hands were set to oblique 8:20/10:10 positions in the first place. It seems unlikely that pre-1920 watchmakers wanted their watches to frown. One possibility is that oblique watch-hand orientations are best at keeping company logos uncovered—but, if so, horizontal positions such as 9:15 or 2:45 would be even better. Because horizontal orientations have never been popular in watch advertisement, we can rule this idea out.

Could it then be that oblique orientations result in higher watch sales than do cardinal—or vertical and horizontal—orientations? The answer may well

(What powerful insight, **what shared brain mechanism**, could cause salespeople to hock their clocks with that setting?)

COURTESY OF SWATCH



Not as cuckoo as you think: all clock sellers use the 10:10 display.



Both 10:10 and 8:20 have a visually arresting shape for the brain. But one is much more commonly used. Why is that?

be affirmative, and the neuroscience of perception and cognition reveals why. Scientists have long known that we can detect cardinal orientations more easily than oblique orientations. The visual cortex, moreover, responds to oblique orientations more weakly, as if they had lower contrast than cardinal orientations of the same physical brightness. In addition, fewer neurons are sensitive to oblique than to cardinal orientations. As a result, obliquely oriented watch hands are a bit more difficult for us to see.

At first, this fact may seem like bad news for marketing timepieces, especially if you think that watch hands should be as visible as possible in ads. But neuroscience tells us why it is actually a benefit. To maximize the potential for sales, you really want your customers to rivet their attention on your product—and the visual challenge of seeing the oblique position draws that attention. Visual attention has the effect of enhancing the perception of low-contrast image elements in perception. As it happens, the enhancement is most valuable when those elements are difficult to detect because attention is stronger when the object of interest is hard to see—such as watch hands that are oriented obliquely.

If *Mad Men* (and *Women*) intuited that obliquely oriented lines are atten-

tion getters, people in other fields may have arrived at similar conclusions. We looked for prominently featured clocks in fine art paintings and—viola!—Marc Chagall used the time 10:10 in his famous series of clock paintings dating as far back as 1914, before the watch industry’s own 10:10 preference.

### Time’s Arrow

Watch manufacturers are not the only companies that have toyed with the interaction of time and illusion in commercial advertising. When you use FedEx courier services to buy yourself some time, you may overlook the clever illusion hidden in the company’s iconic logo: time’s arrow, pointing toward the future. You can see either the white arrow or the FedEx letters, but not both at

**The watch industry was not the first to use 10:10 as an ideal setting for timepieces. Here is an example from artist Marc Chagall’s clock series.**

once, because one is always the background to the other.

The current FedEx logo was shortened from the earlier company name Federal Express and given a new snazzy illusory design element, the background arrow between the “E” and the “x.” Did the company shorten the name to reduce the amount of paint needed for signage on its planes and trucks? That explana-



GETTY IMAGES (top left); SARUN LAOWONG (stockphoto (top right)); BRIDGEMAN-GIRAUDON, Art Resource/Artists Rights Society, New York/ADAGP, Paris (bottom)

(Time may **fly like an arrow**, but it is your attention to time that advertisers care about.)



**FedEx incorporates a forward-pointing arrow into its ambiguous logo (look at the white space in the type). In languages that read left to right, the arrow points right (upper left of image)—and the arrow points left in languages that read right to left, such as Arabic (truck).**

grouped in sequences, such as in the famous representation of human evolution from prehuman to *Homo sapiens*. The direction of the sequence is fundamentally arbitrary, yet if you grouped it the wrong way, it would look like a time reversal.

So time may fly like an arrow, but it is your attention to time that advertisers care about. **M**

STEPHEN L. MACKNIK and SUSANA MARTINEZ-CONDE are laboratory directors at the Barrow Neurological Institute in Phoenix. They serve on *Scientific American Mind*'s board of advisers. Their forthcoming book, *Champions of Illusion*, will be published by Scientific American/Farrar, Straus and Giroux. LEANDRO LUIGI DI STASI is a Fulbright Scholar at the Barrow Neurological Institute and the University of Granada in Spain, who works in the emerging field of neuroergonomics.

tion makes no sense, unless the painters could use only one font size. Once the name was shorter, they could just paint the letters larger to take up the same space and use about the same amount of paint. In fact, according to Linden Leader, the graphic artist who designed the new logo, the FedEx CEO specifically requested that the logo be easily legible on every truck from five blocks away.

Instead the change resulted from a thorough analysis of the company's name recognition in the market. Why might the new logo be more effective? One reason is that the arrow, a symbol that has special meaning to our cognitive system, helps to draw attention to the logo as a whole. Arrows indicate what scientists call "implied motion." Visual neuroscientists Anja Schlack and Thomas Albright of the Salk Institute for Biological Studies have shown that neurons that respond preferentially to specific directions of motion in the world are also activated by arrows pointing in the corresponding direction, even though the arrows are not themselves moving but just represent the concept of motion.

The FedEx arrow pointing to the right signifies motion toward the future for those who write in English and other

left-to-right languages. Moreover, because our motion areas also have more neurons that prefer cardinal rather than oblique directions, here the arrow invokes a powerful competition with the FedEx name itself, so our perception vacillates between "FedEx" and forward momentum. In languages read right to left, the FedEx arrow points toward the left, such as in the Arabic version of the logo, consistent with the corresponding cognitive representation of time's arrow.

This same left-to-right effect works to express temporal order of pictograms

### (Further Reading)

- ◆ **When Sustained Attention Impairs Perception.** S. Ling and M. Carrasco in *Nature Neuroscience*, Vol. 9, No. 10, pages 1243–1245; October 2006.
- ◆ **Unequal Representation of Cardinal vs. Oblique Orientations in the Middle Temporal Visual Area.** X. Xu, C. E. Collins, I. Khaytin, J. H. Kaas and V. A. Casagrande in *Proceedings of the National Academy of Sciences USA*, Vol. 103, No. 46, pages 17,490–17,495; November 14, 2006.
- ◆ **Remembering Visual Motion: Neural Correlates of Associative Plasticity and Motion Recall in Cortical Area MT.** A. Schlack and T. D. Albright in *Neuron*, Vol. 53, No. 6, pages 881–890; March 15, 2007.
- ◆ **Arte e Espressione: Studi e Ricerche di Psicologia Dell'arte.** Alberto Argenton. Il Poligrafo, Padua, 2008.
- ◆ **Task Difficulty Modulates the Activity of Specific Neuronal Populations in Primary Visual Cortex.** Y. Chen, S. Martinez-Conde, S. L. Macknik, Y. Bereshpolova, H. A. Swadlow and J.-M. Alonso in *Nature Neuroscience*, Vol. 11, No. 8, pages 974–982; August 2008.
- ◆ **Why Time Stands Still for Watchmakers.** Andrew Adam Newman in *New York Times Media & Advertising* section; November 27, 2008.

# Taking the Bad with the Good

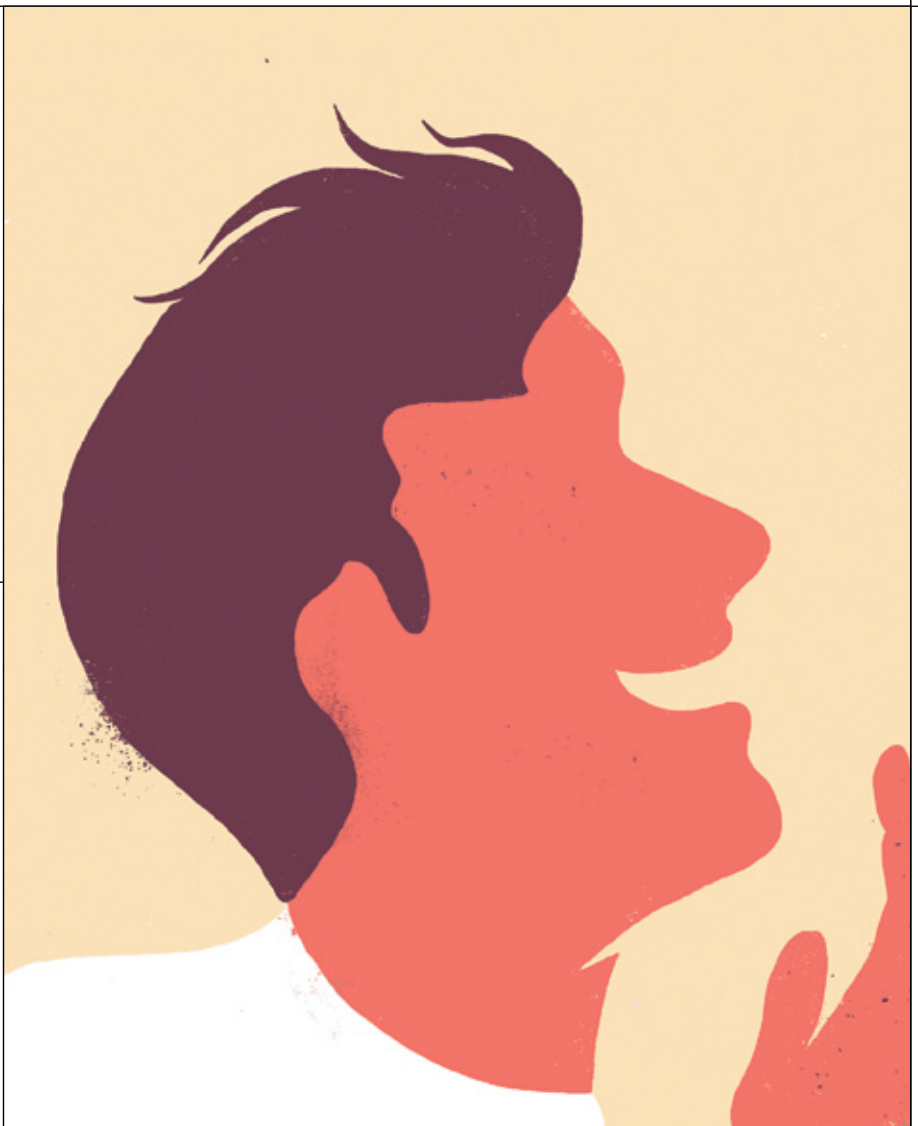
Feeling sad, mad, critical or otherwise awful? Surprise: negative emotions are essential for mental health

BY TORI RODRIGUEZ

A CLIENT SITS before me, seeking help untangling his relationship problems. As a psychotherapist, I strive to be warm, nonjudgmental and encouraging. I am a bit unsettled, then, when in the midst of describing his painful experiences, he says, “I’m sorry for being so negative.”

A crucial goal of therapy is to learn to acknowledge and express a full range of emotions, and here was a client apologizing for doing just that. In my psychotherapy practice, many of my clients struggle with highly distressing emotions, such as extreme anger, or with suicidal thoughts. In recent years I have noticed an increase in the number of people who also feel guilty or ashamed about what they perceive to be negativity. Such reactions undoubtedly stem from our culture’s overriding bias toward positive thinking. Although positive emotions are worth cultivating, problems arise when people start believing they must be upbeat all the time.

In fact, anger and sadness are an important part of life, and new research shows that experiencing and accepting such emotions are vital to our mental health. Attempting to suppress thoughts can backfire and even diminish our sense of contentment. “Acknowledging the complexity of life may be an especially fruitful path to psychological well-being,” says psychologist Jonathan M. Adler of the Franklin W. Olin College of Engineering.



## Meaningful Misery

Positive thoughts and emotions can, of course, benefit mental health. Hedonic theories define well-being as the presence of positive emotion, the relative absence of negative emotion and a sense of life satisfaction. Taken to an extreme, however, that definition is not congruent with the messiness of real life. In addition, people’s outlook can become so rosy that they ignore dangers or become complacent [see “Can Positive Thinking Be Negative?” by Scott O. Lilienfeld and Hal Arkowitz; *SCIENTIFIC AMERICAN Mind*, May/June 2011].

Eudaemonic approaches, on the other hand, emphasize a sense of meaning, personal growth and understanding of the self—goals that require confronting

life’s adversities. Unpleasant feelings are just as crucial as the enjoyable ones in helping you make sense of life’s ups and downs. “Remember, one of the primary reasons we have emotions in the first place is to help us evaluate our experiences,” Adler says.

Adler and Hal E. Hershfield, a professor of marketing at New York University, investigated the link between mixed emotional experience and psychological welfare in a group of people undergoing 12 sessions of psychotherapy. Before each session, participants completed a questionnaire that assessed their psychological well-being. They also wrote narratives describing their life events and their time in therapy, which were coded for emotional con-

SÉBASTIEN THIBAUT

tent. As Adler and Hershfield reported in 2012, feeling cheerful and dejected at the same time—for example, “I feel sad at times because of everything I’ve been through, but I’m also happy and hopeful because I’m working through my issues”—preceded improvements in well-being over the next week or two for subjects, even if the mixed feelings were unpleasant at the time. “Taking the good and the bad together may detoxify

thought prior to sleep. Those who tried to muffle the thought reported dreaming about it more, a phenomenon called dream rebound.

Suppressing thoughts and feelings can even be harmful. In a 2012 study psychologist Eric L. Garland of Florida State University and his associates measured a stress response based on heart rate in 58 adults in treatment for alcohol dependence while exposing them to alco-

You may also try doing mindfulness exercises to help you become aware of your present experience without passing judgment on it. One way to train yourself to adopt this state is to focus on your breathing while meditating and simply acknowledge any fleeting thoughts or feelings. This practice may make it easier to accept unpleasant thoughts [see “Being in the Now,” by Amishi P. Jha; SCIENTIFIC AMERICAN

( We can’t avoid negative feelings altogether, because **to live is to experience setbacks** and conflicts. )

the bad experiences, allowing you to make meaning out of them in a way that supports psychological well-being,” the researchers found.

Negative emotions also most likely aid in our survival. Bad feelings can be vital clues that a health issue, relationship or other important matter needs attention, Adler points out. The survival value of negative thoughts and emotions may help explain why suppressing them is so fruitless. In a 2009 study psychologist David J. Kavanagh of Queensland University of Technology in Australia and his colleagues asked people in treatment for alcohol abuse and addiction to complete a questionnaire that assessed their drinking-related urges and cravings, as well as any attempts to suppress thoughts related to booze over the previous 24 hours. They found that those who often fought against intrusive alcohol-related thoughts actually harbored more of them. Similar findings from a 2010 study suggested that pushing back negative emotions could spawn more emotional overeating than simply recognizing that you were, say, upset, agitated or blue.

Even if you successfully avoid contemplating a topic, your subconscious may still dwell on it. In a 2011 study psychologist Richard A. Bryant and his colleagues at the University of New South Wales in Sydney told some participants, but not others, to suppress an unwanted

hol-related cues. Subjects also completed a measure of their tendency to suppress thoughts. The researchers found that those who restrained their thinking more often had stronger stress responses to the cues than did those who suppressed their thoughts less frequently.

### Accepting the Pain

Instead of backing away from negative emotions, accept them. Acknowledge how you are feeling without rushing to change your emotional state. Many people find it helpful to breathe slowly and deeply while learning to tolerate strong feelings or to imagine the feelings as floating clouds, as a reminder that they will pass. I often tell my clients that a thought is just a thought and a feeling just a feeling, nothing more.

If the emotion is overwhelming, you may want to express how you feel in a journal or to another person. The exercise may shift your perspective and bring a sense of closure. If the discomfort lingers, consider taking action. You may want to tell a friend her comment was hurtful or take steps to leave the job that makes you miserable.

MIND, March/April 2013]. Earlier this year Garland and his colleagues found that among 125 individuals with a history of trauma who were also in treatment for substance dependence, those who were naturally more mindful both coped better with their trauma and craved their drug less. Likewise, in a 2012 study psychologist Shannon Sauer-Zavala of Boston University and her co-workers found that a therapy that included mindfulness training helped individuals overcome anxiety disorders. It worked not by minimizing the number of negative feelings but by training patients to accept those feelings.

“It is impossible to avoid negative emotions altogether because to live is to experience setbacks and conflicts,” Sauer-Zavala says. Learning how to cope with those emotions is the key, she adds. Indeed, once my client accepted his thoughts and feelings, shaking off his shame and guilt, he saw his problems with greater clarity and proceeded down the path to recovery. **M**

TORI RODRIGUEZ is a writer and psychotherapist in private practice in Atlanta.

### (Further Reading)

- ◆ **Mindfulness for Beginners: Reclaiming the Present Moment—and Your Life.** Jon Kabat-Zinn. Sounds True, 2011.
- ◆ **The Antidote: Happiness for People Who Can’t Stand Positive Thinking.** Oliver Burkeman. Faber & Faber, 2012.

# Inside the Dog Mind

New science reveals the multiple intelligences of mankind's best friend

BY GARETH COOK

**JUST ABOUT EVERY** dog owner is convinced their dog is a genius. For a long time scientists did not take such pronouncements particularly seriously, but research now suggests that canines are indeed quite bright and, in some ways, unique. Brian Hare, associate professor in the department of evolutionary anthropology and the Center for Cognitive Neuroscience at Duke University, is one of the leading figures in the quest to understand what dogs know. Founder of the Duke Canine Cognition Center, Hare has written a book, *The Genius of Dogs* (Dutton Adult, 2013), with his wife, journalist Vanessa Woods. Hare recently answered questions from Mind Matters editor Gareth Cook.

**COOK:** What is the biggest misconception people have about the dog mind?

**HARE:** That there are “smart” dogs and “dumb” dogs. There’s still this throwback to a unidimensional version of intelligence, as though there is only one type of intelligence that you either have more or less of.

In reality, there are various types of intelligence. Different dogs are good at different things. Unfortunately, the clever strategies some dogs are using are not apparent without playing a cognitive game. This means people can often underestimate the intelligence of their best friend. The pug drooling on your shoe may not look like the brightest bulb, but she comes from a long line of successful dogs and is a member of perhaps the most successful mammal species on the planet besides us. Rest assured: she is a genius.

**COOK:** What are the “different things” that dogs are good at? What are the areas of dog intelligence you have studied?

**HARE:** We know that, as a species, dogs are remarkable in certain areas, such as taking someone else’s visual perspective or learning from someone else’s actions.



In particular, I’ve been interested in how dogs recruit help. Still, most of my research with dogs has been about the cooperative way they use human communicative gestures. Or put more simply, how they can interpret our gestures to understand us or get what they want.

**COOK:** But other animals are intelligent, right? What makes dogs unique?

**HARE:** Absolutely. Other animals have their own unique genius that was shaped by nature. In the case of dogs, it happens to be their ability to read our communicative gestures. We take it for granted that

dogs can effortlessly use our pointing gestures to find a hidden toy or morsel of food, but no other species can spontaneously read our communicative gestures as flexibly as dogs can. It allows them to be incredible social partners with us, whether it’s hunting or agility or just navigating everyday life. Their ability to interpret our gestures also helps them solve problems they can’t solve on their own.

**COOK:** I see you have created a Web site, Dognition.com. Can you tell me about it?

**HARE:** Dognition is about helping people find the genius in their dog. The only

CORBIS

way to find their genius is to compare them with other dogs. As I said, different dogs use different strategies to solve problems. Does your dog rely on you to solve problems, or are they more independent? Do they pay attention to where you are looking before they decide to sneak food off the coffee table, or are they unaware when you are watching—making it hard for them to be sneaky?

Dognition is all about playing fun games that will give you a window into your dog's mind and that will in turn en-

owner yawning and seeing if their dog yawns back. It's a really simple test, but it can tell you a lot about your dog.

**COOK:** How empathetic are dogs, truly, when it comes to their human partners, and how much is just our imagination or our need to believe that they understand us?

**HARE:** As a scientist, it is hard to design tests that assess whether an animal is empathetic because most research on empathy in humans relies on people re-

Etruscan wolf spread throughout Europe. It was also around this time that humans were emigrating out of Africa.

But the wolf's reign didn't last long. As modern humans became the dominant carnivore, we persecuted other large carnivores to extinction—which is why dogs are such an interesting puzzle. Some have proposed that modern humans adopted wolf puppies and raised them, although this doesn't really make sense. Humans have never had a particularly amicable relationship with wolves. We tend to have a

( One study shows that dogs prefer to spend time with humans rather **than their own species**, which is unusual for an animal. )

rich the relationship you have with your dog. On top of that, the data that you enter will contribute to a huge citizen science project that will help us help all dogs, from shelter dogs to service dogs. Everyone who signs into Dognition will not only get an extensive cognitive profile of their own dog, but the data will also be entered into a database that scientists can use to answer all these burning questions that we have never had the resources to answer, such as about breed differences. The largest single dog study published tested around 15,000 dogs. With Dognition and people's input, we have the potential to test hundreds of thousands or even millions of dogs. It's an incredibly exciting project, and I can't wait to see what we find out.

**COOK:** Like the “yawn test”?

**HARE:** Even as young children, we laugh when we see someone laughing, and we cry when we see someone in distress. Our ability to “catch” the emotions of others is called emotional contagion. A common form of emotional contagion is yawning. If you see, hear or even think about someone yawning, you will probably feel an irresistible urge to yawn yourself. Contagious yawning is related to empathy scores in adults.

It looks like some dogs also contagiously yawn. The yawn test is just the

porting how they feel, and dogs can't talk (or at least not yet in a way we can understand them).

But there is definitely something special about the bond we have with dogs. Their ability to read our communicative gestures makes them seem in tune with us. And their attentiveness to our every move can't help but make us feel special. There is one study that shows that dogs would prefer to spend time with humans rather than their own species, which is unusual for an animal. Every dog owner is familiar with that rise in spirits as a thumping tail greets you at the door—and from the enthusiasm dogs have for us, it's hard to believe the feeling isn't mutual.

There are several measures, such as contagious yawning, that show that dogs probably at least have a basic form of empathy. And studies show that dogs and humans experience a rise in oxytocin, the “hug hormone” when we embrace and pet them (although it seems dogs get a higher boost in oxytocin when they are petted by women, as opposed to men).

**COOK:** What is the “wolf event,” as you call it, and what is its significance?

**HARE:** The “wolf event” was a curious episode in evolutionary history when wolves basically took over Europe. Between 1.7 million and 1.9 million years ago, during one of the ice ages, the relatively small

low tolerance for fanged predators, and the annihilation of wolves in the past 1,000 years almost led to their extinction. Some say humans discovered that tame wolves were excellent hunting partners, but wolves eat a lot of meat. A pack of 10 would need a deer a day. And humans were successful hunters without wolves.

The puzzle is how the big bad wolf was tolerated around humans long enough to evolve into the mutt that now sleeps on the sofa. It took my childhood dog (Oreo), a Russian genius, Siberian foxes, New Guinea singing dogs, Hungarian scientists, bonobos in Congo and a decade of research for me to figure out the answer.

And the answer is ... you'll have to read the book to find out. But to give you a hint, it's not always survival of the fittest. Sometimes it's the friendliest that have an evolutionary edge. **M**

Are you a scientist who specializes in neuroscience, cognitive science or psychology? And have you read a recent peer-reviewed paper that you would like to write about? Please send suggestions to Mind Matters editor Gareth Cook, a Pulitzer Prize-winning journalist at the *Boston Globe*. He can be reached at [garethideas@gmail.com](mailto:garethideas@gmail.com) or on Twitter [@garethideas](https://twitter.com/garethideas).

*Christof Koch's column, Consciousness Redux, will return in the next issue.*

A close-up photograph of a person's open palm, facing upwards, resting on a wooden surface. The palm is marked with the handwritten phrase "EVERYBODY DOES IT..." in black ink. The ink is written in a simple, blocky, sans-serif font. The words "EVERYBODY" and "DOES" are on the first line, and "IT..." is on the second line. The background is a warm, golden-brown wooden surface with visible grain patterns. The lighting is soft, highlighting the texture of the skin and the wood.

EVERYBODY  
DOES IT...



# WHY WE CHEAT

Scientists are unraveling the causes of fraud and dishonesty and devising new strategies for rooting them out

BY FERRIC C. FANG AND ARTURO CASADEVALL

Photoillustration by Aaron Goodman

Cyclist Lance Armstrong has apologized for using performance-enhancing drugs to win seven Tour de France titles. He attributed his cheating to a determination to “win at all costs.” Psychologist Marc Hauser of Harvard University, who once wrote an article entitled “Costs of Deception: Cheaters Are Punished...,” is now out of a job after the U.S. Office of Research Integrity concluded that he “fabricated data, manipulated results in multiple experiments, and described how studies were conducted in factually incorrect ways.” Sixteen banks have agreed to settlements or are under investigation for manipulation of the Libor, an interest rate at which banks may borrow from other banks, in what is said to be the largest financial scam in the history of markets.

These cases are only part of a seemingly unending stream of cheating scandals in the news, affecting sports, science, education, finance and other realms. Although it is comforting to think that most people are essentially honest, cheating—defined as acting dishonestly to gain an advantage—is actually astoundingly common. In a 1997

survey, management professor Donald McCabe of Rutgers University and Linda Klebe Treviño, a professor of organizational behavior at the Pennsylvania State University, revealed that about three fourths of 1,800 students at nine state universities admitted to cheating on tests or written assignments. In 2005 sociologist Brian Martinson of the



HealthPartners Research Foundation in Bloomington, Minn., and his colleagues reported that one third of scientists confessed to engaging in questionable research practices during the previous three years.

Cheating is not limited to humans; it has been documented throughout the living world, wherever there is competition for limited resources. Despite its ubiquity, cheating can be quite detrimental to individuals and to society. Cheaters are stigmatized and may lose their jobs. Resources are squandered on fraudulent work. Individuals who play by the rules are deprived of rewards that they deserve. There is also collateral damage. Armstrong’s cycling teammates were coerced into going along with the doping scheme and bullied when they tried to come clean. Dishonest scientific research can misdirect other investigators, lead to misguided public policy and harm patients when clinical decisions are based on faulty information.

Such problems have led to many effective constraints on cheating—but existing controls in human society may be in need of refinement. In an effort to better understand cheating, scientists have discovered that creativity, fear of loss and the observation of dishonest behavior can motivate cheating or make it more likely. These triggers, along with an increasing appreciation that cheating can be contagious, may help explain the recent “epidemic” of deceit in academia and point to strategies to reduce the spread of dishonest behavior. The scientific enterprise is

BRYN LENNON Getty Images (left); GETTY IMAGES (center); STEVE DUNWELL Getty Images (right)

#### FAST FACTS

### Decoding Dishonesty

- 1** >> Cheating is astoundingly common. One survey revealed that about three fourths of 1,800 students at nine universities admitted to cheating on tests or assignments.
- 2** >> Fraudulent work squanders resources. It may also harm patients and misdirect scientists or public policy makers.
- 3** >> Researchers are trying to better understand cheating in hopes of minimizing its impact on society. So far they have discovered that creativity, fear of loss and observing dishonest behavior can motivate cheating or make it more likely to happen.



far from immune to cheating, but it can help us understand why people cheat and what can be done about it.

### Origins of Deception

In nature, cheating has evolved as a way for organisms to gain advantage over others without incurring the cost of effort. For an individual, the calculus is simple: Can I get something for nothing without being caught and punished? At every level, some critters take the risk. Microbiologist E. Peter Greenberg of the University of Washington has found that some *Pseudomonas* bacteria exploit public goods generated by other cooperating bacteria without sharing in production. Similarly, systems biologist Alexander van Oudenaarden of the Massachusetts Institute of Technology has found that some *Saccharomyces* yeast

by the parrotfish's skin. When a cleaner fish snags mucus rather than parasites, it cheats the parrotfish of its benefit in the arrangement. Biologist Redouan Bshary of the University of Neuchâtel in Switzerland and his colleagues have observed that parrotfish frequently respond to such behavior by fleeing, so that both the cheater and its straitlaced companion lose out on the food. In retribution, the wronged cleaner fish will sometimes chase its partner. The dilemma appears to discourage cheating by cleaner fish, given that cleaners are more likely to cheat when feeding alone.

Yet simply balancing costs and benefits, as these fish do, cannot account for the psychology of the phenomenon in humans. For a closer approximation, we must look to other primates, which have large and deeply convoluted neo-

**SUSPICIOUS SHENANIGANS:** Lance Armstrong (left) admitted to doping to win seven Tour de France titles. Law-enforcement officials speak at a press conference at The Hague after police busted a network suspected of fixing soccer matches (middle). At Harvard University (right), 125 students were investigated for cheating on a final exam.

intelligence is the ability to deceive [see "The Social Genius of Animals," by Katherine Harmon; *SCIENTIFIC AMERICAN MIND*, November/December 2012]. Tactical deception is widespread among primates. Ethologist Hans Kummer of the University of Zurich vividly described cheating behavior in hamadryas baboons in Ethiopia: female juveniles mate with juvenile males while concealing their actions from the alpha male by hiding behind rocks. Primatolo-

**The bigger a species' neocortex, the more members of that society use dishonest tactics to manipulate others.**

cells cheat by using the products of a sugar-metabolizing enzyme made through the labor of other cells.

Moving up the food chain, the diminutive cleaner fish also are known to abuse relationships for personal gain. The cleaner fish species *Labroides*, for example, feast on the parasites that attach themselves to the parrotfish *Chlorurus*, often servicing the larger fish as cooperating male-female pairs. Cleaner fish, however, prefer to eat the mucus secreted

cortices (the outer layers of the brain responsible for conscious thought and language). In contrast, this structure is small and smooth in small mammals and absent in other animals. Primatologists, psychologists and neuroscientists have long suspected that the challenges posed by social primate groups have led to the impressive evolution of the primate neocortex that is responsible for the great leap forward in intelligence.

One major manifestation of social

gist Frans de Waal of Emory University has documented examples of deception by chimpanzees living in captivity. In 2004 psychologists Richard W. Byrne of the University of St. Andrews in Scotland and Nadia Corp, now at Keele University in England, showed that neocortex size predicts the degree to which primates practice deception. The bigger the neocortex in a species, the more individuals in that society use dishonest tactics for social manipulation.



### Everyone Cheats—A Little

Humans are surprisingly quick to cheat when the circumstances are conducive. In 2008 behavioral economist Dan Ariely of Duke University and his colleagues described what happened when they asked college students to solve math puzzles for cash rewards. When the researchers changed the experimental conditions such that the students assumed the examiner could not detect cheating, the average self-reported test score rose significantly. The researchers determined that the scores were not inflated by a few students who cheated a lot but rather by many students cheating a little.

It may seem self-evident that people, as with other animals, are motivated to cheat by the potential benefits. If cheat-

increased the cash reward, the amount of cheating actually declined. Ariely suggests that the students felt guilty when they cheated more or received larger amounts of cash through dishonest behavior. That is, a person's conscience places a lid on the amount of cheating he or she will engage in. Another possibility is that the students thought they would be less likely to attract attention if they cheated only a little.

Not everyone is equally likely to cheat, however. In 2011 Ariely and behavioral economist Francesca Gino of Harvard Business School reported that people who score higher on psychological tests of creativity are more apt to engage in dishonesty—a connection that is perhaps not surprising considering that creativity and tactical deception are

**NATURAL-BORN CHEATERS:** Some yeast cells (left) unfairly nab the chemicals produced from the labor of other cells. Cleaner fish (small fish, center) may steal the mucus of parrotfish (not shown) for supper instead of helpfully consuming their parasites. Among baboons (right), young females cheat the alpha males out of the action by mating with younger guys while hiding behind rocks.

ber 2012]. As Proust observed in *Remembrance of Things Past*, “It is not only by dint of lying to others, but also of lying to ourselves, that we cease to notice that we are lying.” Or as George told Jerry on *Seinfeld* 75 years later, “It’s not a lie if you believe it.” Ironically, the creativity and intelligence that we regard as distinctly human might have arisen alongside our ability to deceive. We are who we are because we cheat.

**When the researchers raised the cash reward for right answers, the amount of cheating actually declined.**

ers used a simple cost-benefit calculation, one might predict that people would cheat as much as possible, not just a little bit. Yet in Ariely's study, students on average reported six correct answers when they got only four right, even though they could have raised their scores to a maximum of 20. In addition, no simple relation exists between the magnitude of the reward and the likelihood of cheating. When Ariely's team

both products of the neocortex. Yet Gino and Ariely believe the two are not just anatomically correlated but causally connected. They submit that creative individuals are better at self-deception: they come up with more inventive rationalizations for cheating as a way of making themselves feel better about doing it [see “Unveiling the Real Evil Genius,” by Ingrid Wickelgren; *SCIENTIFIC AMERICAN MIND*, November/Decem-

Gender, too, plays a role in determining who bamboozles his or her peers. Along with plant pathologist Joan W. Bennett of Rutgers University, we have recently observed that among researchers in the life sciences, males are more likely to cheat. Misconduct is seen among those at all levels of the academic hierarchy, from student to professor, but men are overrepresented among the culprits. Just as they commit more crimes in

THOMAS DEERINCK Science Source (left); DAVE FLEETHAM Corbis (center); RAUL ARBOLEDA Getty Images (right)

society at large, males appear more likely to become charlatans in academia. Although we do not yet know precisely why men are more likely to veer off the moral path, scientists have gained insight into what motivates cheating generally.

In addition to potential gain, fear of loss may drive dishonesty. In fact, marketing researcher Scott Rick, now at the University of Michigan, and behavioral economist George F. Loewenstein, now at Carnegie Mellon University, have not-

2,000 retracted scientific papers, mostly in the life sciences. Last year we reported that the majority of retractions arose from research misconduct, most commonly fraud. Even after correcting for the rapidly rising number of scientific publications, we found that the rate of retractions for fraud has increased nearly 10-fold over the past two decades. This trend parallels the increasing pressure and competition for research grants and academic jobs. The well-known

was “very, very concerned” about his ability to support the researchers in his laboratory. “I was on a treadmill, and I couldn’t get off,” he told the federal judge at his sentencing hearing in June 2006. In a study published last year psychiatrist Donald Kornfeld, an emeritus professor at the Columbia University College of Physicians and Surgeons, concluded that a major impetus for misconduct by research trainees is a fear that they will fail to advance in their career. The potential for loss creates what Rick and Loewenstein call a “hypermotivation” to cheat, which may lead people to overcome their usual ethical constraints.



**DO YOUR OWN WORK:** Cheating on tests is surprisingly common. Targeting self-image is the best deterrent. People will not copy their neighbor’s paper if it makes them feel bad about themselves. A verbal reminder of the honor code just before an exam begins might prevent a lot of peeking.

ed that dread is an even more powerful motivator than the desire for reward. In a commentary on the 2008 paper by Ariely and his colleagues, Rick and Loewenstein observed that many instances of dishonesty in the real world result when people find themselves in a situation in which they face losing money, reputation or their career.

We believe that anxiety over loss is a principal driver of cheating in science. Along with neuroscientist and medical writer R. Grant Steen of Medical Communications Consultants in Chapel Hill, N.C., we surveyed more than

publish-or-perish environment of academia dictates that faculty with insufficient publications or funding may lose their research space, status and jobs. As a result, much of the cheating in academia probably stems from concern over the potential demise of a career rather than the prestige of publication.

Physiologist Eric Poehlman of the University of Vermont, one of the rare scientists who actually spent time in jail for research misconduct, stated that he

### Deception Gone Wild

Cheating can breed more of the same if nothing puts a brake on the process. Once someone has overcome the initial barrier to cheating, subsequent hurdles to dishonest behavior may seem smaller and trivial to surmount. Ariely calls this response the “what the hell” effect, as in “what the hell, I already blew my diet, so I may as well have the dessert.” In our study of retracted papers, we observed serial misconduct by scientists for whom fraud had become a habit. The most extreme example so far is anesthesiologist Yoshitaka Fujii, formerly at Toho University in Tokyo, who is said to have fabricated data in as many as 183 scientific articles.

Another way that cheating can spread is through copycat behavior. Seeing someone else cheat without apparent consequences strongly encourages others to do the same. One need only watch pedestrians waiting at a crosswalk or passengers jumping a queue at a bus stop to observe examples of this phenome-

### (The Authors)

**FERRIC C. FANG** is professor of laboratory medicine, microbiology, medicine and pathobiology at the University of Washington. He studies bacterial pathogenesis and is editor in chief of the journal *Infection and Immunity*. **ARTURO CASADEVALL** is Leo and Julia Forchheimer Chair in Microbiology and Immunology at the Albert Einstein College of Medicine. He studies fungal pathogenesis and mechanisms of antibody action and is editor in chief of the online journal *mBio*.

## In fact, unchecked dishonesty can promote the perception that one must cheat to remain competitive.

non. In 2011 psychologists Agata Blachnio and Malgorzata Weremko of Catholic University of Lublin in Poland described an experiment in which students took a spelling test in a room secretly fitted with a one-way mirror. A dictionary and a thesaurus were in the room, but the students were asked not to use them. Subjects were three times as likely to cheat when an assistant posing as a cheating student was also present. In fact, unchecked dishonesty can promote the perception that one must cheat to remain competitive.

Such observations have led Ariely to refer to cheating as “infectious.” As physicians who specialize in infectious

in females. A more plausible explanation is contagion. The widespread bending of the rules probably led students to conclude that collaborating with other students was okay. (The class was called “Introduction to Congress,” so perhaps the students were simply identifying too much with the material.)

Just as an untreated minor infection may progress to a more serious condition, minor acts of dishonesty that pass without consequences may be followed by more egregious misconduct. Luk Van Parijs was once a promising young postdoctoral trainee in the lab of Nobel laureate David Baltimore at the California Institute of Technology. According to an

drew Wakefield, a gastroenterology researcher at Royal Free Hospital in London, that suggested a link among autism, bowel disease and vaccination. That study, later referred to by editors of the *BMJ* as “an elaborate fraud,” helped to fuel the modern antivaccine movement that even today erodes public confidence in vaccines and leads to cases of infection that could have been prevented.

### Inoculated for Honesty

Psychologist Leda Cosmides and anthropologist John Tooby of the University of California, Santa Barbara, suggest that humans have both the ability to deceive and a specific talent for detecting cheaters. For more than two decades they have argued that people look for social rule violations to identify cheaters specifically in settings in which cheating is most likely to occur, as when a 17-year-old enters a liquor store or attends a party at which alcohol is served. Part of that talent for policing dishonesty is our ability to conduct research that can be used to devise more effective strategies to reduce it. Although there is a natural tendency to resort to stricter penalties to discourage cheating, little evidence supports the notion that harsher penalties are more effective than moderate ones. Instead education to instill and reinforce personal barriers to dishonesty is a more attractive approach.

According to Ariely, self-image is an important constraint on dishonesty. People do not cheat when it makes them feel bad about themselves. When they do cheat, they may construct elaborate rationalizations to make themselves feel better. Thus, reminders about an honor code or having people sign a statement attesting that they will not cheat has a measurable impact on reducing cheating. Ariely suggests that moving the signature line from the bottom to the top of the tax

#### JAYWALKING

**JOCKEYS:** Crossing against the light can become contagious.

If one person ventures into traffic, you might do the same. Otherwise, he'll be on time and you, the rule follower, will be late. Too bad for the cars that have to stop for you. Or for you, if they don't.



diseases, we find his metaphor intriguing. This kind of social contagion may help explain the high prevalence of cheating in relatively small groups of people. For example, 125 Harvard students were recently under investigation for cheating on the final examination in an introductory government course. (More than half these students were told to withdraw from school for up to a year as punishment.) It is statistically unlikely that nearly half the 279 students in that class are sociopaths given the low prevalence of sociopathy—about 3 percent in males and 1 percent

interview with Baltimore published in 2010, Van Parijs had been cutting some corners at Caltech, but Baltimore was unaware of the behavior at the time. After Van Parijs started his own lab at M.I.T., the dishonest behavior escalated. In 2009 the Office of Research Integrity found that he had falsified data in numerous grants, publications and research presentations. Five publications were retracted, and Van Parijs lost his job.

Even single acts of dishonesty can have serious and lasting consequences for society. One famous example is a retracted 1998 article in the *Lancet* by An-



**NOT SO FAST:** Radar speed signs encourage drivers to heed the speed limit because they shame violators by advertising how fast they are going to anyone in the vicinity. Reminders to obey the rules are effective tactics for curtailing cheating.

form might prompt taxpayers to be honest. Signs displaying radar speed are effective in modifying behavior because they shame drivers into observing the speed limit by advertising any violation.

To reduce the hypermotivation to cheat arising from the fear of loss, we need reward systems that improve an individual's sense of security in settings where cheating is problematic. In academia, reducing the dependence of faculty members on funds from research grants may decrease the temptation to enhance or make up results. Recognizing successful teams rather than individuals may also lessen the incentives for misconduct.

Ethics instruction, where it exists in graduate schools and workplaces, should emphasize the costs of cheating and its damaging effects. In 2006 the Commission on Public Relations Education recommended that colleges and universities provide dedicated ethics courses, but most are not yet doing so. Such instruction might reduce the prevalence of cheating in college and clear up confusion among many students about what constitutes plagiarism.

Surveillance and enforcement of penalties for cheaters are critical tools for limiting the spread of the behavior. Just as diagnostic tests reveal infections, sophisticated technology can detect doping by athletes, and careful scrutiny of data, along with statistical tools, may reveal cheating by scientists. In addition, whistle-blowers can act like sentinel ani-

mals in disease epidemics to spot the earliest signs of cheating. Armstrong, Hauser, Poehlman and Van Parijs were each turned in by people from their inner circles. Supreme Court Justice Louis Brandeis once remarked, "Sunlight is said to be the best of disinfectants; electric light the most efficient policeman." Accordingly, the problem of misconduct must be openly acknowledged and discussed.

In epidemiology, an individual can be protected from disease by "herd immunity," whereby most members of a community are resistant to an infectious agent. Thus, parents who vaccinate their children are also protecting unvaccinated children. Similarly, people in settings in which cheating is problematic might be inoculated against cheating by reminders of ethical codes and of instances

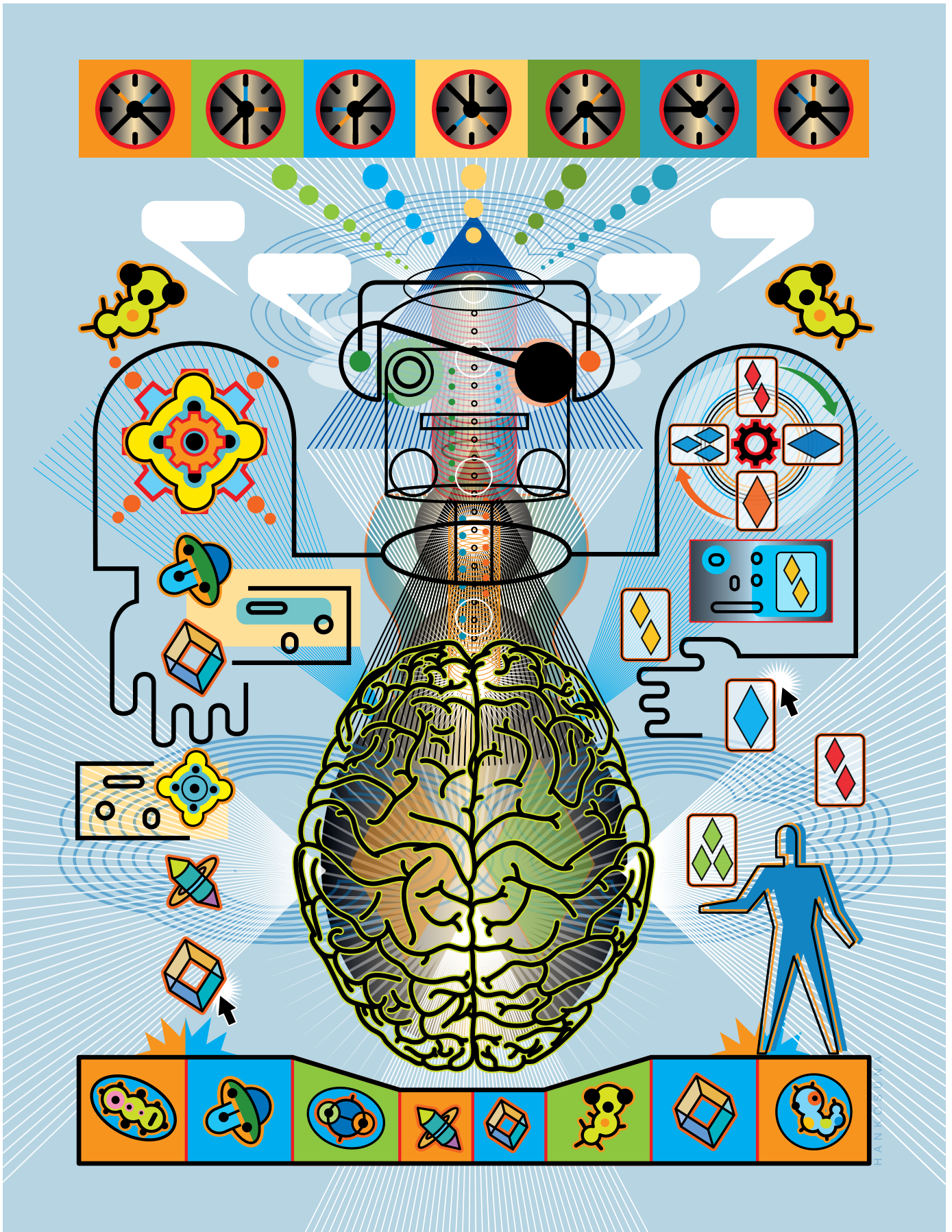
in which cheaters have been caught and punished.

Because minor misconduct may lead to more egregious behavior, even small acts of dishonesty must be taken seriously. This is the basis of the late James Q. Wilson's famous 1982 "broken windows" theory of crime. Attending to lesser infractions such as vandalism may deter petty offenders from developing into hardened criminals, just as treatment of local skin infections may prevent them from progressing to life-threatening septicemia. Perhaps if Van Parijs's penchant for cutting corners had been recognized and addressed while he was a postdoctoral trainee, he might still be in academia today.

Ultimately, combating cheating most likely will require a multifaceted approach to promote a more ethical culture. These elements might include modifying reward systems to recognize teamwork and cooperation, penalizing wrongdoers in a consistent manner, setting up robust protections for whistle-blowers and improving methods to detect cheating. Although cheating may have short-term benefits for the person, such as financial rewards and prestige, it can be costly for both individuals and society. Armstrong was stripped of his titles and banned from sports for life. Hauser was dismissed from his Harvard professorship. As they and so many others have learned to their sorrow, deception has its costs. **M**

### (Further Reading)

- ◆ **Machiavellian Intelligence: Social Expertise and the Evolution of Intellect in Monkeys, Apes, and Humans.** Richard W. Byrne and Andrew Whiten. Oxford University Press, 1989.
- ◆ **How Many Scientists Fabricate and Falsify Research? A Systematic Review and Meta-Analysis of Survey Data.** Daniele Fanelli in *PLOS ONE*, Vol. 4, No. 5, Article e5738, 11 pages; May 2009.
- ◆ **The (Honest) Truth about Dishonesty: How We Lie to Everyone—Especially Ourselves.** Dan Ariely. HarperCollins, 2012.
- ◆ **Winner Takes All.** Arturo Casadevall and Ferric C. Fang in *Scientific American*, Vol. 307, No. 2, page 13; August 2012.
- ◆ **Misconduct Accounts for the Majority of Retracted Scientific Publications.** Ferric C. Fang, R. Grant Steen and Arturo Casadevall in *Proceedings of the National Academy of Sciences USA*, Vol. 109, No. 42, pages 17,028–17,033; October 16, 2012.
- ◆ **Males Are Overrepresented among Life Science Researchers Committing Scientific Misconduct.** Ferric C. Fang, Joan W. Bennett and Arturo Casadevall in *mBio*, Vol. 4, No. 1, page e00640-12; January 22, 2013.





# CALISTHENICS for a Child's Mind

Scientists have concocted mental fitness regimens to strengthen weak thinking skills in students—in effect, making kids smarter **By Ingrid Wickelgren**



A mop of light brown hair shakes as a slender nine-year-old boy named Jack bangs furiously at his keyboard. Jack's eyes are fixed on a clock with six hands, which denote the month, day, hour, minute, second and 60th of a second. As soon as he types 10:28:2:14:56:32, a new clock appears, and he hammers out another set of numbers. An affable 14-year-old student named Marti had just taught me the exercise, and I guessed I could have solved one of these clocks in a few minutes. Jack was finishing one every seven seconds.

Jack's incessant clacking is virtually the only sound in this small classroom of eight- and nine-year-olds. The others work silently. One or two wear an eye patch, copying symbols onto grids. A dark-haired girl listens through headphones to a list of words she must memorize and repeat to a teacher. One boy stares at a Norman Rockwell painting; his job is to extract its main idea and write it down.

Jack, his long red sleeves poking out from under a blue school T-shirt with the initials "EAS," cracks clock codes for 35 minutes almost non-stop. As with others at Eaton Arrowsmith School, a private facility for the learning disabled on the second floor of a building on the campus of the University of British Columbia in Vancouver, Jack attends six periods of brain exercises, among them reading clocks, copying symbols, tracing complex designs, memorizing patterns and performing mental arithmetic. Jack has one period of English and one period of mathematics, but none of his other classes resemble those in an ordinary school.

Arrowsmith students do not learn about the branches of government

ILLUSTRATION BY HANK OSUNA



In a classroom at Eaton Arrowsmith School in Vancouver, B.C., students work independently on computerized and paper-based exercises designed to bolster basic mental processes such as memory and reasoning.

or genres of literature. Their time is devoted instead to fortifying mental processes such as attention, memory and reasoning. For decades psychologists have thought that such fundamental thinking capacities were fixed. In research circles, evidence is mounting that they may not be.

The Arrowsmith program is intensive, requiring students to dedicate 80 percent of their day for three to four years to brain remediation before returning to regular school. Although the school boasts a number of success stories, support for its regimen's effectiveness is mainly anecdotal. Nevertheless, a commitment to its style of brain fitness for children is gathering steam in the scientific, clinical and even mainstream educational communities.

A small collection of brain-training workouts has emerged from neuroscience and psychology laboratories in recent years, and several are now being marketed and sold. Some build working (short-term) memory, a kind of mental whiteboard that is linked to intelligence. Others target basic number

sense, for math, or sound perception, for reading. Another trains reasoning.

In many cases, the tools are aimed at learning problems such as dyslexia, dyscalculia or attention-deficit hyperactivity disorder (ADHD). But some educators are starting to offer brain training to the general school population. "I see the technology as making it possible to individualize training and learning for everybody," says psychologist Allyson P. Mackey of the Massachusetts Institute of Technology. "Even kids performing fairly well might have a weakness, and if you patch that up, they would perform much better."

The extent to which children can overcome intellectual deficits or raise their IQ through mental calisthenics is largely unknown. Although data suggest that the training can be useful, it does not always work. In addition, researchers are only now beginning to explore whether the measured gains in their thinking skills translate into academic achievement.

Still, many scientists and educators now believe that with the proper tools, students can increase their intellectual capacity—an idea that could transform lives. "The question is: What are we capable of as human beings?" asks Howard Eaton, a learning disabilities specialist who founded Eaton Arrowsmith. The notion that people can fundamentally alter their brains, he says, "changes your whole perspective on human possibility."

### Levers for Learning

Of course, school has long been based on the premise that the brain is flexible: learning new information and skills involves changes at the neural level. Still, people have assumed that a person's *capacity* to learn is fairly stable. Part of this capacity lies in executive functions, a set of faculties gov-

#### FAST FACTS

### Beefing Up Young Brains

- 1» Psychologists have long believed that thinking capacities such as attention, memory and reasoning were fixed, but evidence is mounting that they are not.
- 2» A smattering of brain-training workouts has emerged from neuroscience and psychology laboratories, and several of the programs are now being marketed and sold.
- 3» In many cases, the brain workouts are aimed at kids with learning problems, but some educators are offering them to all children as part of regular instruction.

COURTESY OF SANDRA HEUSEL/Eaton Educational Group

**“I see the technology as making it possible to individualize training and learning for everybody,”** says one psychologist.

erned by a structure called the prefrontal cortex that sits just behind the forehead. These faculties are working memory, cognitive flexibility—the ability to find alternative solutions to problems and shift from one idea or action to another—and self-regulation, the ability to inhibit competing or inappropriate actions.

School is not traditionally designed to alter executive function, nor is it typically structured to tweak basic math ability or facility for listening to language. It does not do these things in part because people assumed those basics of the brain were immovable.

Yet it is no secret that environment can have a powerful effect on intellectual capacity. Stressful circumstances such as those that accompany poverty, for example, can virtually shut down executive functions [see “Treating a Toxin to Learning,” by Clancy Blair; *SCIENTIFIC AMERICAN MIND*, Sep-

and emotional maturity [see “The Education of Character,” by Ingrid Wickelgren; *SCIENTIFIC AMERICAN MIND*, September/October 2012]. Meanwhile other scientists have set out to design interventions aimed more squarely at an individual child’s intellectual capacity.

One critical lever on intellect is working memory. Various cognitive skills depend on this mental scratchpad. Attention, in particular, entails mentally taking note of important information. “If you can’t hold a plan in mind, you’ll get distracted,” says cognitive neuroscientist Torkel Klingberg of the Karolinska Institute in Stockholm.

In 1997 Klingberg was studying the neural basis of working memory when he came across a paper showing that kids with ADHD very often had limited working memory capacity. Although working memory was widely believed to be a static trait, Klingberg was radically optimistic about its pliability.



tember/October 2012]. A child’s socioeconomic class can also strongly influence language skills that are fundamental to reading. “For a four- or five-year-old, the difference in language exposure between a child from a low socioeconomic class and one from a high socioeconomic class can be as much as 30 million words,” says neuroscientist William M. Jenkins, chief scientific officer at Scientific Learning Corporation in Oakland, Calif.

In that light, the notion that tailored coaching could *boost* a child’s potential to learn is less difficult to fathom. In recent years researchers have devised curricula designed to promote self-regulation, a skill essential to both academic success and social

ity. “I thought of it as a muscle that could be trained,” he recalls.

With attention deficits in mind, Klingberg and his colleagues created workouts for recalling locations—such as directions to a shopping mall—as well as verbal information. In some exercises, users try to reproduce the order in which an array of red bulbs or asteroids light up. As with all good training programs, these adapt to the child: as her performance improves, the game gets harder. At higher levels, the asteroids move, or the grid of lights rotates before the player has to recall the order. A verbal task requires remembering a series of digits and repeating it in reverse.

In Cogmed working memory training, players try to click on asteroids (*left*) in a sequence that matches the one they just saw. They also punch numbers on a keypad (*right*) in the order opposite to the one they just heard.

COURTESY OF NCS PEARSON

In a study published in 2005 by Klingberg's team, 22 kids aged seven to 12 who had severe attention problems played these games for 35 to 40 minutes a day for 25 days. The children improved significantly more on a standard assessment of working memory than did 22 kids with ADHD who used much easier versions of the same games. In addition, parents of the trained youths said their

training for five to seven weeks; the others received a less taxing version of the program. By the end of the instruction, the children who did the more intensive exercises showed a big boost in all aspects of working memory, whereas the other kids reaped only minimal gains. Moreover, six months later the kids who got the real training scored significantly higher on a standardized test of mathematical rea-

**Among kids who score in the lowest 10 percent on working memory tests, more than four fifths have academic troubles.**

children became more attentive. Based on such results, Klingberg founded a company called Cogmed, now owned by Pearson, the education firm, to market the software.

Scientists have since garnered additional support for these games as remedies for ADHD. In 2010 psychologist William B. Benninger of Ohio State University and his colleagues found that children and adolescents with ADHD who did the drills at home became more attentive, better organized and had fewer symptoms, according to their parents, than those who did not exercise their recall. In 2012 psychologist Julie B. Schweitzer of the University of California, Davis, School of Medicine and her associates reported that the training significantly reduced "off-task" behavior in 12 children with ADHD while doing schoolwork—that is, looking away from a worksheet, a more real-world measure of focus.

Working memory can have a profound effect on learning in general. Among children who score in the lowest 10 percent of the population on working memory tests, more than four fifths have considerable problems in reading or math, or both. From a test of 345 children between the ages of eight and 11, psychologist Darren L. Dunning of the University of York in England and his colleagues identified 42 children who fell in the lowest 15 percent in working memory ability. They assigned 22 of them to intensive, in-school Cogmed

soning than they had at the beginning of the trial, indicating that they used their trained brains to learn more math.

### Getting Out of a Jam

Another critical component of academic success is reasoning, the capacity to think logically, connect ideas and solve problems in novel situations. Reasoning is a higher-level skill that depends on executive functions such as working memory and attention. The clock puzzles Jack solves so expertly are supposed to train reasoning by building a child's understanding of relations such as those between the different hands on a clock.

Several years ago M.I.T.'s Mackey, then a psychology graduate student at U.C. Berkeley, wanted to see if she could sharpen reasoning in disadvantaged children. Collaborating with her colleague, psychologist Silvia A. Bunge, Mackey selected computer and commercial board games that rely heavily on reasoning. In one board game, called Rush Hour, players need to figure out how to get a car to escape a traffic jam while still obeying the laws of the road. Other games depended on logic or on integrating different pieces of information. They asked 17 students, aged seven to 10, from an elementary school in a high-poverty neighborhood in Oakland, Calif., to play the games for an hour a day, two days a week, for eight weeks. Another 11 students played games that taxed processing speed—how quickly they could make sense of information—instead.

The kids who played the reasoning games saw their scores jump by more than 30 percent on a standard test of that skill—and their IQ scores rose 10 points on average. The students who played games that exercised processing speed upped their ranking on a test of that ability by 30 percent. "We were really surprised at how big the gains were," Mackey says.

She is now trying to reproduce her results in a larger sample of kids at risk for school failure and



Playing games such as Rush Hour (above) that require reasoning upped the IQ scores of kids from a low-income community.

### (The Author)

INGRID WICKELGREN is an editor at *Scientific American Mind* and author of the blog *Streams of Consciousness* at [ScientificAmerican.com](http://ScientificAmerican.com).

COURTESY OF THINKFUN, INC. [www.thinkfun.com](http://www.thinkfun.com)

determine whether the training translates into gains in academic achievement. “If we can show these kinds of games lead to better test scores, we’ve taken a huge forward,” Mackey says.

### Five Dots or Six?

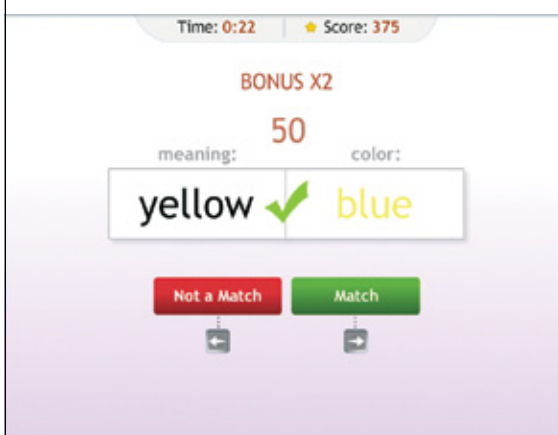
Computerized training programs can bolster basic math ability, too. Doing mental math depends heavily on working memory, which we use to hold and manipulate numbers. One Arrowsmith exercise involves adding one small number to the next as the digits appear sequentially, keeping a running total, and reporting the sum at the end.

Other programs train number sense, a basic sense of quantity that enables us to immediately compare, say, the number of dots in two different arrays or subtract or add dots. Scientists have tied this sense to a location in the brain: a narrow indentation on its surface called the intraparietal sulcus. Without a well-developed sense of number, children will have trouble with math and may develop dyscalculia, a mathematical learning disability that afflicts about 7 percent of the population. A nine-year-old with dyscalculia might, for example, confuse five dots with six or be unable to say whether 50 is greater or less than 100.

Several years ago neuroscientist Stanislas Dehaene of the French National Institute of Health and Medical Research and his colleagues created a Web-based game called Number Race, in which players compare quantities of dots and associate them with number symbols and learn some basic addition and subtraction facts. In 2006 the researchers reported that 15 seven- to nine-year-olds with dyscalculia who played Number Race got somewhat better at comparing numbers, making quick visual assessments of quantity and subtracting one-digit numbers.

Three years later the researchers tested the software on younger children at risk for math difficulties: 53 French kindergartners from low socioeconomic backgrounds. Some of the children played Number Race for six 20-minute sessions while others used a commercially available reading program, after which the kids switched tasks. Number Race, but not the reading software, improved the kids’ ability to compare numbers represented as symbols, suggesting that the program honed the ability to connect number symbols to quantity. The team has since developed a more advanced game, called Number Catcher, that exercises basic calculation skills and represents numbers in different ways.

Lumosity, a company based in San Francisco, offers a suite of brain-training games aimed at various



capacities, including several related to math. One involves arithmetic problems that appear in falling raindrops that must be solved before the drops splash into water at the bottom of the screen. In another, users compare the value of mathematical expressions presented in pairs. A third exercises problem solving. Players deduce the rule—“blue,” say, or “animals”—behind the sorting of words or objects.

Such drills have shown promise in boosting math proficiency in children with inborn impediments to learning the subject. In a 2011 pilot study psychiatrist Shelli R. Kesler of Stanford University

Lumosity games target core thinking skills. Spot the bird before it vanishes while remembering the letter (*top*) to train your focus. Compare the word on the left with the color on the right (*middle*) to stretch your cognitive flexibility. Type the answers before the drops hit the water (*bottom*) to tune your problem-solving ability.

and her colleagues found that playing these games 20 minutes a day for six weeks ameliorated characteristic math-related deficiencies in 16 girls who had a genetic condition called Turner syndrome. After the training, the girls scored significantly higher on tests of number sense, processing speed and cognitive flexibility. Their knowledge of math facts and calculation ability also improved to a lesser extent.

### Sounding It Out

As with math, reading involves a complex set of intellectual capacities, including reasoning and executive skills. Dyslexia, a reading disability in which the brain has trouble recognizing and processing words, afflicts 5 to 17 percent of children. In the early 1990s neuroscientist Paula Tullal of Rutgers University hypothesized that a root cause in many cases was auditory, specifically, a deficit in detecting rapid changes in similar sounds, such as “da” and “ba.” Such difficulties, she argued, prevented children from acquiring good language skills, leading to dyslexia.

other colleagues, reported significant improvement in language and reading skills in 22 children with dyslexia who used the program 20 minutes a day five days a week for eight weeks. They also saw in these kids increased activation in brain circuitry responsible for processing rapidly changing sounds. In a 2008 investigation neuroscientist Helen J. Neville of the University of Oregon and her colleagues found evidence that Fast ForWord Language improved the ability of children with and without language impairments to pay attention to auditory stimuli. The kids also showed gains in language comprehension.

Not all studies back up Fast ForWord’s efficacy. In a 2011 meta-analysis (quantitative review) of six large studies, psychologist Charles Hulme of the University of York and his colleagues concluded that the program had little effect on children’s language or reading difficulties. The mixed results may reflect differences in how the software was tested, including the degree to which adults monitored its use and motivated children to engage with it. After

A program called Fast ForWord Language asks users to distinguish sounds such as “ada” and “aba” by choosing the acorn that uttered the target phoneme (left) and to parse sentences such as “The girl is chasing the dog” by clicking on the picture the sentence describes (right).



In 1996 Tullal and neuroscientist Michael Merzenich, now an emeritus professor at U.C.S.F., founded Scientific Learning to develop computer software to correct auditory-processing problems in children with reading difficulties. The program, called Fast ForWord Language, helps children hear and discriminate phonemes by first slowing them down and emphasizing certain rapidly changing parts of speech, Jenkins says. Then it gradually speeds up and softens the emphasis. The software also morphs the sounds, making them more or less similar, depending on a child’s proficiency.

Several small studies indicate that the program is helpful. In 2007 neuroscientist Nadine Gaab of Harvard Medical School, along with Tullal, among

all, kids who quit using the program out of frustration or boredom are unlikely to benefit. In addition, not all children with dyslexia suffer from auditory problems. Indeed, the latest versions of Fast ForWord drill executive functions, among other skills critical to reading proficiency. These exercises may reach a wider swath of the student population than the original program did.

### Playing for IQ Points

Most of the current student brain-training programs are aimed primarily at those with diagnosable deficits. The several hundred U.S. schools that have adopted the Cogmed software, for example, typically offer it to students with attention deficits

COURTESY OF SCIENTIFIC LEARNING CORPORATION

and other learning disabilities. More than 500 clinics in the U.S. and Canada also use Cogmed, primarily with clients who have ADHD.

Yet the programs are also trickling into the educational mainstream. Although Fast ForWord is geared toward kids with reading problems, many of the more than 3,000 schools that have the software include it as part of regular instruction. So far 12,000 students in more than 325 schools world-

so late trying to reread and understand," she told me last year. "I ended up crying because I was overwhelmed with homework." Marti has since graduated from the program, and her ninth grade December report card displayed straight A's. School officials have data on numerous children who, like Marti, have been helped by the curriculum.

Outside scientists often find the Arrowsmith approach intriguing but say it lacks rigorous scientific

**Eventually, the educational community may support adding at least a dollop of brain fitness to children's usual scholastic fare.**

wide have played a suite of brain games offered through the Lumosity Education Access Program (LEAP), and more than a quarter of Lumosity.com online users are younger than 21. At least one private parochial school in New York City has made Cogmed software available to the kids in its fifth and sixth grades. "This isn't limited to students with learning difficulties," says Nicole F. Ng, a former teacher who now manages LEAP. "It applies to a healthy student who wants to improve his cognitive capabilities."

Some data hint that brain training could benefit the typical learner. In an unpublished study conducted by Ng and her colleagues, 949 students aged six to 18 years in 43 schools played 28 Lumosity games for an average of six hours total during a semester. These youths raised their scores on a battery of neuropsychological tests significantly more than did 443 students who did not perform the exercises. The more hours a student trained, the more he or she improved on skills such as memory, processing speed and reasoning. Students who spent at least 10 hours of training saw measurable benefits, Ng says. She is now leading a study of 100 schools to determine whether the cognitive benefits translate into better grades and test scores.

In other studies, psychologist John Jonides of the University of Michigan and his colleagues have raised the IQ scores of typical elementary and middle school children with their own working memory regimen, but that method does not always produce the intended improvement [see "Building Better Brains," by John Jonides, Susanne M. Jaeggi, Martin Buschkuhl and Priti Shah; *SCIENTIFIC AMERICAN MIND*, September/October 2012]. It may be, therefore, that the training is sensitive to the circumstances.

Before arriving at Eaton Arrowsmith, Marti had struggled in regular school. "I'd be staying up

support. "I saw one kid doing math on a computer faster than I could do it," says Adele Diamond, a developmental cognitive neuroscientist at the University of British Columbia. But, she warns, "I'd like to see data that it helps." Indeed, one small, eight-month investigation of the school's curriculum led by educational psychologist Linda Siegel of the University of British Columbia failed to show that it significantly improved students' scores on a battery of cognitive and achievement tests.

Yet science does increasingly suggest that the brain is far more supple than we once assumed. Eventually the educational community may decide that the data support the adding of at least a dollop of brain fitness to children's usual scholastic fare. Although no one knows exactly the form such training will take, putting children's mental muscles through the paces on a regular basis could lead to lasting benefits. "I envision improvement of cognitive skills as part of education much more than it is right now," Mackey says. **M**

### (Further Reading)

- ◆ **A Pilot Study of an Online Cognitive Rehabilitation Program for Executive Function Skills in Children with Cancer-Related Brain Injury.** Shelli R. Kesler, Norman J. Lacayo and Booil Jo in *Brain Injury*, Vol. 25, No. 1, pages 101-112; January 2011.
- ◆ **Differential Effects of Reasoning and Speed Training in Children.** Allyson P. Mackey et al. in *Developmental Science*, Vol. 14, No. 3, pages 583-590; May 2011.
- ◆ **How to Build a Better Learner.** Gary Stix in *Scientific American*, Vol. 305, No. 2, pages 50-57; August 2011.
- ◆ **Training the Brain: Practical Applications of Neural Plasticity from the Intersection of Cognitive Neuroscience, Developmental Psychology, and Prevention Science.** Richard L. Bryck and Philip A. Fisher in *American Psychologist*, Vol. 67, No. 2, pages 87-100; February-March 2012.
- ◆ **Will Working Memory Training Generalize to Improve Off-Task Behavior in Children with Attention-Deficit/Hyperactivity Disorder?** Chloe T. Green et al. in *Neurotherapeutics*, Vol. 9, No. 3, pages 639-648; July 2012.





# An Appetite for Aggression

The peculiar psychology of war likely holds answers for avoiding future atrocities

By Roland Weierstall, Maggie Schauer and Thomas Elbert

**“I really tortured others.** At night we went out and raided villages. We killed whomever we saw. If we happened to see a woman, we raped her.... Fighting is all there is in the life of a man. Whenever I hear guns go off, I want nothing more than to fight. This thirst lies deep within me.”

The young man who is describing these unbelievable horrors has a gaunt but friendly face. We are in Goma, a bleak city at the eastern edge of the civil war taking place in the Democratic Republic of the Congo. Our team of German researchers from the University of Konstanz and an aid organization, called vivo international, sits shivering in our encampment.

The United Nations houses former child soldiers at this site. They are brought here by truck or helicopter from hundreds of miles away in the bush, and they are nervous. Many of them have been taking drugs daily and are going through withdrawal symptoms. One young man is suffering from pneumonia. We hear the rattling in his chest every time he takes a breath, and he groans from fever and pain. Others have arrived with gunshot wounds that are now infected.

First they are interrogated by U.N. peacekeepers, who are cold and suspicious. “What unit were you in? Who is your commander? How large is your unit? Where is it located? And don’t try to lie to us, bud-

## FAST FACTS

### For the Love of Battle

- 1» Appetitive aggression, in which violent excesses are experienced as sensually pleasurable, may occur in war.
- 2» Humans may have evolved an instinct to hunt that arises in combat situations, leading to this apparently pathological behavior.
- 3» The traumas of war change the psyche of soldiers. A deeper understanding of the psychology of violence can help civilians and fighters process such challenging experiences together.

ILLUSTRATION BY BRIAN STAUFFER

dy!” After the questioning, they finally get some food and, if they are lucky, some painkillers. Then they go talk with the whites—the psychologists from Germany—assuming they are willing. As it turns out, they all want to talk.

We have learned from hard experience in war-torn areas that research into violence must involve the perpetrators, and so we are interviewing hundreds of fighters. First, we listen to the sufferings that these Congolese warriors have had to endure. Some of them were not even born when the First Congo War, in 1996, sent the country spiraling into a humanitarian crisis. The realities of war in this enormous, inaccessible region in the heart of Africa can seem completely foreign to many of us: primitive at times, often brutal and sadistic, and impossible to reconcile with any conventional notion of morality. Our challenge is to gain insight into how people respond in the face of constant brutalization.

Fear is a pure form of stress; we all try as best we can to avoid this emotion. Yet fear is key to survival. When we recognize we are in acute danger, our brain triggers a cascade of physical alarms. Our senses sharpen to soak up information about prospective threats, blood rushes to our muscles and the body releases chemicals that suppress pain. At this point, all animals, including humans, are ready to run for cover or stand and fight. An aggressive move is often enough to make an enemy back down.

Lashing out in self-defense is a familiar response, one that researchers refer to as facilitative or reactive aggression. There is another form of violence, however, an “evil” form, which we have called appetitive aggression. It arises from the thrill of the hunt. Even the act of planning an attack can arouse intense excitement.

What is truly frightening is that ap-



A child soldier rides his bicycle in the Democratic Republic of the Congo.

petitive aggression is a surprisingly common phenomenon. The more that young men perceive that violence gives them feelings of superiority and pleasure that are otherwise lacking in their daily lives, and the more frequently they engage in aggressive acts, the more they will seek the stimulation that hunting and killing affords. Inflicting pain on our fellow humans is part of our fundamental repertoire of behaviors, every bit as much as caring for the sick and injured. The question is: Why?

### Stress and Survival

A few million years ago our hominin ancestors began to hunt and consume

meat. For the first time, the human diet had access to a concentrated source of energy that was lacking in our earlier all-vegetarian diet. According to one popular theory, eating meat allowed our energy-intensive brains to grow bigger and more complex, giving us some of the cognitive edge that has helped our species dominate the planet. The most successful hunters could feed more offspring, attract more sexual partners and attain higher status in a group.

Humans do not only hunt other animals, however. When conflicts arise, we also hunt members of our own species. Culture is what constrains us from wanton violence by delineating who is friend and who is foe. We are socialized into a code of conduct that frowns on antagonizing those who belong to our own group.

Little attention has gone to understanding what happens when that code of

conduct gets violated on a grand scale. Insights into the psychology of war are crucial if we are to help societies rebuild after periods of conflict. One robust finding in trauma research, for example, is that the greater a person’s exposure to life-threatening events, the greater his or her likelihood of developing post-traumatic stress disorder (PTSD). This connection has been observed in soldiers and civilians alike. Yet we wondered if the story were really so simple. In our evolutionary past, the killing of our own kind could easily have evolved as an in-born strategy for securing greater reproductive success. Violence might not always lead to trauma.

Our first opportunity to examine this question was with 269 Rwandan prisoners who were accused or convicted of crimes relating to the genocide in 1994. We asked them about the types of traumas they encountered and crimes they committed. We also assessed the severity of their PTSD symptoms and probed whether they had discovered a taste for

### (The Authors)

**ROLAND WEIERSTALL** and **MAGGIE SCHAUER** are psychologists working with **THOMAS ELBERT**, professor of clinical psychology and neuropsychology, at the University of Konstanz in Germany. Schauer runs the Center of Excellence for Psychotraumatology and is currently president of the international aid organization *vivo international*.

violence. Two such queries were “Once fighting has started, do you get carried away by the violence” and “Once you get used to being cruel, do you want to be crueler and crueler?”

About a third of men answered “yes” to the two questions above; significantly fewer women agreed. Two other questions elicited affirmative responses from more than half the men in our survey—they agreed that they tended to get carried away by the violence of a fight and that defeating an opponent was more fun when they saw blood. For women, 30 and 40 percent said yes, respectively. Although women were less likely to develop an appetite for aggression, they were not immune to it.

We noticed some other trends in the data we collected from Rwanda and, later, from Ugandan child soldiers and South African criminal offenders. The more violent events a fighter had witnessed or committed, the higher his or her rating on our appetitive aggression questionnaire. These higher scores also predicted fewer symptoms of PTSD. Having a taste for violence benefited their mental health.

Further, our results show that observing atrocities and engaging in them predicts the enjoyment of cruelty. As much as these findings conflict with our deeply held sense that violence is morally repulsive, they might help us comprehend how conflicts perpetuate—and how so many people can perish so quickly in an event such as the Rwandan genocide.

In 2011 military historian Sönke Neitzel and social psychologist Harald Welzer published excerpts from the transcripts of World War II Allies who had eavesdropped on captured soldiers from the German Wehrmacht. The recordings revealed a fascination with violence and the hunting down of humans among some of the fighters. The revelations caused an uproar, especially among former participants in the war, who feared being labeled as monsters. Yet these transcripts are consistent with our studies.

Another urgent question that we are beginning to investigate is what happens when combatants return to society. Our

research hints at a “perpetrator mode” that may wear off once a fighter reenters civilian life. Of the soldiers we interviewed, those who had spent more time in society between the end of the genocide and their arrest scored lower on aggression but showed more trauma symptoms than those who were rounded up

## **We should not be amazed by the brutality of soldiers at places such as Abu Ghraib or Guantánamo.**

sooner. Violence may be perceived differently by a person in perpetrator mode than by someone exposed to the tempering effects of culture.

What all these data suggest to us is that the thrill of the kill is neither a sign of mental illness nor is it uncommon. Our ancestors on the hunt were not so different from contemporary combatants: both groups experience great hardships. Sometimes they must track their prey for days. They must suppress their fear of being injured or snuffed out entirely. For us to be willing to endure these conditions, behaving brutally must somehow become rewarding—potentially even pleasurable.

This is not to say that human beings enjoy murder. Only child soldiers, who are recruited by force before reaching pu-

berty, sometimes describe their first kill in glowing terms; virtually everybody else experiences extreme stress. But incessant battle can break down moral inhibitions and alter our perception of our own actions. We should not be amazed by the brutality of soldiers observed at places such as Abu Ghraib or Guantánamo. War changes everyone.

### **Altered Values**

Half a year after our visit to Goma, we again met the young men we had tested before. Too many of those who had scored high for appetitive aggression had returned to the bush—to armed groups that, though impoverished, hungry and often riddled with disease, nonetheless provided them the opportunity to fight, rape and kill.

The men who remained at the camp reported an overwhelming sense of isolation. They told us about the heroic deeds that other fighters understood but that civilians rejected out of hand. As one of them recounted, “I miss being a soldier. I miss the power! Sometimes I killed people just for the fun of it. Others did as well. The sight of blood can really get you going. So much so that it is impossible to stop killing.”

Because most of us struggle to comprehend what happens in war, soldiers often lack adequate social support once they return to civilian life. They may struggle with emotions that conflict with the values of their surrounding culture. They may fail to adjust to new opportunities and ways of life. Only by understanding the experience of combatants in the heat of war can we start to counsel them, integrate them and curb the immense tragedies brought on by violence. **M**

### **(Further Reading)**

- ◆ **The Thrill of Being Violent as an Antidote to Posttraumatic Stress Disorder in Rwandese Genocide Perpetrators.** Roland Weierstall et al. in *European Journal of Psychotraumatology*, Vol. 2, Article 6345; 2011.
- ◆ **When Combat Prevents PTSD Symptoms: Results from a Survey with Former Child Soldiers in Northern Uganda.** Roland Weierstall et al. in *BMC Psychiatry*, Vol. 12, No. 41. Published online May 14, 2012.
- ◆ **Attraction to Cruelty Ameliorates Continuous Stress and Maintains Functioning: A Study on Former Young Offenders in Two Townships in South Africa.** Roland Weierstall et al. in *Peace and Conflict: Journal of Peace Psychology* (in press).

# Solving the Mystery of MS

New medicines for multiple sclerosis have made a big difference in patients' lives, but a breakthrough in therapy may require rethinking the origins of the disease **By James D. Bowen**

ILLUSTRATION BY VIKTOR KOEN

**S**ix years ago, when she was 24, Rachelle Alston woke up one morning and noticed she was having trouble seeing out of her left eye. “Everything was blurry from the bridge of my nose down,” recalls the slim Seattle native. “I thought my contacts must have scratched my eye or I had dry eyes, so I left my contacts out and went to work.”

She mentioned the problem to her co-workers. “I thought it was no big deal and I’d give it a few days, but they were older and pretty much pushed me out the door telling me I had to go see a doctor—now.” She saw an optometrist. He examined her and immediately referred her to a neuro-ophthalmologist, who sent her for an MRI of her brain. The scan revealed bright patches along nerves, a sign of the type of damage that characterizes multiple sclerosis.



Width: 501 Level: 203  
Rid: 02925  
Ser: 001203  
Inst: 009215

S1220

R Signa 1.5T  
.0 mm

0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100

ST/I  
TR: 617  
TE: 10.0 1/1  
256x192/2.0 NEX  
FOV: 24 cm  
Thk: 5.0 mm Mode: Multi:  
Imge: 15/03:59 PSeq: ME



Rachelle Alston was diagnosed with multiple sclerosis six years ago, when she was 24. The latest medications have helped her manage the illness.

“I went home and started looking up MS on the Internet. Boy, that’s one thing you should not do!” Alston recalls. “I couldn’t believe it. Here I was at the beginning of my life, wanting to have a family and a career, and I thought, How can I keep a job, and who would want to marry someone with this disease? Imagine saying to your date: ‘Hi, I

have MS. Want to take care of me?’”

Multiple sclerosis is a disease of the brain and spinal cord that leads to a wide variety of motor, sensory and cognitive problems. It affects an estimated 2.5 million people worldwide, about half of whom will become disabled within 10 to 15 years of their diagnosis. Indeed, MS is the leading cause of non-traumatic disability among young adults: the disorder typically strikes between the ages of 15 and 50 years, with an average age at diagnosis of about 30.

Despite this grim prognosis, a stream of new treatments have brightened the prospects for patients’ quality of life. Based on taming a damaging immune response, these therapies reduce the frequency and severity of symptoms and may slow the progression of the disease. During the past 19 years the U.S. Food and Drug Administration has approved nine new medications, and two more are up for review in the next few months.

Still, the cause of MS remains unknown, and eventually most patients will progress to an advanced phase of the disorder that remains unresponsive to medicine’s best therapies. As research into more effective immune-altering remedies continues, many scientists are turning their attention to understanding what causes the progressive degeneration of neurons that lies at the heart of

MS, with the goal of developing treatments that can completely halt or even prevent the disease.

### Targeted Treatments

Over the years MS has been blamed on diet, infections, toxins and even repressed memories. Based on these theories, patients have been subjected to a host of treatments, many of which are potentially harmful. They were placed in hot boxes, infected with malaria, injected with milk and treated with radiation. In 1936 American neurologist Richard Brickner published a 29-page list assessing 158 different therapies in use at that time to treat MS.

Meanwhile advances in immunology in the early 1900s led to an appreciation of the immune system’s role. In 1933 researchers found that they could produce an MS-like disease called experimental autoimmune encephalomyelitis in rhesus monkeys by injecting them with extracts of rabbit brains, which triggered the monkeys’ immune system to mistakenly react to something in their own brain. Ultimately, researchers discovered that the targets of the immune attack were proteins in myelin, the fatty, protein-packed insulating material that surrounds the long tendrils of neurons called axons. Myelin nurtures these cells and allows them to conduct impulses efficiently. The discovery of this animal model bolstered the theory that MS is primarily an autoimmune disease and helped scientists study the disorder and test new treatments.

Most scientists now believe that in MS, the body’s white blood cells attack these myelin proteins. The onslaught is thought to begin when susceptible individuals are exposed to a virus, bacterium or other environmental culprit that contains proteins similar to those in myelin. The encounter spurs the production of immune cells that “mistake” myelin for a foreign protein. According to the autoimmune model of MS, damage from this immune attack initially disrupts transmission of nerve signals and eventually destroys the nerves themselves. Yet scientists, despite decades of research, have

#### FAST FACTS

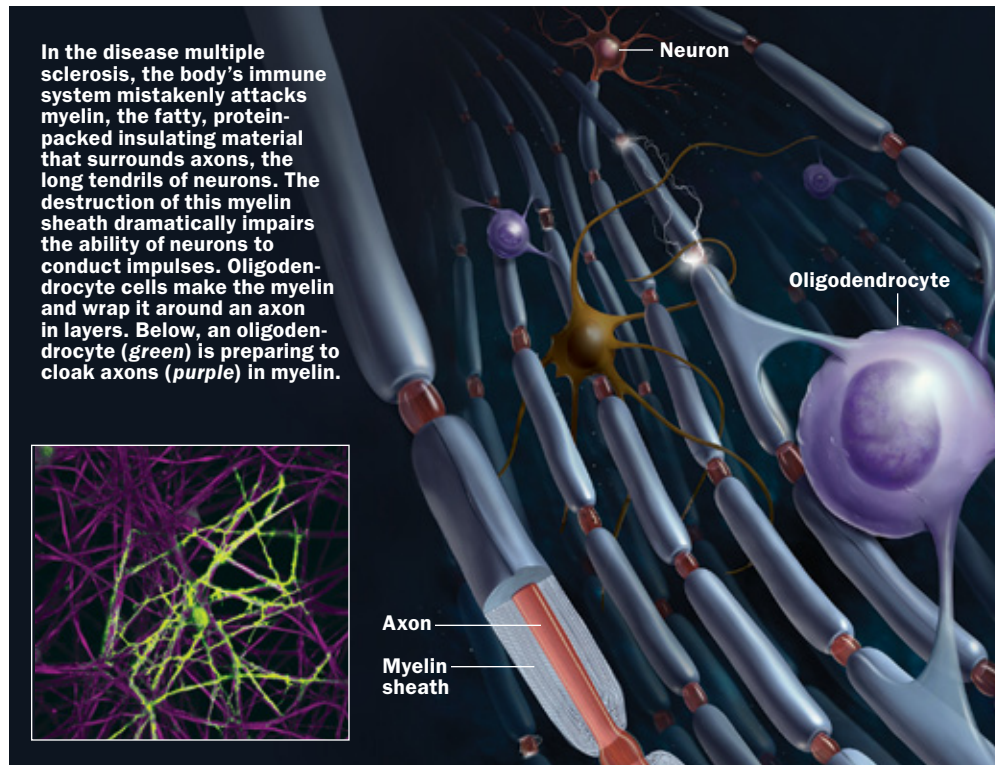
#### Deferring Disability

**1** Multiple sclerosis, a disease of the brain and spinal cord, is the leading cause of nontraumatic disability among young adults. The average age at diagnosis is about 30.

**2** During the past 19 years the U.S. Food and Drug Administration has approved nine new medications for MS, and two more are up for review in the next few months.

**3** Although current medications keep early symptoms at bay, they do not stop the degeneration of neurons. Scientists are now formulating new theories about the cause of MS in hopes of developing drugs that can halt its progression or even prevent its onset.

## Insulation Breakdown



not yet discovered what this trigger is.

MS afflicts only the central nervous system—that is, the brain, spinal cord and optic nerves. Areas of inflammation tend to move, flaring and fading in one area, then reappearing weeks, months and even years later somewhere else. At different times, a patient might experience any of a variety of possible symptoms in different body regions, including numbness and tingling, “pins and needles” sensations, pain, muscle weakness and tremor, and emotional, psychological or cognitive disturbances. For example, weakness in a leg may fade, only to be followed by facial paralysis. The waxing and waning of symptoms characterizes the most common form of the disorder, termed relapsing-remitting MS [see box on page 55]. After the first attack, patients may go months—even years—in remission before another relapse.

Almost all existing treatments are aimed at rolling back the immune attack. Back in the 1960s, patients took

adrenocorticotrophic hormone, which stimulates the adrenal glands to produce cortisol, a powerful immune suppressor. Synthetic corticosteroids, such as methylprednisolone, are still used to treat flare-ups, but because of their severe side effects—which include diabe-

disability. Studies conducted over the past few years show that continuous treatment not only reduces the frequency and severity of relapses but also appears to delay the onset of disability.

Some of the newer treatments target, while blunting the actions of, particular classes of immune cells now known to be involved in an MS attack. Others work even more subtly. For example, in MS, part of the immune reaction promotes changes in the blood-brain barrier, a tightly knit network of cells surrounding capillaries in the central nervous system. This filter normally keeps white blood cells, among other substances, from slipping into the brain or spinal cord. Yet the blood-brain barrier becomes more porous in MS, allowing immune cells to cross into the central nervous system. One new drug, the antibody (immune system protein) natalizumab, blocks receptors on blood vessel walls that white cells grab and use to pull themselves across the blood-brain barrier and into the brain or spinal

MS has been blamed on diet, infections, toxins and even repressed memories. Patients were placed in hot boxes, infected with malaria, injected with milk and treated with radiation.

COURTESY OF ALAN HOOFRING NIH Medical Arts (Illustration); COURTESY OF R. DOUGLAS FIELDS National Institutes of Health (micrograph)



## Who Gets Multiple Sclerosis?

Multiple sclerosis, a disease of the brain and spinal cord that produces myriad symptoms, does not strike the population evenly. Your risk for the disease is deter-

mined by genetics, gender and even where you live. All three factors hint at a role for the environment in the disease.



If you are an identical twin who acquires the disease, your twin, who has nearly the same genetic material as you, has a 20 to 30 percent chance of getting it, too. Among fraternal twins, who share half their genes, the risk is only 5 percent. To date, researchers have identified about 50 genes that appear to increase the risk to some degree. All these genes play a role in immune function, but no one gene or genes have been identified as the culprit.



Together, however, these genes explain only about 10 percent of a person's risk of acquiring MS, with the three genes with the strongest ties to the disease accounting for around just 4 percent of the risk. Thus, additional genes, coupled with environmental exposure, are very likely to be involved as well.



MS is more common among Caucasians, especially those of northern European ancestry, and much less so among Asians and people of African descent. Although such differences could reflect genetics, geography also appears to be important. MS seems to be more common at higher latitudes where the climate is temperate—that is, in Europe, the U.S., Canada, New Zealand and Australia—and rare in the tropics (parts of Asia and Africa). The highest prevalence is on the Orkney Islands, north of Scotland, where residents have the disease at the rate of 270 per 100,000 (compared with 90 per 100,000 in the U.S.). Interestingly, migration studies suggest that if you move from a low-risk country to a high-risk one before adolescence, you acquire the risk of your new home country. If you move after adolescence, however, you retain the risk profile of your country of origin. This pattern suggests that something in the environment affects risk, possibly an infectious agent or insufficient levels of sunlight.



Three to four times as many women as men are diagnosed with MS, a statistic that parallels the increased risk for autoimmune disease in women. No one knows the cause of the gender discrepancy in MS, but one clue, which hints at an emergent environmental factor, is that the gap has widened in recent decades. In the 1950s a woman's risk of developing the disorder was only about 1.4 times that of a man's.



Sunlight, in particular, affects vitamin D levels. Some studies have found that these amounts are lower in MS patients and that those with lower levels are more likely to have attacks, or relapses, than patients with higher levels. Vitamin D has also been shown to influence immune function, making a link between the vitamin and MS plausible. To date, however, there is no definitive proof that taking vitamin D supplements will prevent MS or help treat it. Nevertheless, because the vitamin is generally safe, many neurologists will recommend vitamin D as a supplement.

cord. Disabling these molecular handholds means that far fewer immune cells slip into the central nervous system, where they can wreak havoc.

In another current approach, a pill called fingolimod prevents white blood cells called lymphocytes from leaving the lymph nodes and entering the circulation, so that they cannot reach the brain and spinal cord. Because the drug does not destroy these cells, they can still perform

many of their important roles in normal immunity, and patients can fight off ordinary infections. Another oral agent, teriflunomide, approved in late 2012, stops rapidly dividing immune cells involved in MS from proliferating, thereby blunting the immune attack, while sparing cells that multiply more slowly and are important to normal disease resistance. Because these newer pharmaceuticals are designed to inhibit particular biochemical processes underlying MS, they are safer than treatments that suppress the immune system more broadly.

One treatment that the FDA is expected to approve this year is BG-12 (dimethyl fumaric acid), now is used to treat the skin condition psoriasis. This drug has anti-inflammatory and antioxidant effects that are thought to help protect neu-

rons. It may also modulate immune cell function to reduce inflammation. In a large-scale study published in 2012, neurologist Robert J. Fox of the Cleveland Clinic and his colleagues found that patients with relapsing-remitting MS who took BG-12 for two years had fewer attacks, slower progression of disability and less pronounced lesions as seen on an MRI than did those taking a placebo pill.

### Rebooting the Immune System

Not all the latest remedies are so delicate, however. Another emerging medicine under FDA review is an injectable drug called alemtuzumab. This antibody is now an approved treatment for chronic lymphocytic leukemia, a blood cancer. It destroys large numbers of white cells and causes severe immuno-

#### (The Author)

**JAMES D. BOWEN** is medical director of the MS Center at the Swedish Neuroscience Institute in Seattle and clinical associate professor of neurology at the University of Washington.



suppression. In MS, it is designed to reboot the immune system in the hope that after recovering from the drug's effects, the body's built-in defenses will no longer attack myelin. In a clinical trial, 376 patients taking alemtuzumab had 55 percent fewer relapses than did 195 patients receiving a standard treatment (the anti-inflammatory agent interferon beta-1a). In addition, 30 percent fewer patients receiving the experimental therapy became disabled during the two-year trial.

Still, the treatment carries a risk of infection: 67 percent of those taking alemtuzumab developed mild to moderate infections compared with 45 percent of those taking interferon. In addition, 20 to 30 percent of patients who received alemtuzumab ended up with thyroid disease that resulted from an immune system assault on the thyroid gland. Why this adverse event occurred is unknown, but scientists suspect it resulted from a defect in immune regulation that could be behind MS as well.

Another approach to restarting the immune system involves a bone marrow transplant. Last year my colleagues and I reported treating 26 seriously disabled MS patients, many of whom could not walk, with a combination of radiation, chemotherapy and antibody treatments

The drug is designed to reboot the immune system in the hope that after recovering from the medicine's effects, the body's built-in defenses will no longer attack myelin.

that kills almost all of a patient's immune cells. We then gave them a bone marrow transplant to restore their immune systems—bone marrow contains stem cells that give rise to all blood cell types. We hoped that the reconstituted immune systems would no longer attack myelin.

The immune system did seem to back off its assault. The treatment appeared to reduce the flare-ups of symptoms, and it stabilized the disease for as long as six years in some of the patients, all of whom had previously been going rapidly downhill. In 11 patients, however, the illness continued to progress, leaving them less and less able to engage in normal daily activities. The approach, moreover, is

not without risk. One patient died as a result of treatment-related complications, and another succumbed seven years later to a blood disorder to which the therapy may have contributed. Overall, patients with less advanced disease benefited more from the transplant, suggesting that reconstituting a patient's immune system might be more effective earlier on—a theory we are now testing in a follow-up study.

The fact that such severe immunosuppressive treatments fail to cure MS, however, suggests that autoimmune activity cannot fully explain the illness. In recent years researchers have come to understand that an apparently relentless neurodegenerative process appears to occur in parallel with the sporadic autoimmune attacks and may be at least partially independent of it. After all, destruction of neurons in MS continues even after the immune attacks appear to abate later in the disease.

### A Theory Turned Inside-Out

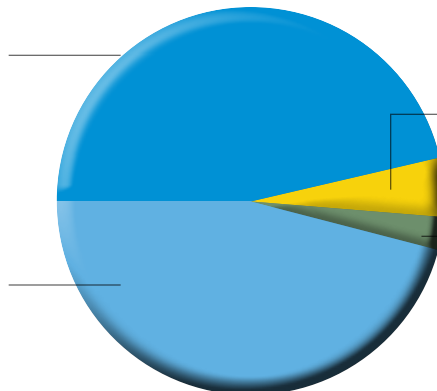
Scientists have developed three different theories to account for such phenomena. Some propose that the damage from years of immune attacks triggers a self-perpetuating destructive cascade in neurons or in oligodendrocytes, which make myelin. This process severs and destroys

## Patterns of Difficulty

Nearly 150 years after French neurologist Jean-Martin Charcot described a condition he called "*la sclérose en plaques disséminées*," scientists have characterized different forms of multiple

sclerosis. The types differ in the pattern of symptoms a patient experiences, with some patterns being far more common than others. Here are the main forms of this neurological disorder:

- In about 85 percent of patients, the disease follows a relapsing-remitting pattern in which symptoms worsen, or flare up, followed by a remission in which they remain stable, fade or disappear. During flare-ups, symptoms can range from mild to severe and in rare cases can even cause paralysis and death.
- About half of people who have the relapsing-remitting variety will eventually acquire secondary progressive MS, in which symptoms slowly worsen between relapses.



- About 10 percent of patients have primary progressive MS, in which symptoms steadily worsen from the outset in the absence of attacks.
- Less than 5 percent of the time, a patient is afflicted with progressive relapsing MS, in which the symptoms initially progress steadily but years later are punctuated by intermittent relapses.

axons and causes the death of neurons themselves. Other scientists suggest, meanwhile, that a chronic, smoldering autoimmune attack continues undetected throughout the illness. It persists despite immunosuppressive treatment and may rebound afterward, causing progressive neurodegeneration.

The most controversial hypothesis is that MS is primarily a neurodegenerative, rather than an autoimmune, disease. In this “inside-out” theory, neurons, oligodendrocytes or other cells in the central nervous system fall apart as a result of an inherited defect or environmental culprit, such as a virus. Products of this degeneration, perhaps proteins from dying cells, then provoke an autoimmune reaction. According to this view, an autoimmune attack may accelerate the neurodegeneration in MS, but it is not the principal cause of the disorder. This theory would explain why MS progresses in the face of aggressive immunosuppression. It would also clar-

Another approach is to transplant stem cells that can restore damaged tissue. These cells are thought to work by releasing chemicals that stimulate cellular repair.

ify why some patients have lost neurons and axons in areas with little evident autoimmune activity.

In addition, this last theory jibes with other recent findings regarding the timing and location of the damage in MS. For decades scientists assumed this damage was confined to white matter—which is made up of axons surrounded by myelin—and occurred late in the disease, a pattern consistent with an im-

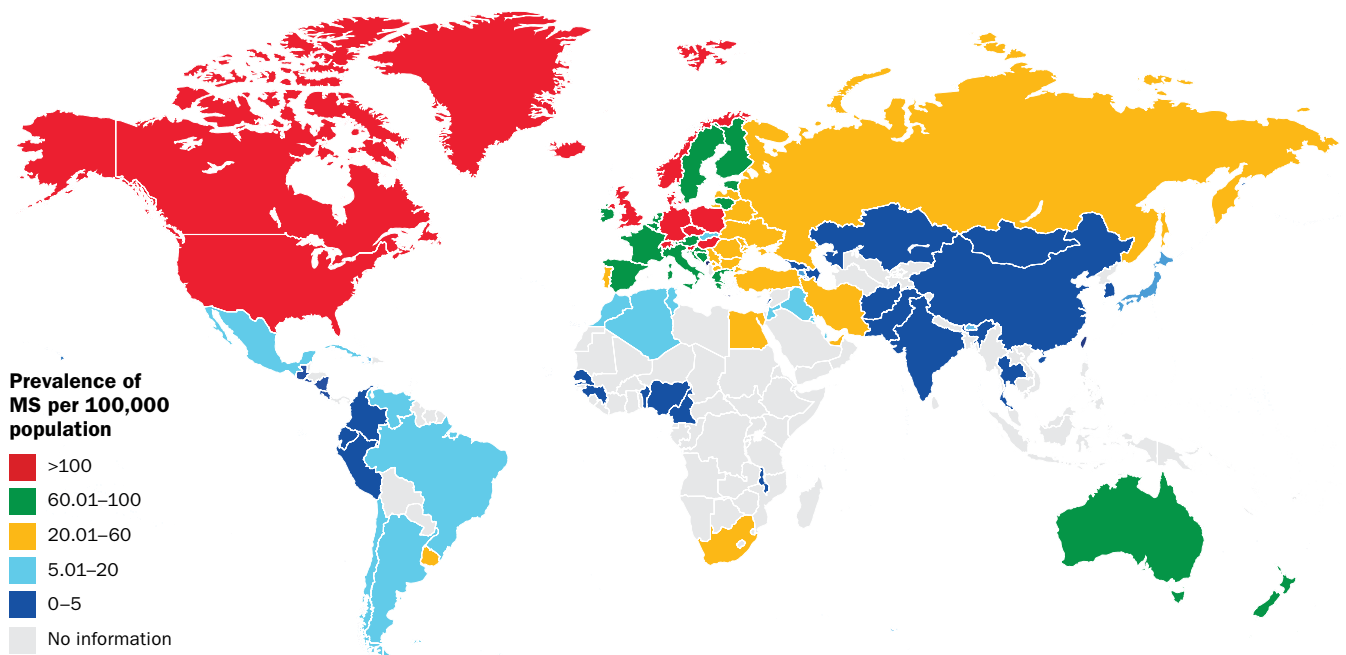
mune attack on myelin. The latest data, however, show that the neuronal cell bodies in the brain’s cerebral cortex, its outer covering, degenerate very early in the disease. (This cortical damage may, in fact, more closely parallel a patient’s early symptoms than the often lesser damage to myelin.) Yet the immune onslaught does not directly target these cortical neurons, hinting that they may be victims of an early, independent degeneration process.

Although no neuroprotective drugs have been approved for MS, some of the immune-altering medications used to treat the disease—particularly BG-12—are thought to protect neurons, which may explain some of their positive effects. Researchers are also investigating whether other, approved drugs with neuroprotective effects may be useful in MS. These agents include the anemia drug erythropoietin, the hormones estrogen and testosterone, and the antiseizure drug lamotrigine. Yet another approach

## Where in the World Is Multiple Sclerosis?

The prevalence of multiple sclerosis, a disease of the brain and spinal cord, varies dramatically by geographic location. The condition is relatively common in North America, but quite rare in much of Asia

and parts of Africa and South America. The reasons for the variation are unclear but likely involve genetics as well as an environmental factor, such as an infectious agent or sunlight.



ISTOCKPHOTO

## Treatments for Multiple Sclerosis

Name (Generic)	How Given	Year Available	Mode of Action
<b>Betaseron</b> (interferon beta-1b)	Injected through the skin every other day	1993	Reduces inflammation by lowering levels of immune chemicals called cytokines and by hampering the traffic of immune cells across the blood-brain barrier
<b>Avonex</b> (interferon beta-1a)	Injected into the muscle once a week	1996	Similar to Betaseron (interferon beta-1b)
<b>Copaxone</b> (glatiramer acetate)	Injected through the skin daily	1996	Not known, but may interfere with the function of immune cells that would otherwise target a protein in myelin
<b>Novantrone</b> (mitoxantrone)	Injected intravenously every three months	2000	A chemotherapy drug used primarily to treat cancer, mitoxantrone disrupts DNA synthesis and repair, which inhibits immune cell proliferation, suppressing the immune system
<b>Rebif</b> (interferon beta-1a)	Injected through the skin three times a week	2002	Similar to Betaseron (interferon beta-1b)
<b>Tysabri</b> (natalizumab)	Injected intravenously every four weeks	2004	Inhibits the traffic of white cells into the central nervous system by binding molecules that the cells use to move across the blood-brain barrier
<b>Extavia</b> (interferon beta-1b)	Injected through the skin every other day	2009	See “Betaseron”
<b>Gilenya</b> (fingolimod)	Pill taken once a day	2010	Prevents white blood cells called lymphocytes from moving from the lymph nodes into the bloodstream so they cannot travel to the brain and spinal cord
<b>Aubagio</b> (teriflunomide)	Pill taken once a day	2012	Inhibits rapidly dividing immune cells involved in MS, blunting the immune attack, but spares less rapidly dividing cells important to normal immunity
<b>Tecfidera</b> (BG-12)	Pill taken twice a day	2013	Not known, but may activate a cellular pathway that helps to protect neurons, myelin and the blood-brain barrier from oxidative damage caused by the immune attack; it may also reduce inflammation
<b>Lemtrada</b> (alemtuzumab)	Injected intravenously for five consecutive days once a year	Under review	Severe immunosuppression; thought to allow immune system to “reboot” to a less aggressive status

is to transplant stem cells that can stimulate the restoration of damaged tissue. Doctors have used these cells, called mesenchymal stem cells, to try to mend damaged hearts. They are thought to work by releasing chemicals that stimulate cellular repair systems.

Until such treatments are ready, the goal is mainly to keep patients from getting worse by taming the immune system. The latest medicines seem to make a significant difference. By taking fingolimod, Alston has been able to keep her symptoms at bay—and live the life she always wanted. She is married with two children, Langdon and Katie, and works full-time at an e-commerce company.

How fast her disease will progress remains to be seen. But advances in our understanding of the biology of MS hold

out the promise that we will soon have remedies that can roll back the disease and perhaps, one day, cure it. **M**

### (Further Reading)

- ◆ **Multiple Sclerosis: New Insights in Pathogenesis and Novel Therapeutics.** D. Ontaneda, M. Hyland and J. A. Cohen in *Annual Review of Medicine*, Vol. 63, pages 389–404; 2012.
- ◆ **Autologous Hematopoietic Cell Transplantation following High-Dose Immunosuppressive Therapy for Advanced Multiple Sclerosis: Long-Term Results.** J. D. Bowen et al. in *Bone Marrow Transplantation*, Vol. 47, No. 7, pages 946–951; July 2012.
- ◆ **Placebo-Controlled Phase 3 Study of Oral BG-12 or Glatiramer in Multiple Sclerosis.** R. J. Fox et al. in *New England Journal of Medicine*, Vol. 367, No. 12, pages 1087–1097; September 20, 2012.
- ◆ **Mesenchymal Stem Cell Transplantation in Multiple Sclerosis.** Jeffrey A. Cohen in *Journal of the Neurological Sciences*. Published online January 4, 2013.
- ◆ National MS Society: [www.nationalmssociety.org](http://www.nationalmssociety.org)



**PSILOCYBIN, THE ACTIVE INGREDIENT IN MAGIC MUSHROOMS, IS BEING EXPLORED AS A THERAPEUTIC TOOL TO IMPROVE THE LIVES OF PEOPLE WITH A LIFE-THREATENING ILLNESS BY ERICA REX**

ILLUSTRATIONS BY PETER HORVATH



## Calming a Turbulent Mind

I was lying on a lumpy off-white sofa under a mountain of blankets, wearing an eye mask and listening to a Brahms symphony playing through my headphones. The notes of a violin solo lit three strands of deep red light, which trickled like water in my right visual field. Deeper tones poured from above in huge blue clouds in the middle distance. Another violin flourish turned the sky yellow and brought with it a comet's tail

of body parts flying from the upper left of my visual field to the lower right, disappearing behind me.

This all happened within the first hour of my swallowing a capsule of psilocybin, the psychoactive ingredient in “magic mushrooms,” as a study subject at the Johns Hopkins University School of Medicine’s Behavioral Pharmacology Research Unit (BPRU). Patients with cancer are given the drug to improve mood and outlook and to help regain a sense of existential meaning in the face of a deadly disease.

I was diagnosed with breast cancer in 2009. A year on from a lumpectomy and radiation therapy, my prognosis seemed good. But rather than cheerfully getting on with life, I was spending most days at my desk crying. I began searching the Web for a way to kill myself that wouldn’t be either messy or too painful. The man I had married, who had made it possible for me to move to England



#### FAST FACTS

### Psychedelic Solutions

- 1**» Scientists are taking a second look at the therapeutic potential of psychedelic drugs, in particular psilocybin. This hallucinogen may offer faster, more effective treatment for individuals in a spiritual deficit state.
- 2**» A spiritual deficit state encompasses the severe distress and emotional suffering associated with deeply threatening events, such as a terminal illness. Modern medicine has typically struggled to assuage this condition.
- 3**» A few doses of psilocybin, in a carefully tailored setting and with a therapist's guidance, have been shown to calm the psychological turbulence of people afflicted with a number of conditions, including depression and alcohol addiction.

and continue cancer treatment under the U.K.'s universal health plan, could not cope with my depression and left for weeks at a time.

By the time my three-year mammogram rolled around at the beginning of 2012, I was living alone. Sitting in the waiting room at Barts Cancer Center in London, I felt so alienated by the pink ribbons, the flowered wallpaper and the yapping television that I fled before being called for my scan. A staff member pursued me, first down the stairs, then later on the phone. With each imprecation to reschedule, I declined more earnestly. "You can have my breast," I'd think to myself. "I'll leave it off for you in a bag."

Both here in the U.K. and in the U.S. where I had my surgery, medicine excels at finding cures for disease and saving lives. All that excellence has created a void, however, wherein the emotional and existential needs of patients often go neglected. My demoralization is common among cancer patients. We ob-

ness about survival and what the future holds for us. The system is not structured to help doctors carry us across the minefield of emotional and personal issues that cancer lays out before us.

But I am also fortunate. After decades of banishment to the netherworld of Schedule I (Class A in the U.K.), hallucinogens are making a reprise on the clinical stage. Drugs such as psilocybin have the potential to improve patients' sense of psychospiritual well-being and with it overall quality of life, a central focus in today's palliative care protocols. We stop worrying about the future and about death. A scant handful of researchers are exploring the hallucinogenic option as an adjuvant to cancer treatment for the first time in a generation, reintroducing a means of addressing the existential crises many cancer patients experience. Hallucinogens have also been studied as treatments for other conditions: a 2005 pilot study at the University of Arizona demonstrated that psilocybin successfully treated severe refractory obsessive-compulsive disorder, and cluster headache sufferers report that psilocybin arrests the headache cycle in a way no other drugs have touched.

Before their prohibition in the 1970s—the regulatory response to the explosion in street use during the late 1960s—hallucinogens were prescribed to approximately 40,000 research subjects. The results showed remarkable promise in helping terminally ill people overcome pain, fear, psychological isolation and depression. Now researchers are revisiting some of psilocybin's forgotten virtues. Not only does it diminish patients' symptoms immediately, it also improves therapeutic outcomes for months, even years afterward. Many patients undergo what Charles S. Grob, principal investigator at Harbor-U.C.L.A. Medical Center, terms a “psychospiritual epiphany.”

These scientists have been waiting a long time for the tide to turn.

### Flesh of the Gods

Indigenous cultures have used plants with hallucinogenic powers for centuries as a chemically mediated entryway to curative religious experiences. The Aztecs of Mexico and Central America called psilocybin-containing mushrooms *teonanacatl*, meaning literally “flesh of the gods.” Then, in the 17th century, *teonanacatl* was condemned by the

Spanish Inquisition. Practitioners were forcibly converted to Christianity. For three centuries ceremonial practices were thought to have been eradicated.

In 1955 banker-cum-amateur-mycologist R. Gordon Wasson journeyed to the hills of Oaxaca, Mexico, where he was permitted to attend a ritual healing ceremony conducted by a native healer, which he described in an article for *Life* magazine. A few years later, in collaboration with French botanist Roger Heim, then director of the French National Museum of Natural History, the two men



collected and identified the families of Strophariaceae and the genus *Psilocybe* used by the native practitioners. They provided samples to chemist Albert Hoffman of Sandoz in Basel, Switzerland, who in 1938 had synthesized LSD from ergotamine, an alkaloid produced by another fungus, *Claviceps purpurea*, a rot that grows on rye. Until 1991, when a new drug was finally introduced, ergotamine was the only available treatment for migraine.

Hoffman identified and isolated two active alkaloids, psilocybin and psilocin, from the mushroom samples. Clinical experimentation on psilocybin began quickly. Both it and LSD showed immense promise when administered to terminally ill patients and subsequently to intractably depressed and alcoholic patients. They provided relief to groups previously dismissed as untreatable.

Prolonged illness is not a modern phenomenon. But now—unlike 400 years ago—most people in the Western world do not die of fast-acting infectious diseases such as typhoid and plague. Those have given way to chronic, lingering disease processes lasting months or years. The accompanying

Drugs such as psilocybin could improve patients' sense of **psychospiritual well-being** and with it overall quality of life.

psychospiritual distress also afflicts those suffering from compulsive or habit-based disorders, such as alcoholism or nicotine addiction. “The issues around alcohol addiction and terminal illness are the same thing,” says Stephen Ross, principal investigator of New York University’s Psilocybin Cancer Anxiety Study. “These are people in an acute spiritual deficit state.”

A spiritual deficit state has been defined as “severe distress and emotional suffering associated

who do. “Existential terror in the dying is the most taboo conversation in medicine,” says Anthony Bossis, clinical assistant professor of psychiatry at N.Y.U., and co-principal investigator of the study there. “You can count on clearing the room of interns the moment you mention death.”

### A Skeleton Key

In the early 1990s the FDA and the National Institute on Drug Abuse began loosening their legal

## The healing constituent of psilocybin lies within the **intrapsychic world** the drug evokes during a session.

with events that threaten the intactness of the person”; in other words, it makes many sufferers feel that life is now worthless. It destroys patients’ ability to manage their affairs or connect in any meaningful way with loved ones. The knowledge of their impending death depletes their sense of autonomy. Psychotherapy may address some of these issues, but for many patients it is a poor option—if it is available. If you are facing imminent death, talk therapy is unlikely to bring relief quickly enough.

Spiritual deficit is not modern medicine’s cup of tea. Today a patient receiving a terminal diagnosis is not likely to be offered sessions with a counselor or psychotherapist unless he or she asks for them. A very small number of hospitals give patients the option of taking part in structured palliative care, where they receive consultations with palliative care physicians and home visits by specialist nurses. Some hospitals and doctors offer support groups and meditation classes or refer patients to charities

throttle on the study of hallucinogens. Even so, psilocybin researchers today obtain funding from private rather than federal sources, among them the Heffter Research Institute in New Mexico, the Multidisciplinary Association for Psychedelic Studies in California, and the Beckley Foundation in England.

The therapeutic benefit of psilocybin lies in its capacity to provide a neurochemical bridge between spiritual guidance and talk therapy. Although questions remain about psilocybin’s precise mechanism of action, researchers agree on this point: the drug’s value depends entirely on the patient’s feelings and perceptions during the session and the way he or she processes the memories afterward. Patients who undergo a transcendent peak while taking psilocybin describe it as among the most meaningful events in their lives. “The drug is a skeleton key which unlocks an interior door to places we don’t generally have access to,” says psychologist William A. Richards of BPRU, one of the researchers who successfully treated terminally ill patients with hallucinogens from the early 1960s until 1977, when the work was shut down. “It’s a therapeutic accelerant.”

Unlike psychoactive drugs, anxiolytic medications such as Xanax help patients only while they are taking them. The effect wears off when the body clears the drug from the system. Patients must repeat the regimen, often increasing the dosage to obtain the same effect. In contrast, the healing constituent of psilocybin lies within the intrapsychic world the drug evokes during a session. Psilocybin treatment consists of only one or two doses.

Grob and his colleagues carried out the first contemporary clinical study using psilocybin to treat depression at Harbor-U.C.L.A. Medical Center between 2004 and 2008. They assessed 12 patients with advanced-stage cancer using standard-

Grassroots movements may help legalize the therapeutic use of hallucinogens. AIDS sufferers and their advocates launched the campaign for medical marijuana clinics (below).



ROBYN TWOMEY Redux Pictures





Ritual is an important part of a psilocybin session. Researchers today carefully survey a patient's mental and physical landscape to channel the drug's effects toward healing.

ized psychological measurements of depression and mood, as well as screening for other psychiatric symptoms, such as paranoia and grandiosity.

All the patients who took part in the study reported sustained mood improvement and anxiety reduction after the sessions. The effects lasted for at least six months. Everyone in this group has since died. “The profession itself forgot about the promise of the early findings,” Grob says. “Forty years later here we are.”

Psilocybin is a naturally occurring alkaloid found in several species of mushrooms. Structurally, it is similar to the neurotransmitter serotonin. Once ingested, psilocybin is rapidly metabolized to psilocin, which causes a powerful physiological reaction involving three serotonin receptors—sites on the surface of a brain cell where neurotransmitters can attach to activate a cellular function. One receptor of particular interest is known as 5-HT<sub>2A</sub>. Depressed and suicidal patients have been found (at autopsy) to have more 5-HT<sub>2A</sub> receptors than normal patients. Psilocin binds to the 5-HT<sub>2A</sub> receptor in place of serotonin, which may partly explain psilocybin's positive effect on mood.

The lasting effects of a psilocybin session are generally thought to result from psychological insights gained from the experience, although an observed physiological change may further explain the

drug's lingering benefits. Animal studies show that LSD, another potent 5-HT<sub>2A</sub> agonist, causes a prolonged decrease in the number of 5-HT<sub>2A</sub> receptors. Psilocybin very likely has the same effect.

Recently a study by researcher Robin L. Carhart-Harris of the Neuropsychopharmacology Unit at Imperial College London yielded some surprises about the way psilocybin works. He found that overall blood flow to brain regions associated with consciousness and the concept of self decreased by 20 percent, contradicting a long-standing assumption that psilocybin increases blood flow to some areas of the brain. This new information helps to explain the ego dissolution that usually accompanies subjects' descriptions of psilocybin. Instead of augmenting the brain's day job of filtering and classifying, psilocybin removes internal constraints on our perceptions, thoughts and feelings.

Carhart-Harris performed functional MRI studies in healthy volunteers who had been given

### (The Author)

ERICA REX is an American journalist based in the U.K. She has written for the *New York Times*, the *Times* (U.K.) and numerous other venues.

psilocybin. He focused on two key structural hubs, the posterior cingulate cortex (PCC) and the medial prefrontal cortex (mPFC), which tend to activate in concert, like the first violin and the kettle drum in a symphony orchestra. With psilocybin, they became far less synchronized. The mPFC, in the front part of the brain, and the PCC, tucked in the middle, participate in the brain's default-mode network (DMN), a set of regions whose activity has been closely linked to our sense of self. Looking inward at oneself, as happens in depression, activates the DMN. "Tightly constrained, ruminative thinking is associated with hyperactivity and connectivity in the DMN," Carhart-Harris says. Psilocybin reduces DMN activity and, with it, the narrowing thought processes associated with anhedonia—the inability to experience pleasure—and depression.

Although the PCC and mPFC still play together on psilocybin, it is as though the conductor has left the room. The music changes character. If the brain in its normal state is Beethoven's Violin Concerto, on psilocybin it becomes improvisational jazz. The mind no longer dwells on questions limned by the ego such as "How will I survive if I'm laid off" and "I wonder if he's having an affair?"

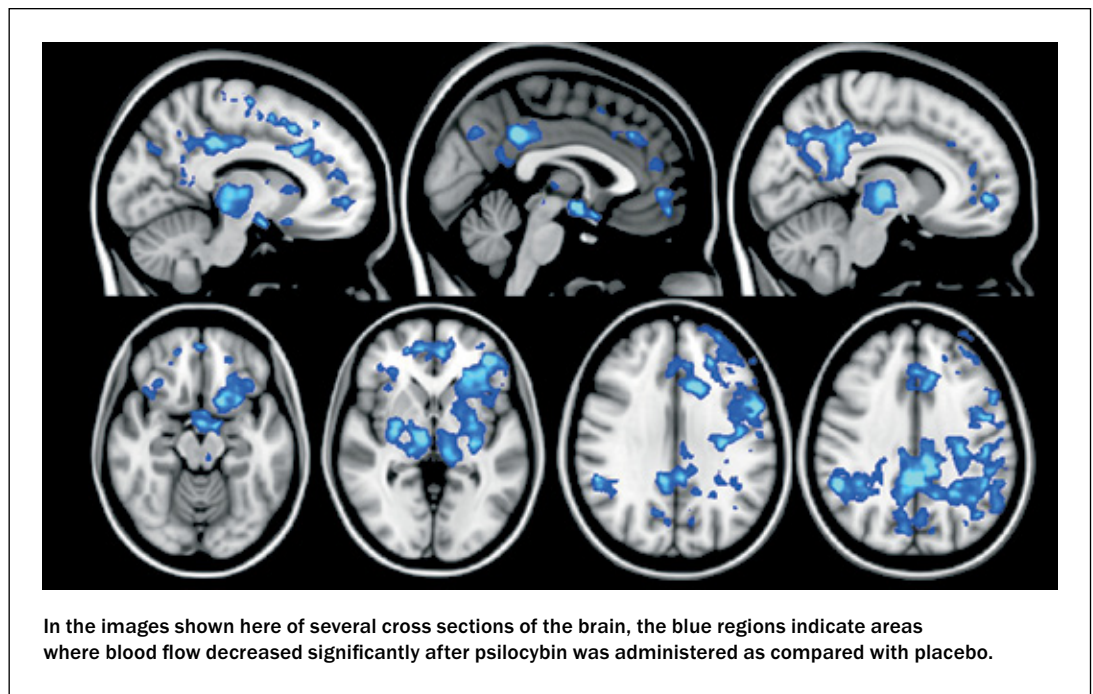
### Radical Curiosity

Subjects visit the Baltimore clinic twice, receiving a low dose of psilocybin on one visit and a moderately high dose on the next. We are screened for

mental, emotional and physical problems before we are officially admitted into the study. Giving psilocybin to people who have underlying psychotic disorders or schizophrenia can be catastrophic. Many volunteers are sent home after a day.

The researchers also brief us on "set and setting," a concept that was introduced in the early 1960s by LSD pioneer Timothy Leary to describe the optimal scenario for using hallucinogens as therapeutic tools. Set and setting are key factors in the equation. Set refers to "mind-set"—the patient's mental and emotional attitude toward the hallucinogenic experience. Setting is the physical and social environment—the room or space itself and the people who are present with the subject throughout the experience.

Set must include a willingness to move toward repellent or frightening thoughts and images, rather than trying to flee from them—either by trying to leave the room, which has happened with at least one subject at BPRU, or through emotional avoidance. For this reason, part of the set and setting equation includes complete trust in the guides, trained psychotherapists who remain throughout the entire session. The images and feelings can be beautiful and transcendent or terrifying and disgusting—or all of these over the course of a day. "Radical curiosity," said neuroscientist Roland Griffiths, study director at BPRU, when we first met. "That's how you have to approach this."



FROM "NEURAL CORRELATES OF THE PSYCHEDELIC STATE AS DETERMINED BY FMRI STUDIES WITH PSILOCYBIN," BY ROBIN L. CARHART-HARRIS ET AL., IN PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES USA, VOL. 109, NO. 6, FEBRUARY 7, 2012

“What do you think about God?” he asked me. “Where do we go **when we die?**” I didn’t know the answers.



Although modern medicine has helped prolong life for many people, including many breast cancer sufferers, it has largely failed to help patients cope with existential terror.

Four different psychotherapists and the study’s coordinator interviewed me for hours. They asked questions such as “If you had to spend the day being nauseated, could you tolerate it?” and “Do you ever think there are people or other beings who are transmitting secret coded messages to you alone?”

I filled out more than 50 pages of questionnaires, including assessments of optimism and pessimism, pain scales, depression scales, queries about my lifestyle and my habits, as well as one called Assessment of Spirituality and Religious Sentiments. My blood pressure was monitored every 15 minutes for two hours. The physical exams often uncover maladies that subjects themselves were not aware of. Borderline diabetes, heart arrhythmia or slightly off-par liver function will get you excluded, as well as traces of alcohol or drugs. All feelings and experiences—from childhood trauma to attitude to internal conflicts—are subjected to scrutiny. The guides have to know the lay of the psychic land so they can be supportive if

complex or painful feelings arise. They often do.

I met with Griffiths before my session. “What do you think about God?” he asked me. “Where do we go when we die?” I didn’t know the answers. By the end of the third day, I felt as though I had been flayed. But I’d passed, and I was in.

When my session day arrived, I was brought into a softly lit, comfortably decorated lounge, invited to lie down on a sofa and listen to music. Then I swallowed a purple capsule of psilocybin.

Some time later, when I was deeply within the world of the drug and the imagery it evoked, I found myself inside a steel industrial space. I became aware of my animosity toward my two living siblings. A woman seated at the end of a long table, wearing a net cap and white clothes and working busily, turned and handed me a Dixie cup. “You can put that in here,” she said. So I did. The cup filled itself with my bilious, sibling-directed feelings. “We’ll put it over here,” she said, and placed it on a table at the back of the room. Then she went matter-of-factly back to

work, along with now numerous busy women who occupied this space.

My guide, Fred, asked me what was happening. I sat up. As I recounted the scene, I began to laugh out loud, and my own laughter appeared to me in a midnight blue, cloud-dark sky as an effusion of twinkling gemstones, glittering in time with my peals of laughter, like a metronome.

Not all subjects have an all-encompassing transcendent experience during their sessions, wherein they feel a profound oneness with all things, a union with the universe or with God. I did not—and at first I was disappointed. But as the months have passed, I realize what I did gain is immeasurable.

harshness has ebbed. I am now able to feel more compassion both toward myself and toward others. I no longer spend my days worrying about what the future holds and whether I'll have a cancer recurrence or whether I'll die alone.

### Legal Hurdles

Grassroots movements may help push legalization of hallucinogens, as they did with medical marijuana. Initiated by AIDS sufferers and their advocates, the original California law, Proposition 215, effectively made possession of marijuana legal for pharmaceutical purposes in 1996 without prior FDA approval or the buy-in of pharmaceutical com-

## I no longer spend my days worrying about **what the future holds** and whether I'll have a cancer recurrence and die alone.

Since my session, my mood has improved, and my sense of myself as a person occupying a certain space in the universe has altered.

I have come to realize the universe consists of more than what readily meets the eye. An abiding sense of the inexplicable vastness of what is real and what is possible has affected my worldview. I no longer define myself by what has happened to my body, or even my emotional life, since my cancer diagnosis.

The vision of my own laughter producing a sky spilling jewels provided me with a kind of affirming metaphor. Shaking his finger at me at the time I told him, Fred commented: "Let that be a lesson to you, young lady."

It was.

Later on, when talking about my hallucinations with the clinicians and my guides, I found they provided me some profound truths about my life. My tendency to judge myself with a kind of murderous

panies. Seventeen other states and the District of Columbia have since followed suit.

But whereas marijuana can be safely self-administered, hallucinogens cannot. Traditional societies sequestered the experience of brain disinhibition within a ritual context supervised by shamanic healers for very good reasons. The powerful images and emotions they elicit require both context and guidance. Set and setting have to be honored because the drugs can be dangerous.

As the population ages and as more people face prolonged illness and end-of-life issues, the demand for improved palliative care and the inclusion of psychospiritual considerations is altering the way medicine will be practiced. The camel's nose is under the tent, and he's already halfway in.

Richards has far-reaching hopes for the future of hallucinogenic-assisted psychotherapy. He envisions the possibility of administering psilocybin to incarcerated sociopaths as an adjunct to talk therapy, perhaps enabling them to discover their empathic feelings toward themselves and others and eventually to reenter society's mainstream. A trial in the U.K., based at Imperial College, is recruiting patients suffering from intractable depression, whose illness has not responded to any conventional treatment.

When I asked David Nutt, director of the Neuropsychopharmacology Unit in the Division of Brain Sciences and clinical director of the upcoming Imperial College study about the obstacles presented by legal bans against psychoactive drugs, he said: "We'll change the law."

I hope he's right. **M**

### (Further Reading)

- ◆ **The Use of Psilocybin in Patients with Advanced Cancer and Existential Anxiety.** Charles S. Grob in *Psychedelic Medicine: New Evidence for Hallucinogenic Substances as Treatments*, Vol. 1. Edited by Michael Winkelman and Thomas B. Roberts. Praeger, 2007.
- ◆ **Neural Correlates of the Psychedelic State as Determined by fMRI Studies with Psilocybin.** Robin L. Carhart-Harris et al. in *Proceedings of the National Academy of Sciences USA*, Vol. 109, No. 6, pages 2138–2143; February 7, 2012.
- ◆ **Implications for Psychedelic-Assisted Psychotherapy: A Functional Magnetic Resonance Imaging Study with Psilocybin.** Robin L. Carhart-Harris et al. in *British Journal of Psychiatry*, Vol. 200, No. 3, pages 238–244; March 2012.



# A Trip Out of Depression

**KETAMINE, AN ANESTHETIC AND ILLICIT PARTY DRUG, IS EMERGING AS A FAST-ACTING ANTIDEPRESSANT**  
**BY SIMONE GRIMM AND MILAN SCHEIDEGGER**

ILLUSTRATION BY PETER HORVATH

For 20 years Joan\* quietly suffered from an unrelenting desire to commit suicide. She held down a job as a special-education teacher and helped care for her family in the northeastern U.S. Yet day after day she struggled through a crushing depression and felt neither joy nor pleasure. Except for the stream of psychiatrists recommending different antidepressant treatments—all of which failed to provide relief—Joan kept her condition private. She says it was the fear of hurting her students or abandoning her father that kept her alive. “I really don’t know how I survived,” she says.

*\*A pseudonym to protect the patient’s privacy.*



The sense of dissociation that a large dose of ketamine can generate has made it a popular recreational drug.

A few years ago Joan got a break. She came across a clinical trial for a drug called ketamine that had succeeded in treating patients with intractable major depressive disorder. She enlisted. Following one dose, she experienced her first reprieve from suicidal thoughts in two decades. She realized the drug was working while she was sitting outside on a pleas-

ant day and noticed that the leaves on a tree looked bright green and that a spider was building a web. “It sounds crazy, but normally everything was clouded and gray,” she says. “Nothing stirred me.”

Depression ranks among the most prevalent psychiatric conditions in the U.S. Research from 2008 suggests that approximately 14.3 million, or 6.4 percent, of American adults experience a major depressive episode in a given year. Only about half the people who try antidepressant drugs respond to them, however. When they do, several weeks or even months may elapse before a patient experiences relief, a critical failing for people at immediate risk for suicide. Ketamine, in contrast, appears to ease the most severe symptoms of depression within minutes or hours, even in patients who have a dismal track record with other treatments. The effects of a single dose can last at least a week in some patients.

Ketamine’s promise has ignited excitement, as well as controversy, among clinicians and neuroscientists for the past several years. A Schedule III drug under the Controlled Substances Act, ketamine—commercially sold as Ketalar—is primarily used as

#### FAST FACTS

### Defeating Depression

- 1» Ketamine is an analgesic, an anesthetic and a hallucinogen—yet the drug also seems to alleviate depression.
- 2» More commonly known as a party drug, ketamine changes the neurotransmitter balance in the brain, thereby affecting consciousness.
- 3» Deciphering ketamine’s mechanism of action could pave the way for a new generation of antidepressants.

GETTY IMAGES

# The **speedy relief** of ketamine sets it apart from typical antidepressants, as does **the way it interacts** with the brain.

an anesthetic in veterinarian medicine, particularly for horses, and as a short-term anesthetic and analgesic in hospitals during surgery or other painful procedures. The U.S. Food and Drug Administration has not approved it for treating depression, because its side effects can be harmful. The speedy relief it offers, however, sets it apart from typical antidepressants, as does the way it interacts with the brain. These factors combined have made ketamine a rising star in the world of depression research.

## Rave Reviews

Ketamine was originally synthesized in the 1960s as an alternative to phencyclidine, more commonly known as PCP or “angel dust.” Anecdotal reports of ketamine’s mood-enhancing action have circulated in the medical community for more than 20 years. At the same time, it developed a growing reputation as a “rave” drug, with effects similar to the psychoactive drug ecstasy. Depending on the dose, a person taking ketamine may experience altered physical, spatial and temporal states; larger quantities may induce hallucinations and dissolution of the self.

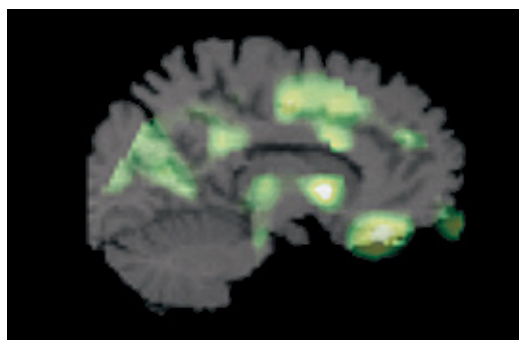
The first controlled study of ketamine for treating depression was conducted in 2006 by psychiatrist Carlos A. Zarate, Jr., and his colleagues at the National Institute of Mental Health. They intravenously administered either ketamine or a saline solution to 17 severely depressed patients. On average, the participants had already tried six different antidepressant regimens without success.

The outcomes exceeded all expectations. For half the patients, symptoms of depression dropped by 50 percent within two hours. By the end of the first day, 71 percent of the patients had responded to the drug—a third of them were virtually free of symptoms. Some of the study participants continued to feel relief from that single dose of ketamine for at least a week. “To our knowledge, there has never been a report of any other drug or somatic treatment that results in such a dramatic, rapid and prolonged response with a single administration,” says lead investigator Zarate.

The researchers had similar success with patients suffering from bipolar disorder who were given ketamine during a depressive phase of their illness. Last year Zarate and his team published a study showing that thoughts of suicide decreased

rapidly in these patients a mere 40 minutes after receiving a short intravenous infusion of the drug. The positive effect lasted for up to three days and was experienced by 79 percent of the treated test patients.

Yet the work is still new, and the drug needs to be tested in many more patients to verify the findings so far. The results of different ketamine studies have varied widely, ranging from a positive response rate as low as 25 percent to as high as 85 per-



Moderate doses of ketamine increased neuronal activity in numerous areas of the brain (shown in green). These regions include the prefrontal cortex and the thalamus.

cent one day after a ketamine infusion. Part of the ambiguity may arise from the difficulty of designing a convincing control group for an experiment. During a ketamine infusion, patients immediately feel dissociated and drugged, so the challenge is to keep them unaware of whether they are receiving ketamine or a placebo. Psychiatrist James Murchough of Mount Sinai Hospital says studies are in the works in which some patients will receive a placebo that causes a temporary reaction that simulates the effects of ketamine.

Yet other scientists posit that the psychoactive effect of ketamine may in fact ease depression. Along with psilocybin—the psychoactive substance in certain mushrooms—and mescaline, which is derived from a Central American species of cactus, psychiatrist Franz X. Vollenweider of the University Hospital of Psychiatry Zurich considers ket-

## (The Authors)

**SIMONE GRIMM** is a psychologist working at the University Hospital of Psychiatry in Zurich and at Charité University Medical Center in Berlin. **MILAN SCHEIDEGGER** is currently earning an M.D.-Ph.D. degree at the Swiss Federal Institute of Technology’s Institute for Biomedical Engineering and at the University Hospital of Psychiatry Zurich.



**Depression changes the way we view the world, often depriving it of beauty. Ketamine has helped some patients improve their outlook for several days at a time.**

amine a promising candidate for a psycholytic approach to therapy, in which psychoactive substances are used to alter a patient's mind.

### Alternative Thinking

Clinicians treating patients are not the only ones keenly studying ketamine's potential. Neuroscientists have hailed the drug as the first breakthrough in depression medication research in 50 years because ketamine works on a different pathway in the brain than most antidepressants. Conventional drugs aim to elevate concentrations of serotonin, dopamine or noradrenaline, neurotransmitters that ferry important information between neurons.

Ketamine, on the other hand, briefly floods the space between two connected neurons with glutamate, a different neurotransmitter, which is abundant in the brain and crucial for learning and memory processes. Researchers are still attempting to understand exactly how ketamine's effect on the glutamate system mitigates depression, but studies show that various areas of the brain associated with

depression respond after administration of the drug.

One hypothesis suggests that ketamine quickly and dramatically increases the function and density of synapses, the junctions between neurons, in areas of the brain where cells have atrophied because of stress or depression. The prefrontal cortex—a region essential to complex decision making, learning and memory—is one such area. In depressed people, it appears to have reduced volume and less activation than in healthy individuals, as well as fewer synapses on neurons in one subregion. A rodent study conducted by a team led by Ronald S. Duman of Yale University found that ketamine caused a burst of glutamate in the prefrontal cortex and a sudden increase in the formation of new synapses. Duman hailed ketamine as being “like a magic drug.”

The ability of synapses to adjust their strength is essential to the function of a healthy brain, and their increased plasticity could be the neurobiological reason for the apparent change in perspective of patients who take ketamine. We hypothesize that depression is associated with an imbalance in the way glutamate

CORBIS



regulates the brain and that when the neurotransmitter floods the synapses it temporarily returns the system to a healthy, balanced state. Many chronically depressed patients have a glutamate deficiency, and the initial findings by our team in Zurich, along with Martin Walter of Otto von Guericke University in Magdeburg, Germany, support the idea that correcting the shortage normalizes brain activity associated with depression. Namely, we have observed that an increase in glutamate levels causes the prefrontal cortex to activate more intensely to emotional stimuli.

cians at Mount Sinai found that out of 21 patients who received up to six infusions of ketamine over 12 days, 17 had lapsed back into depression a median of 18 days after the end of the treatment, whereas only four had not relapsed after 83 days when the study concluded. On the positive side, the participants experienced no notable adverse side effects.

Even if ketamine's efficacy becomes more strongly established, the road forward is unclear. Because ketamine has been available for decades, there is no patent for it and little financial incentive

## Ketamine **floods the space** between two neurons with glutamate, a chemical **crucial for learning** and memory.

The amygdala, which is often hyperactive in depressed individuals, becomes less responsive. [For more on glutamate and synaptic plasticity, see "A Lifeline for Addicts," by Michele Solis; SCIENTIFIC AMERICAN MIND, March/April 2013.]

Depressed patients also are low on glutamate in the anterior cingulate cortex, a region in the frontal lobes important in motivation and cognitive control. Psychiatrist James M. Stone of Imperial College London observed an uptick in glutamate concentrations in the anterior cingulate cortex of healthy human subjects within as little as 30 minutes of a ketamine infusion.

A short-term rise in glutamate does not alone explain its antidepressant action, of course. The buildup occurs because ketamine blocks the neurotransmitter from binding to a receptor known as NMDA. This blockage causes other types of glutamate receptors to become more strongly stimulated. That shift, too, can ultimately increase the density of nerve synapses. Numerous mechanisms most likely contribute to resetting the connections not only between individual neurons but also among the broader brain networks that regulate mood.

### A Sense of Hope

In spite of progress on deciphering how it works, ketamine in its current form may never develop into an accepted treatment for depression. Research on ketamine addicts and those who take it in large doses as a party drug has uncovered unsavory side effects: users may experience learning and perception problems, as well as memory disorders, and in some cases can develop a severely inflamed bladder. Another concern is that ketamine's benefits may actually be relatively fleeting. A recent study by physi-

for pharmaceutical companies to research the drug and collect FDA approval for its use as an antidepressant. Given its drawbacks, some researchers hope instead to eventually develop new, less troublesome drugs based on ketamine's chemistry.

A few doctors in private practice have taken matters into their own hands. Glen Zehnder Brooks, an anesthesiologist in New York City, for example, recently opened a ketamine infusion clinic and treats depressed patients who are under the care of a psychiatrist. Brooks reports that "to see the transformation [in patients] is just amazing." He often works with Princeton, N.J., psychiatrist Steven P. Levine, who has gained a reputation for providing patients with ketamine. In fact, Joan discovered Levine through the Internet, after five years of participating in ketamine clinical trials. In each trial she responded positively and then relapsed, a pattern that left her filled with hope yet frustrated. "You know your brain will respond to the right stuff, so then why can't I get it? This is a terminal illness." Now she can schedule an infusion whenever her spirits sink dangerously low.

For the first time in decades, she says she is optimistic about the future. **M**

### (Further Reading)

- ◆ **Ketamine Use: A Review.** Celia J. A. Morgan and H. Valerie Curran in *Addiction*, Vol. 107, No. 1, pages 27–38; January 2012.
- ◆ **Ketamine for Depression: Where Do We Go from Here?** Marije aan het Rot, Carlos A. Zarate, Jr., Dennis S. Charney and Sanjay J. Mathew in *Biological Psychiatry*, Vol. 72, No. 7, pages 537–547; October 1, 2012.
- ◆ **Synaptic Dysfunction in Depression: Potential Therapeutic Targets.** Ronald S. Duman and George K. Aghajanian in *Science*, Vol. 338, pages 68–72; October 5, 2012.



# Are Doctors Diagnosing Too Many Kids with ADHD?

Some boys may be labeled incorrectly with the condition, but undertreatment may be the bigger problem

BY SCOTT O. LILIENFELD AND HAL ARKOWITZ

A GERMAN children's book from 1845 by Heinrich Hoffman featured "Fidgety Philip," a boy who was so restless he would writhe and tilt wildly in his chair at the dinner table. Once, using the tablecloth as an anchor, he dragged all the dishes onto the floor. Yet it was not until 1902 that a British pediatrician, George Frederic Still, described what we now recognize as attention-deficit hyperactivity disorder (ADHD). Since Still's day, the disorder has gone by a host of names, including organic drivenness, hyperkinetic syndrome, attention-deficit disorder—and now ADHD.

Despite this lengthy history, the diagnosis and treatment of ADHD in today's children could hardly be more controversial. On his television show in 2004, Phil McGraw ("Dr. Phil") opined that ADHD is "so overdiagnosed," and a survey in 2005 by psychologists Jill Norvilitis of the University at Buffalo, S.U.N.Y., and Ping Fang of Capitol Normal University in Beijing revealed that in the U.S., 82 percent of teachers and 68 percent of undergraduates agreed that "ADHD is overdiagnosed today." According to many critics, such overdiagnosis raises the specter of medicalizing largely normal behavior and relying too heavily on pills rather than skills—such as teaching children better ways of coping with stress.



Yet although data point to at least some overdiagnosis, at least in boys, the extent of this problem is unclear. In fact, the evidence, with notable exceptions, appears to be stronger for the undertreatment than overtreatment of ADHD.

## Medicalizing Normality

The American Psychiatric Association's diagnostic manual of the past 19 years, the *DSM-IV*, outlines three sets of indicators for ADHD: inattention (a child is easily distracted), hyperactivity (he or she may fidget a lot, for example), and impulsivity (the child may blurt out answers too quickly). A child must display at least six of the nine listed symp-

toms for at least half a year across these categories. In addition, at least some problems must be present before the age of seven and produce impairment in at least two different settings, such as school or home. Studies suggest that about 5 percent of school-age children have ADHD; the disorder is diagnosed in about three times as many boys as girls.

Many scholars have alleged that ADHD is massively overdiagnosed, reflecting a "medicalization" of largely normative childhood difficulties, such as jitteriness, boredom and impatience. Nevertheless, it makes little sense to refer to the overdiagnosis of ADHD

unless there is an objective cutoff score for its presence. Data suggest, however, that a bright dividing line does not exist. In a study published in 2011 psychologists David Marcus, now at Washington State University, and Tammy Barry of the University of Southern Mississippi measured ADHD symptoms in a large sample of third graders. Their analyses demonstrated that ADHD differs in degree, not in kind, from normality.

Yet many well-recognized medical conditions, such as hypertension and type 2 diabetes, are also extremes on a continuum that stretches across the population. Hence, the more relevant question is whether doctors are routinely di-

COURTESY OF SCOTT O. LILIENFELD (Lilienfeld); COURTESY OF HAL ARKOWITZ (Arkowitz); ILLUSTRATION BY JAN FELDT

agnosing kids with ADHD who do not meet the levels of symptoms specified by the *DSM-IV*.

Some studies hint that such misdiagnosis does occur, although its magnitude is unclear. In 1993 Albert Cotugno, a practicing psychologist in Massachu-

used. About 80 percent of children diagnosed with ADHD display improvements in attention and impulse control while on the drugs but not after their effects wear off. Still, stimulants sometimes have side effects, such as insomnia, mild weight loss and a slight stunt-

stimulant treatment compared with the 5 percent of children in that region who would be expected to meet criteria for ADHD. Moreover, increasing numbers of individuals with few or no attentional problems—such as college students trying to stay awake and alert to study—are

(About 17 percent of the 1,000 mental health professionals surveyed **mistakenly diagnosed the kids with ADHD.**)

setts, reported that only 22 percent of 92 children referred to an ADHD clinic actually met criteria for ADHD following an evaluation, indicating that many children referred for treatment do not have the disorder as formally defined. Nevertheless, these results are not conclusive, because it is unknown how many of the youth received an official diagnosis, and the sample came from only one clinic.

Clearer, but less dramatic, evidence for overdiagnosis comes from a 2012 study in which psychologist Katrin Bruchmüller of the University of Basel and her colleagues found that when given hypothetical vignettes of children who fell short of the *DSM-IV* diagnosis, about 17 percent of the 1,000 mental health professionals surveyed mistakenly diagnosed the kids with ADHD. These errors were especially frequent for boys, perhaps because boys more often fit clinicians' stereotypes of ADHD children. (In contrast, some researchers conjecture that ADHD is underdiagnosed in girls, who often have subtler symptoms, such as daydreaming and spaciness.)

### Pill Pushers?

Published reports of using stimulants for ADHD date to 1938. But in 1944 chemist Leandro Panizzon, working for Ciba, the predecessor of Novartis, synthesized a stimulant drug that he named in honor of his wife, Marguerite, whose nickname was Rita. Ritalin (methylphenidate) and other stimulants, such as Adderall, Concerta and Vyvanse, are now standard treatments; Strattera, a nonstimulant, is also widely

ing of height. Behavioral treatments, which reward children for remaining seated, maintaining attention or engaging in other appropriate activities, are also effective in many cases.

Many media sources report that stimulants have been widely prescribed for children without ADHD. As Dutch pharmacologist Willemijn Meijer of PHARMO Institute in Utrecht and his colleagues observed in a 2009 review, stimulant prescriptions for children in the U.S. rose from 2.8 to 4.4 percent between 2000 and 2005. Yet most data suggest that ADHD is undertreated, at least if one assumes that children with this diagnosis should receive stimulants. Psychiatrist Peter Jensen, then at Columbia University, noted in a 2000 article that data from the mid-1990s demonstrated that although about three million children in the U.S. met criteria for ADHD, only two million received a stimulant prescription from a doctor.

The perception that stimulants are overprescribed and overused probably has a kernel of truth, however. Data collected in 1999 by psychologist Gretchen LeFever, then at Eastern Virginia Medical School, point to geographical pockets of overprescription. In southern Virginia, 8 to 10 percent of children in the second through fifth grades received

using stimulants, according to ongoing studies. Although the long-term harms of such stimulants among students are unclear, they carry a risk of addiction.

### A Peek at the Future

The new edition of the diagnostic manual, *DSM-5* (due out in May), is expected to specify a lower proportion of total symptoms for an ADHD diagnosis than its predecessor and to increase the age of onset to 12 years. In a commentary in 2012 psychologist Laura Batstra of the University of Groningen in the Netherlands and psychiatrist Allen Frances of Duke University expressed concerns that these modifications will result in erroneous increases in ADHD diagnoses. Whether or not their forecast is correct, this next chapter of ADHD diagnosis will almost surely usher in a new flurry of controversy regarding the classification and treatment of the disorder. **M**

SCOTT O. LILIENFELD and HAL ARKOWITZ serve on the board of advisers for *Scientific American Mind*. Lilienfeld is a psychology professor at Emory University, and Arkowitz is an associate professor of psychology at the University of Arizona.

Send suggestions for column topics to [editors@SciAmMind.com](mailto:editors@SciAmMind.com)

### (Further Reading)

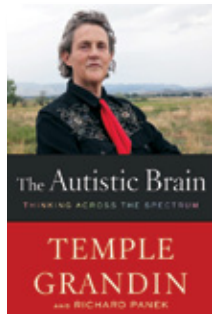
- ◆ **Is ADHD Diagnosed in Accord with Diagnostic Criteria? Overdiagnosis and Influence of Client Gender on Diagnosis.** Katrin Bruchmüller, Jürgen Margraf and Silvia Schneider in *Journal of Consulting and Clinical Psychology*, Vol. 80, No. 1, pages 128–138; February 2012.

books

EXPERIENCING AUTISM

The Autistic Brain: Thinking across the Spectrum

by Temple Grandin and Richard Panek. Houghton Mifflin Harcourt, 2013 (\$28)



When Grandin, best-selling author and autism activist, began giving lectures on the disorder in the 1980s, it wasn't difficult to spot the audience members with autism because they were mostly on the severe end of the spectrum. Today, however, her audiences are filled with shy kids and those she calls "Steve Jobs, Mrs."

Diagnosed with autism in 1949 at age two, just two years after it was first proposed as a disorder, Grandin has had a front-row seat to the entire history of

autism. Psychoanalytical theories of the 1950s and 1960s that blamed cold, distant mothers gave way to diagnostic categories based on checklists of behaviors. Although these categories are tweaked, the idea that autism is defined by its behaviors has stuck. Grandin believes that a new era of science will finally look beyond these outward manifestations to the biological underpinnings of autism.

Grandin has always been an eager participant in brain-imaging studies, from the earliest MRIs to the latest high-definition fiber tracking, which can pinpoint brain abnormalities similar to the way x-rays reveal broken bones. Perhaps the extra connections in her white fiber tracts account for her superior visual memory, and maybe her extra long left ventricle explains her poor working memory. Researchers now accept that no single brain configuration or gene is responsible for autism but more likely represents aggregates of traits: underconnectivity or overconnectivity between different brain regions or "risk" genes that make a child more susceptible to envi-

ronmental factors. Grandin runs through dozens of candidates, occasionally in numbing detail, but the overall effect is palpable excitement over an emerging biological definition of autism.

Paradoxically, Grandin says, even as autism has become more recognized, those on the spectrum may feel more powerless. She cautions against "labelled" thinking that gives those with a diagnosis an overwhelming sense of their deficits. She advises parents and educators to identify individual strengths—she describes visual, verbal and pattern thinkers—and to develop these into job skills. *The Autistic Brain* can both enlighten readers with little exposure to autism and offer hope and compassion to those who live with the condition.

Movingly, Grandin urges researchers to solicit more self-reports from people with autism, a resource often dismissed as unreliable and too subjective. But subjectivity is the point, she says. Many autistic behaviors, from rapid eye blinking to temper tantrums, may be coping mechanisms for a variety of sensory problems that go untreated. How would you know what it feels like to live with autism if you don't ask? —Nina Bai

THE GOOD APE

The Bonobo and the Atheist: In Search of Humanism among the Primates

by Frans de Waal. W. W. Norton, 2013 (\$27.95)



Chimpanzees are said to be about as clever as toddlers, but who is the more superstitious ape? In one study that set out to investigate this question, young chimps observed a researcher using a stick to retrieve candy from a clear plastic box, employing both effective and ineffective motions. The chimps quickly discerned the candy-releasing moves and proceeded to repeat only those. Four-year-old children who watched the same demonstration, however, imitated the entire routine, including the unnecessary moves. The children seemed to put their trust in the experimenter and thus invest some magical significance or "blind faith" in actions of no practical value—perhaps a symptom of the human predisposition for superstition, de Waal posits.

The ease with which our brain suspends reality—call it irrationality, imagination or faith—has been crucial to the development of religion in human culture, according to de Waal, a respected primatologist and avowed atheist. He has a scientist's curiosity about religion. Unlike prominent neo-atheists of our time, he has no interest in disproving God's existence or proving that religion poisons everything. Instead, in this richly observed and intelligent book, de Waal ponders our natural receptiveness to religion, how religion evolved and what if anything might take its place.

De Waal's dispute with religion is its self-assigned monopoly

on morality. The greatest enforcer of good behavior isn't the wrath of an omniscient deity or any dogmatic ethical framework, the Emory University primatologist says, but our emotions. De Waal offers vivid examples of emotionally guided moral behavior in animals: elephants recruiting friends to help pull a heavy box, chimps refusing undeserved rewards and bonobos comforting losers after a fight. Empathy and reciprocity, the basis of prosocial behavior, appear to have deeper evolutionary roots than religion.

If morality comes from emotions and religion from superstitions, what explains their entanglement? De Waal suggests that as communities grew larger and more impersonal, religion gained influence as a supervisor of moral behavior. But he believes secular humanism could serve a similar role and do so by appealing to human potential rather than defaming human nature.

Along the same lines, de Waal rejects Darwinian fundamentalism, which supposes that all our actions, whether ostensibly naughty or nice, are dictated by selfish genes. We can extrapolate only so much about human nature from genes and social insects that lack the neural circuitry necessary for empathy.

De Waal's view of human nature is optimistic but not naive. The good news is that if we didn't already lean in an ethical direction, moral rules "would be like seeds dropped onto a glass plate." The bad news is that both our innate empathy and the religions we create have strong in-group biases. In an ever more globalized society, humanity's greatest moral innovation—to make prosocial sentiments universal and impartial—will demand more than clashing faiths or biology. —Nina Bai

► SHAPING PERCEPTION

**Drunk Tank Pink: And Other Unexpected Forces That Shape How We Think, Feel, and Behave**



by Adam Alter. Penguin Press, 2013 (\$20)

At the 2004 Summer Olympics, researchers asked six athletes in different sports to wear red uniforms instead of their usual more subdued colors. All of them won gold. Although the color red, associated with sex, dominance and aggression,

did not convey magical powers, it may have provided subconscious cues to the athletes and their opponents that swayed the outcome of the competition.

In his new book, social psychologist Alter reveals how seemingly innocuous things, such as colors, symbols, even names, influence how we think and behave. To prove his point, Alter starts with work that began in the 1970s, which showed how pink walls in confined spaces, jails and locker rooms changed men's behavior—calming those prone to violence, even decreasing their strength.

Subtle changes to the environment can also tweak people's behavior. In one study, researchers showed 300 students the Apple or IBM logos at 77 frames per second, too fast for humans to see or process consciously. Participants exposed to the Apple but not the IBM logo performed much better on a subsequent creativity test in which they were asked to find alternative uses for a paper clip. The study revealed that subliminal exposure to a powerful cultural symbol can be enough to prompt people to think outside the box.

Changes to our social scene can also have similar effects. For instance, OPower, an energy company, pits neighbor against neighbor in a friendly game to reduce electricity use. It awards digital smiley faces to clients who conserve more than their neighbors. The system works: since its launch, the firm has accumulated savings of one billion kilowatt-hours from the U.S. electrical grid.

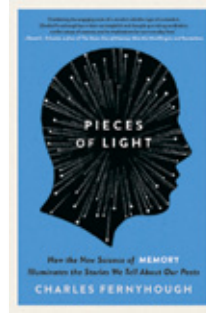
Competing with others does not always bring out our best, however. Pressure from opponents often makes people perform poorly, like when taking a test alongside your peers.

By offering a peek into human perception, *Drunk Tank Pink* may help us reevaluate our surroundings, making us aware of small cues that may direct our thoughts.

—Brian Mossop

► GRASPING OUR PAST

**Pieces of Light: How the New Science of Memory Illuminates the Stories We Tell about Our Pasts**



by Charles Fernyhough. HarperCollins, 2013 (\$26.99)

Andy Warhol had an unusual grooming habit. The artist and pop culture icon liked to wear the same cologne for three months, then store the bottle and never use it again. He hoped to associate the scents with events in a certain time period, so that sniffing the bottles later might evoke those memories.

Most of us know from experience how evocative smells can be and how they can make us recall something, often from early childhood. Unlike Warhol, most people make associations unconsciously, and retrieval occurs automatically. Warhol's "scent museum" is one of the many fascinating stories in *Pieces of Light*, by writer and psychologist Fernyhough.

For Fernyhough, our memories are basically stories. We use them to construct the narratives of our lives and those of loved ones we have lost. Often, however, the tales we tell ourselves do not match reality but are subtly altered every time we recollect them. Here Fernyhough examines his personal stories, stepping back into time to trace the memories he thought were reliable. He

seamlessly intersperses the personal aspects of this journey with descriptions of cutting-edge research into spatial navigation and memory manipulation, as well as new ideas about how memory works.

For instance, when Fernyhough revisits Cambridge, England, where he studied in the 1980s, he thinks he will be able to find his way around.

Yet he quickly gets lost. He experiences a kind of amnesia in which his mental maps have become blurred over time. He also showcases how unreliable autobiographical memory can be. Fernyhough finds that his memories have been tainted by popular clichés of the famous city.

Although most people think that memory works like a DVD, recording events as they happened, Fernyhough's examples help to clarify that this is not the case. He suggests that memory may have evolved not to recall the past but to help predict the future. In other words, we use fragments of memories to simulate upcoming events to figure out the best course of action.

Throughout, the author uses his remarkable storytelling skills to examine memory, leaving us in no doubt that it is an active, ongoing process, incorporating not only what happened then but also who we are now and who we may become.

—Moheb Costandi

ROUNDUP  
►► Defining Me

Three books explore the outside forces that influence our inner world

Find yourself feeling emotionally satisfied after a long gab session? In **Friendfluence: The Surprising Ways Friends Make Us Who We Are** (Doubleday, 2013),



former *Psychology Today* editor Carlin Flora unravels what science says about how our buddies affect our behavior and well-being. Research shows, for instance, that having a close friendship (but not a spouse) can help reduce the risk of dying from coronary disease. Flora's investigation of friendship, its benefits and pitfalls, may help readers improve their own relationships.

Brushing your teeth may have become so routine that you do it without thinking. Although habits help to "free up our processing power for other thoughts," writes psychologist Jeremy Dean, there is a flipside to this automatic pilot mode:

some behaviors, like smoking, can be detrimental. In **Making Habits, Breaking Habits** (Da Capo Lifelong Books, 2013), Dean discusses our difficulties forming and breaking habits and reveals that changing our surroundings or rethinking an action can help add a good one or modify a bad one.


From mean-spirited taunts to subtle jibes, insults can pit people against one another. In **A Slap in the Face: Why Insults Hurt—And Why They Shouldn't** (Oxford University Press, 2013), philosophy professor William B. Irvine discusses why we hurl invective and how we can protect ourselves from the sting. Insults carry weight because we care how others view us, and Irvine suggests the best way to deal with them is to keep our cool and not fire back.

—Victoria Stern

# asktheBrains

Attempting to consciously control an automated skill may disrupt a person's ability to execute it effectively.

Why do top athletes suddenly develop “the yips,” a tendency to choke under pressure? —**Matthew Robison**, *Contoocook, N.H.*

 **Jürgen Beckmann**, chair of the Institute of Sport Psychology at the Technical University of Munich, explains:

A SINGLE SHORT putt is necessary to win the tournament, but suddenly the golfer's hands cramp up, and the putt goes wide. According to several studies, as many as 48 percent of serious golfers have experienced such motor skill failures, known as the yips. It is most often used to describe golf-related errors, although the yips can strike athletes in any sport.

There is no clear explanation as to why pro athletes, who frequently encounter high-stakes moments, still choke under pressure. One suggested explanation is a neurological condition called focal dystonia that results in involuntary muscle contractions when performing a motor task and tends to affect a muscle

group that is used frequently and repeatedly. The cause is unclear, but the contractions may involve abnormalities in neural communication.


Overthinking appears to heighten the yips. Psychologist Debbie Crews found that golfers who performed poorly when putting under pressure also exhibited heightened activity in the left hemisphere of the brain, typically responsible for analytical thinking, and diminished activity in the right hemisphere, associated with coordination and visual ability. Thus, concentrating too intently appears to overshadow other important factors, such as balance and timing. Crews concluded that maintaining a balanced brain, in which both hemispheres are working at similar intensities, is ideal.

Studies have also shown that attempting to consciously control an auto-

ated skill may disrupt a person's ability to execute it and that overusing specific muscle groups may cause them to cramp.

There is hope for those who suffer from the yips. Some work suggests that changing the usual conditions under which an athlete performs a task can reverse a flawed automatic pilot setting. Neuroscientist Christian Marquardt believes that a tailored training program, which analyzes the technical issues athletes encounter in tense situations, can help them overcome the yips. Recently my colleagues and I found that increasing activity in the right hemisphere (by clenching the left fist) actually decreases an athlete's risk of choking under pressure. Other athletes, however, may simply choose to live with their yips.

How does the brain react to a romantic breakup? —**Chelsea Brennan**, *Minneapolis*

 **Xiaomeng (Mona) Xu**, a postdoctoral research fellow at the Warren Alpert Medical School at Brown University and at the Miriam Hospital, responds:

YOU'RE IN THE MIDST of a breakup and feel like a different person. You find yourself spending a lot of time longing for your ex, constantly checking her Facebook updates, and wondering what went wrong. This shift in patterns of thought and behavior may be caused by neural changes that occur after a breakup.

Neuroimaging studies have found that being rejected, even by a stranger, activates many of the same regions in the brain as when experiencing physical pain. In one study, biological anthropologist Helen Fisher of Rutgers University recruited brave participants who held still in a functional MRI scanner while they looked at pictures of the person who had recently dumped them. These participants exhibited increased brain activity in several regions associated with reward, motivation, addiction and obsessive-compulsive disorder, which helps to explain why you might struggle to let go after a romantic relationship ends.

Grief can also be a part of the breakup process. In another

brain-scanning study, researchers asked women who had gone through a recent breakup to think about their ex in an fMRI machine. They found patterns of brain activity consistent with feelings of sadness, rumination and chronic depression.

For some people, heartache can continue months after a split. A team of German investigators, studying a small group of people who were still hung up on an ex up to six months after the relationship had ended, also found brain patterns consistent with depression, such as decreased activity in the insula and the anterior and posterior cingulate cortices.

Although such studies show that heartbreak is associated with obsession and grief, the findings are limited. Our understanding primarily comes from research in which participants are asked to actively think about their ex, something people probably don't do *all* the time. Additionally, studies tend to be about the heartbroken, rather than the heartbreakers, and focus only on the period of misery postsplit. Luckily for many people, the heartache from a lost relationship fades over time, and life goes back to normal. For some, the rupture might even become a positive experience, allowing a person to get away from a dysfunctional relationship and fall in love again. **M**

Have a question? Send it to [editors@SciAmMind.com](mailto:editors@SciAmMind.com)



# MAKE IT YOUR MISSION

TO FIGHT HEART DISEASE IN WOMEN

Heart disease is still the No. 1 killer of women, taking the life of 1 in 3 women each year.

Give the women you care about the power to save their lives at [GoRedForWomen.org](http://GoRedForWomen.org).



# Head Games

Match wits with the Mensa puzzlers

## 1 MINI CROSSWORD

**Across**

- 1) Charade
- 4) "Scat!"
- 5) Refine
- 6) Hurricane center

**Down**

- 1) Skipper's cry
- 2) Pylon shape
- 3) Water tester?
- 4) That woman

	1	2	3
4			
5			
6			

## 2 MAGIC SQUARE

Complete the square below by inserting the nine letters into the grid, one per square, to create the same words reading across and down.

D E E E E L O O P

E	A	C	H
A			
C			
H			

## 3 TRIVIA SCRAMBLE

Which of the following scrambled words is least like the others?

RSHEPIGN  
ELE  
TTOANP  
HLLCCIUR

## 4 ADDING DIGITS

In the following addition example, all the digits from 0 to 9 have been used once and only once. Three digits have been filled in to get you started. Complete the example.

$$\begin{array}{r} 8 \times \times \\ + 6 \ 7 \times \\ \hline \times \times \times \times \end{array}$$

## 5 PATTERN RECOGNITION

Determine the next number in each sequence. Then convert each numerical answer to a letter (A = 1, B = 2, C = 3, and so on) to form a word reading down.

- 64, 32, 16, 8, 4, \_\_\_\_\_
- 0, 3, 6, 9, 12, \_\_\_\_\_
- 3, 4, 6, 8, 12, \_\_\_\_\_
- 2, 3, 5, 8, 13, \_\_\_\_\_
- 110, 109, 105, 96, 80, 55, \_\_\_\_\_

## 6 ANAGRAMS

Find three words made from the same five letters to complete the following story.

**The young boy \_\_\_\_\_ when he looked at his bicycle. The \_\_\_\_\_ had cracked, and a piece had broken off and lodged itself in the spokes. Much as he hated to do it, he had to \_\_\_\_\_ with his older brother for help.**

## 7 BETTING SAVVY

Al and Bob are racing over hills and flat territory. Exactly half the course is hilly, and half the course is flat. The uphill and the downhill are also exactly equal lengths. Al's pace is six miles per hour, no matter the terrain. Bob runs at 6 mph on the flat, 4 mph uphill and 8 mph downhill. Who will win the race?

## 8 MISSING LINK

What one letter, indicated by the question mark, combines with the letters in each box to form a common word?

R	I
H	
E	T

O	
	M
O	

A	Z
E	

N	
	O
E	Z

?

## Answers

1. Al. On a course that is eight miles long, for instance, Al will take one hour and 20 minutes, or 80 minutes. Bob will take 85 minutes.  
2. "D": DITHER, DOOM, DAZE, DOZEN.

3. CHURCHILL. The others were all generals: PERSHING, LEE, PATTON.  
4.  $824 + 679 = 1,503$   
5. The word is BONUS. The patterns are descending powers of 2: multiples of 3; prime numbers plus one; sums of the two preceding terms; and preceding terms minus successive squares (1, 4, 9, 16, 25, 36).  
6. PALED, PEDAL, PLEAD.

E	A	C	H
A	L	O	E
C	O	P	E
H	E	E	D

	1	A	3
	2	C	T
	4	H	S
	5	O	N
	6	Y	E



YOUR  
STORY  
CAN  
CHANGE  
SOMEONE  
ELSE'S.



**ADDICTION IS HOPELESS WITHOUT YOU**

Share your story of recovery or message of hope with someone who needs to hear it. Visit [drugfree.org](http://drugfree.org) and join The Hope Share.

THE PARTNERSHIP<sup>®</sup>  
AT [DRUGFREE.ORG](http://DRUGFREE.ORG)

# BATTERED BRAINS

by Dwayne Godwin and Jorge Cham

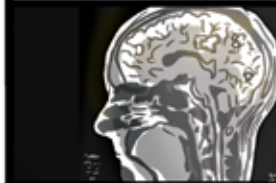
As long as there have been humans, there have been hits to the head.



Living brains are as soft as tofu (or hard gelatin).



And they are protected by the skull ...



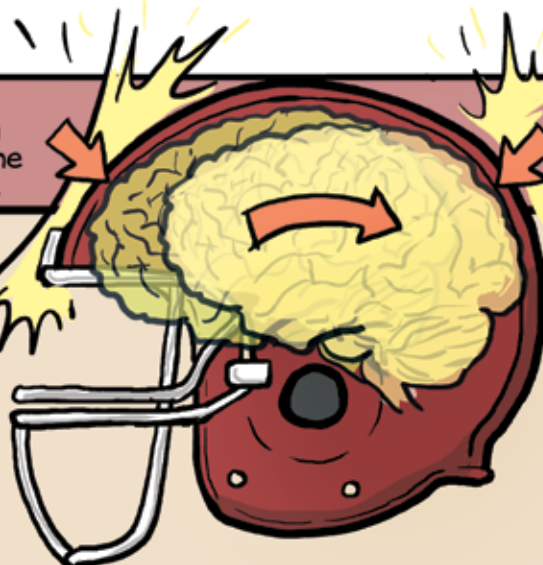
... but not perfectly.

A hit to the head gives the brain an initial smack from one side of the skull ...

... and then a second hit might happen as it rebounds on the opposite side.



Soldiers, boxers or other athletes involved in contact sports are at risk.



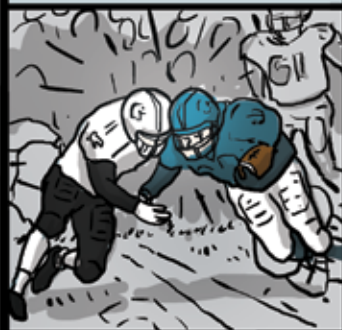
These impacts can tear apart brain connections and damage blood vessels, causing swelling and inflammation.

Recent studies of the brains of former NFL players have found an abnormal accumulation of a protein called tau.



It's a condition called Chronic traumatic encephalopathy (CTE).

CTE has some features similar to Alzheimer's disease, including memory loss and impulsiveness ...



... that correlate with the number of head injuries suffered.

Given that millions of kids risk head injuries from sports ...



... increasing their safety should be a NO-BRAINER.

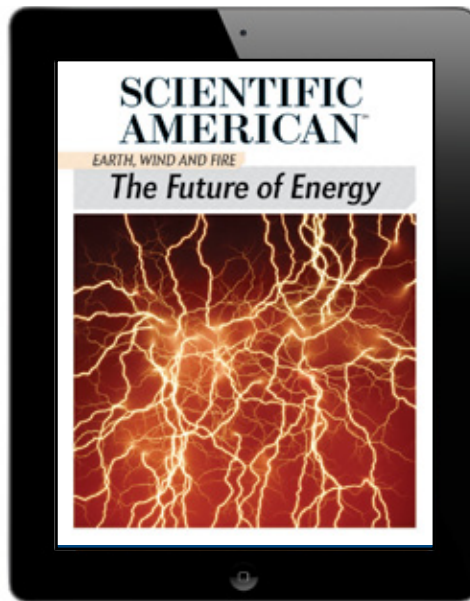
● Dwayne Godwin is a neuroscientist at the Wake Forest University School of Medicine. Follow him on Twitter @BrainyActs  
Jorge Cham draws the comic strip Piled Higher and Deeper at [www.phdcomics.com](http://www.phdcomics.com).

# EBooks that raise your tablet IQ

Science to enrich your life in a format to fit your lifestyle  
From the Editors of Scientific American



Recent years have seen a lot of hype about Higgs. Does it exist? Have scientists really found it? Do we need to worry about it creating a black hole? This eBook chronicles the continuing search for the elusive Higgs boson: the theories, the search and the ongoing questions. In essence, what you need to know to separate Higgs from hype.



For our continued survival, humanity has no choice but to change the way we power our lives. But how? Renewable energy comes in many forms, each with its own merits and drawbacks. This eBook examines sustainable energy technology from wind turbines to geothermal plants to hydroelectric power to alternative sources of fuel.



What is time? Time is precious. Time is money. Time is relative. Perhaps one of the reasons we have so many idioms for time is because it is so difficult to define. This eBook summarizes what science has discovered about how time pervades both our physical and our inner mental worlds.

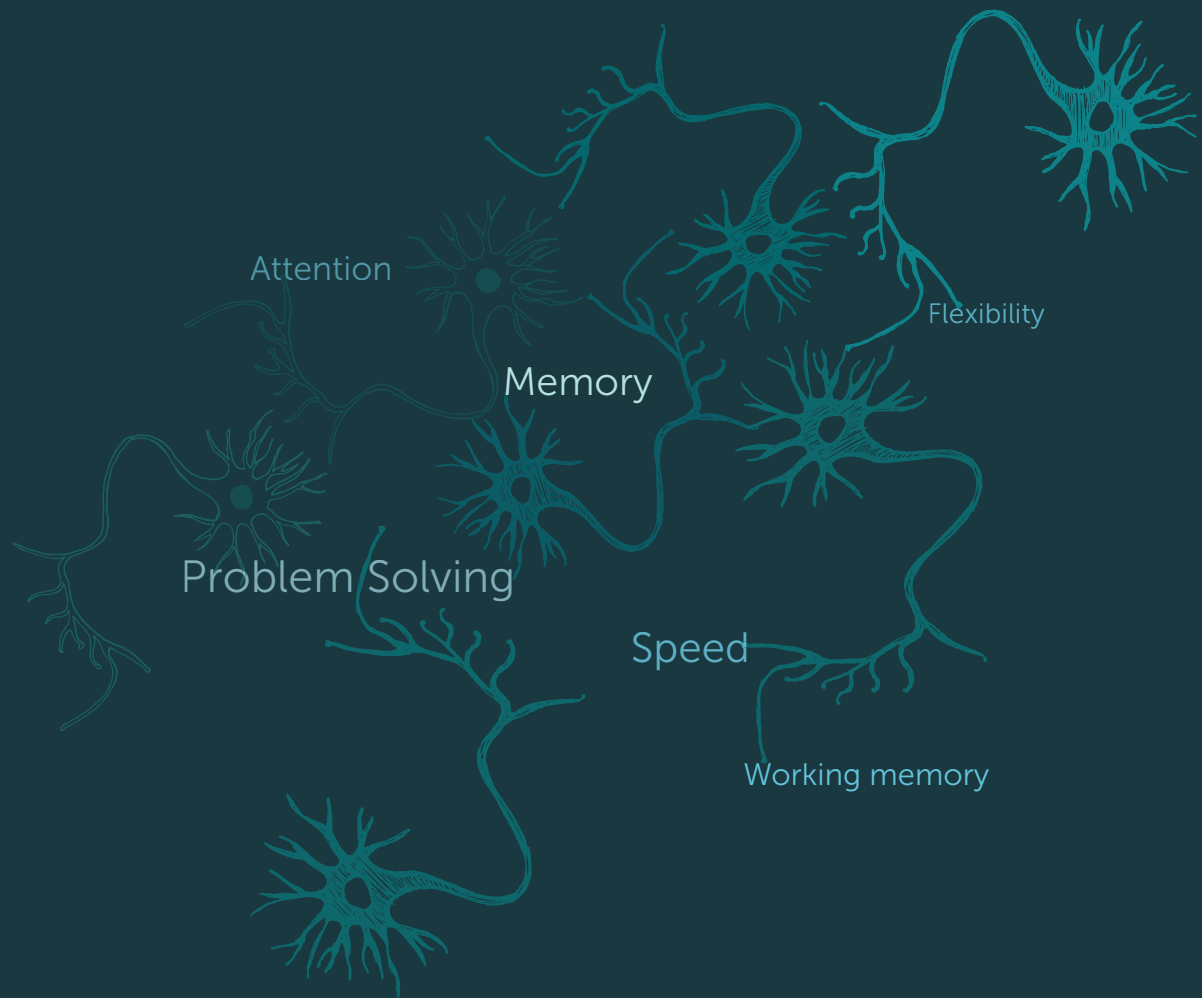
## LOOK FOR THESE OTHER TITLES

**Storm Warnings: Climate Change and Extreme Weather**  
**Beyond Human: A.I. and Genius Machines**  
**Understanding Autism: The Search for Answers**  
**Cyber Hacking: Wars in Virtual Space**  
**Lights Out: How It All Ends**

Download Scientific American eBooks now, available wherever eBooks are sold.

| [books.scientificamerican.com/sa-ebooks](http://books.scientificamerican.com/sa-ebooks) |

**SCIENTIFIC  
AMERICAN™**



## In 2013, unlock the secrets of your brain.

With **35 million users** worldwide and the **largest database** on human cognition ever assembled, Lumosity's brain training program helps leading **research collaborators** understand the human brain.

Now **you** can advance neuroscience research and unlock your own amazing potential in the process: sign up for Lumosity training today.

Every user's progress helps neuroscientists understand the brain a little better. That's how Lumosity makes the world a brighter place.

Unlock your potential at [lumosity.com](https://lumosity.com)

