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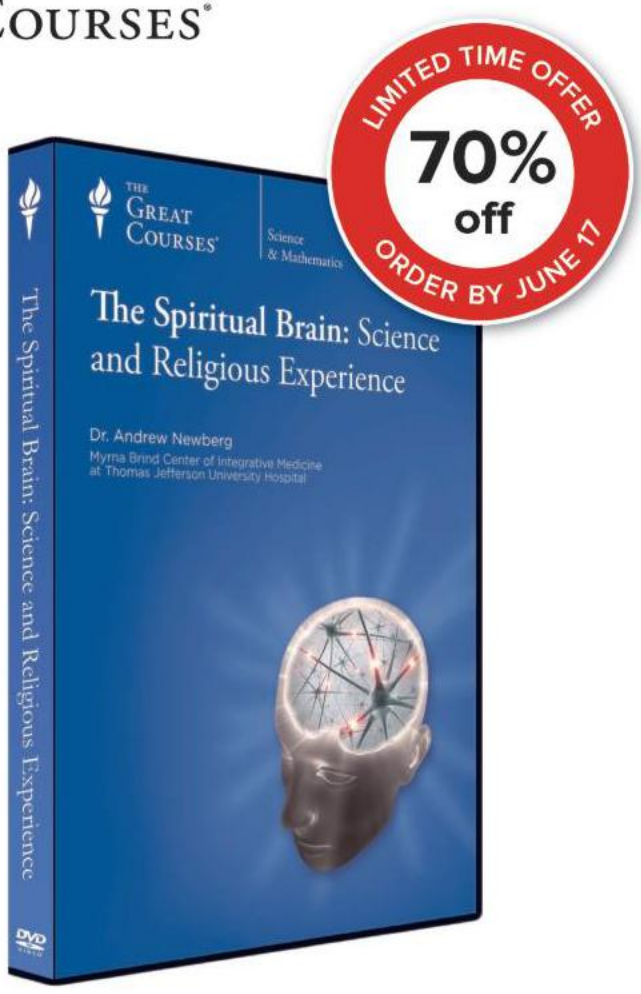

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FROM THE EDITOR

Maybe it's your back, or your neck, or your knees. Perhaps it is a constant dull ache, a pulsating throb or a shooting flare. All of us feel pain from time to time, but an estimated 100 million American adults endure it day in and day out. Finding relief can be a headache in itself. In recent years well-meaning medical efforts to control pain have produced a secondary health crisis: widespread opioid addiction and a quadrupling of overdose deaths from prescription opioids since 1999.

This tragic trend has made it clear that we need better, safer ways to relieve pain, especially chronic pain. This is the point of departure for our cover article, written by Stephani Sutherland, a journalist and neuroscientist. Her story, which begins on page 28, takes us inside the Pain Management Center at Stanford University for a look at how cutting-edge experts spell relief.

In the second part of our special report on pain, beginning on page 36, neurologists R. Allan Purdy and David W. Dodick bring us up-to-date on migraine research. Progress has been made both in deciphering the neural basis of migraine and in developing medications—which should come as good news to the one in five women and one in 16 men in the U.S. who suffer from this condition.

At the far end of the experiential spectrum from pain is laughter. And this issue is leavened with a delightful article by developmental psychologist Gina C. Mireault, who studies the giggles and glee of babies (*page 44*). "Laughter," she writes, reveals much "about infants' understanding of the physical and social world."

This magazine has often covered heroic efforts by scientists to solve a mystery or cure a disease, but sometimes the research heroes are the patients. In an article that starts on page 56, journalist Yudhijit Bhattacharjee chronicles the vital role that Ian Burkhart, a young quadriplegic, has played in helping scientists at Ohio State University develop a brain-machine interface for restoring mobility to paralyzed limbs. As one researcher told Bhattacharjee, "It's because of him that we are making these strides."

And now a final note. This will be the last regular print edition of *Scientific American Mind*. Subscribers will continue to receive a new digital version, and as a bonus, they will also receive monthly issues of *Scientific American* for the remainder of their subscription. (For more details, go to www.ScientificAmerican.com/Transfer.) It has been a joy to edit this magazine for these past two years, and let me remind you that you can always find great reporting on neuroscience, mental health and psychology at www.ScientificAmerican.com/mind.

Claudia Wallis
Managing Editor
editors@sciam.com

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SCIENTIFIC AMERICAN MIND
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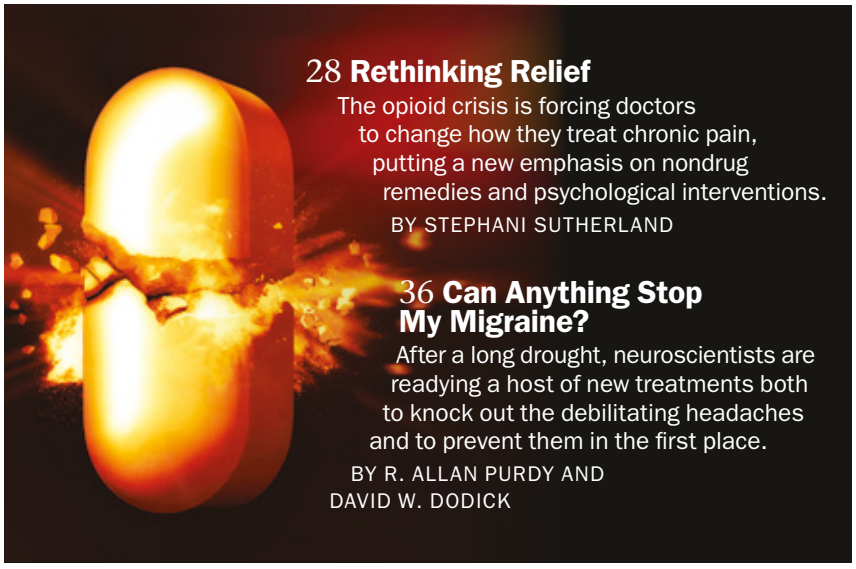

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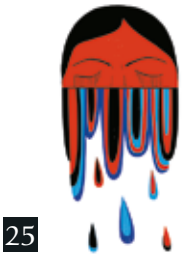

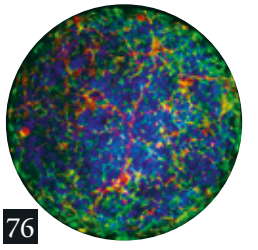

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EXERCISING AWAY DEPRESSION

In "Head Strong," Ferris Jabr writes about the mounting evidence suggesting that, for some people, moderate to vigorous exercise may be the safest, cheapest and most effective treatment for depression. Some readers shared comments on Facebook about their own experiences.

Clare Emmett writes, "I have lifelong treatment-resistant depression and exercise is the only thing that works for me," but she cautions that "it's not a one-size-fits-all solution.... It doesn't work for everyone." **Jeroen Zuiderwijk** also points out "the problem is that depression kills the motivation to exercise.... So in that respect, it's like telling people with obesity the solution is to eat less as it will reduce the craving." Psychiatrist **Elizabeth Bartlett** writes, "Exercise is really helpful.... However, as someone who has suffered from depression I am aware that it is virtually impossible to motivate myself to exercise." **Melissa Dawn** notes, "It's ... not a quick fix, but ... working out for at least 45 minutes, four times a week helps tremendously."

ACADEMICALLY GIFTED, EMOTIONALLY STUNTED?

I found Tom Clynes's article "Nurturing Genius" a bit disturbing. I began to worry when the author wrote of skipping grades as an unqualified good. After I skipped second grade, I was then the smallest, weakest and most emotionally immature kid in class for many years. This meant I got bullied savagely, without hope of recourse, and had an absolutely terrible personal life, especially when I got old enough to notice girls. The academic benefits were zero, as far as I can tell. There was no consideration in the article of emotional growth and getting along with others.

E. N. Anderson
University of California, Riverside

As a single parent to one of those peculiar creatures in that 99.9th percentile group, I feel that a community's ability to nurture gifted children lies in early identification. Virginia, for example, is where my son's intellectual abilities were first identified. There the school system reached out to parents to help them better understand what giftedness means for them and their child. We moved to Michigan 18 months ago, and I was disappointed by the state's resources for gifted education. Even if a public education system can't provide specific programs for intellectually gifted kids, it should at least implement early-identification programs.

Erin K. Dunn
Lake Orion, Mich.

How tiresome that we're still having the same old arguments about how to realize the potential of gifted children that I was hearing when I was in high school 50 years ago. It happens to be Super Bowl Sunday as I'm writing, so I propose this thought experiment: imagine switching our approaches between the development of physically versus mentally gifted children.

Picture a football team in which the coaches focused their attention primarily on the weak and mediocre players, while the most promising athletes were essentially ignored (because they would probably "succeed on their own") and socially ostracized as "nerds" and "geeks." Would you bet on that team getting anywhere near a championship?

Robert Salvage
Indialantic, Fla.

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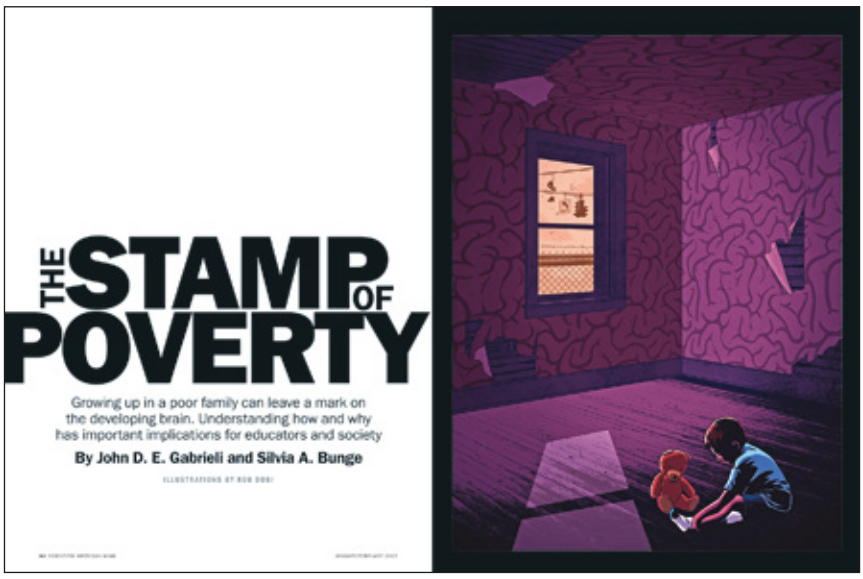

THE POVERTY GAP

John D. E. Gabrieli and Silvia A. Bunge's article "The Stamp of Poverty" struck a chord with some of our readers. On Facebook, **Matteo Rivera** writes, "All [those] people saying you can find a way out of [poverty] with hard work and believing in yourself are the ones who maintain the meritocratic system that keeps the poor being poor." **Paul Harbin** adds, "It only makes evident the level of problem which slavery and racism have created." Others point to possible upsides to experiencing poverty. **Kenneth Shattles** writes, "I can see reasons why poverty could lead to problem-solving skills and other benefits as well as being detrimental to the development of cognitive skills."

HIGH-TECH CRIME PREVENTION

Regarding "Computer Judges," by Jason G. Goldman ["Tomorrow's Criminal Justice," Head Lines], a field study in Chicago used an Internet-based test to identify teens and adults at high risk of violence, targeting them with jobs, mentors and anger management. From 2009 to 2015 the effort saved an estimated total of 324 lives and about $2 billion (as my psychology colleagues and I described in the *Review of European Studies* in March 2016). The use of tests to identify at-risk individuals has been replicated by, among others, University of Chicago economist and *Freakonomics* co-author Steven Levitt. Overidentifying violates civil rights. Underidentifying puts citizens at risk of becoming victims of sex offenses, robbery, assault, arson or murder.

Robert John Zagar
Chicago

PERSONALITY'S MISSING PIECE

In "The Morality Factor," Taya R. Cohen writes that the turning point in discovering the new dimensions of personality beyond the "big five" model was when researchers included in their study 400 adjectives used in South Korea. They found the moral dimension of honesty-humility. If they were searching the adjectives in North Korea, they would probably find a factor of unconditional obedience—to the deep satisfaction of the selection procedures in the Western corporate world. Is there any chance in the future of finding factors such as independent thinking, civilian courage, social sensitivity and proneness to activism?

Blaz Mesec
Ljubljana, Slovenia

OCTOPUS CAMOUFLAGE

"The Mind of an Octopus," an excerpt from the book *Other Minds: The Octopus, the Sea, and the Deep Origins of Consciousness,* by Peter Godfrey-Smith, contains very interesting information about the complexities of the animal's brain/mind. It was disappointing, however, not to find more about what is perhaps the most astounding capability of cephalopods: their ability to adapt their color to that of their surroundings. While a considerable amount is known about the pigment-bearing cells, or chromatophores, in their skin, little or nothing is known about the neurological processes that make it possible for these animals to camouflage in their environment. It is evident that they must be able to somehow match the light reflectance of their background, regardless of what color-vision systems their enemies or potential food sources have.

It is a very remarkable capability (for humans only achievable with much technology), and knowing how it operates in cephalopods is of much interest.

Rolf Kuehni
Tybee Island, Ga.

EDITORS' NOTE: *Although our excerpt did not include research on octopus camouflage, the topic is explored elsewhere in Godfrey-Smith's excellent book.*

SAD: JUST IN WINTER?

The Mind in Pictures cartoon "Winter Blues," by Dwayne Godwin and Jorge Cham, discusses seasonal affective disorder (SAD): what it is, how to cope, and so on. At the end, individuals suffering from SAD are "reminded" that spring and summer—brighter seasons—are just around the bend.

Is SAD also diagnosed in people who become gloomy when the weather gets brighter or when winter changes to spring (rather than fall to winter, say)?

Andrea Dasilva
via e-mail

THE EDITORS REPLY: *Although seasonal affective disorder is typically associated with winter, in rare cases (about one in 10) it can strike in summer. Such individuals are more likely to suffer depression symptoms such as insomnia, appetite and weight loss, and agitation or anxiety. For these people, sometimes a cool-climate getaway is all that's needed to lift the summer blues.*

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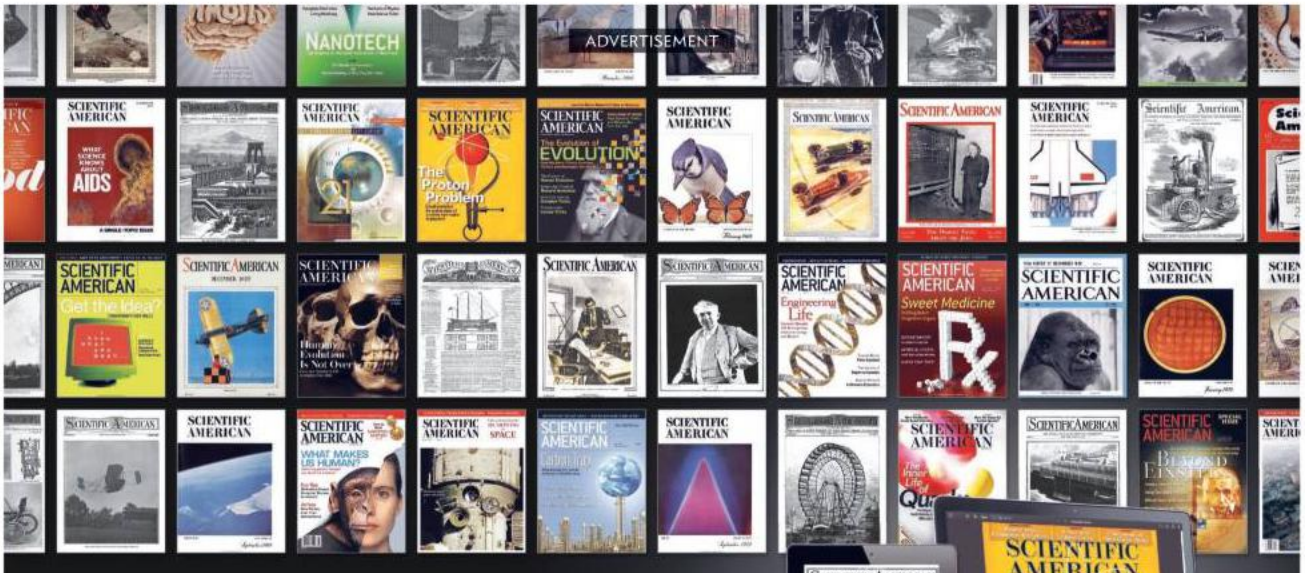

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Head Lines

A USER'S GUIDE TO THE BRAIN

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Marvelous Mirth

Laughter comes in many flavors: the giddy giggle, the mild chuckle, the lusty guffaw, the sarcastic "ha!" Its meaning is just as varied, signaling everything from amusement to discomfort to disdain. For researchers, understanding how our brain interprets this complex behavior is serious business.

ILLUSTRATIONS BY AARON McCONOMY

Real or Faux Hilarity?

Our brain knows the difference

Most of us will laugh at a good joke, but we also laugh when we are not actually amused. Fake chuckles are common in social situations—such as during an important interview or a promising first date. "Laughter is really interesting because we observe it across all human cultures and in other species," says Carolyn McGettigan, a cognitive neuroscientist at Royal Holloway, University of London. "It's an incredibly important social signal."

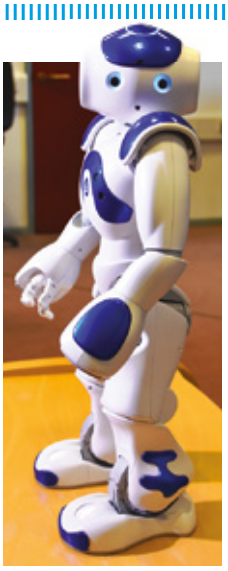
In a 2013 study, McGettigan, then a postdoctoral researcher at University College London, and her colleagues scanned the brains of 21 participants while they passively listened to clips of laughter elicited by funny YouTube videos or produced on command (with instructions to sound as natural as possible). Subjects whose medial prefrontal cortex "lit up" more when hearing the posed laughter were better at detecting whether laughs were genuine or not in a subsequent test. (This brain region is involved in understanding the viewpoint of others.) "If you hear a laugh that seems ambiguous in terms of what the person means," McGettigan explains, "it makes sense that you're going to try to work out why this person sounds like this."

In a follow-up study in 2016, McGettigan and her colleagues recruited a fresh set of participants to rate the laugh tracks on various qualities, such as authenticity and positivity. They compared these findings with the original brain data and found that the activity in the medial prefrontal cortex was negatively correlated with the genuineness of the laughs. Their analyses also revealed that both types of laughter engaged the auditory cortices, although activity in these brain regions increased as the laughs became happier, more energetic and more authentic.

Greg Bryant, a cognitive scientist at the University of California, Los Angeles, who was not involved in the study, says the findings are consistent with his research. "It doesn't look like the brain is really working that hard to classify laughs as much as it's working to figure out the vocalizer's intention," he observes.

"Evolutionarily speaking, it's good to be able to detect if someone is authentically experiencing an emotion versus if they're not," McGettigan says, "because you don't want to be fooled."

—Diana Kwon



COURTESY OF PAUL COULTER (*robot*)

Teaching Robots to Laugh

Expressing humor is a key part of being human

When robot Nao laughs, he does so with his whole body: slapping his knees, shaking his head. But the adorable android, made by SoftBank Robotics, is not merely good at expressing mirth; he can correctly identify as much as 65 percent of happy laughter outbursts in humans, according to a study presented in 2015 at a nonverbal language workshop in the Netherlands. Once robots like Nao master human laughter, they will make far more likable and realistic companions.

Nao's creators and other scientists are studying the minutiae of human laughter—acoustics, breath, body movements and vibrations—to translate them into algorithms that robots and avatars can learn.

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No Laughing Matter

A select number of people suffer from a fear of being the target of amusement

Humor has been touted as a panacea that boosts the immune system, smooths the way to success at work and even helps us to live longer. But for some people, chuckles are no laughing matter.

Those who suffer from gelotophobia, or fear of being laughed at, dread even well-intentioned jokes. "They don't trust friendly laughter—that someone is just enjoying themselves. Any laughter is bad laughter," says psychologist Willibald Ruch of the University of Zurich, who pioneered research on the unusual condition in the mid-2000s. Ruch recalls one case he observed in his laboratory: "This person would always wait for the next bus if no seat in the last row was free. He couldn't stand the idea that someone would sit behind him and laugh."

Like most phobias, this one exists on a spectrum from mild to severe. To assess the extent of the problem, scientists ask people to rate how much they identify with statements such as "It takes me very long to recover from having been laughed at" or "When others laugh in my presence, I get suspicious." Studies across the globe suggest anywhere between 1.6 and 13 percent of people suffer from gelotophobia. "We [see] the lowest numbers in countries where people are more equal, like Denmark and the Netherlands, and very high scores in countries where honor is particularly important and shame is used for social control," such as some Asian countries, Ruch says.

Researchers are just beginning to understand how gelotophobia develops. In addition to culture, parenting may play a role. In a study of 100 families, mothers and fathers who were prone to punishment and control were more likely to have kids who feared laughter. Several studies have shown that gelotophobes were often victims of bullying. Also, a 2012 study suggested a partial overlap with social anxiety, finding that 36 percent of gelotophobes meet the criteria for the disorder.

Brain-imaging studies show that gelotophobes process humor differently from other people. A 2016 electroencephalographic study revealed that when the former listen to the sounds of laughter or angry shouting, they show more activity along pathways linking their prefrontal and posterior cortices. The study's lead author, Ilona Papoušek, a psychologist at the University of Graz in Austria, believes this linkage shows they are "more sensitive to actual or supposed malicious aspects of laughter."

Another experiment published in 2016 showed that compared with a control group, gelotophobes have lower activation in their brain's reward circuits when listening to jokes. It remains unclear, though, what comes first: gelotophobia or atypical processing of laughter in the brain.

The good news, Ruch suspects, is that gelotophobia should respond to the same kind of therapies used for other phobias. The bad news is it might be hard to convince someone who dreads laughter to visit a therapist, who might smile at patients to put them at ease. ***—Marta Zaraska***

And that includes learning how to be funny. In 2016 researchers in South Korea and Singapore showed that Nao is already quite good at telling jokes. When he did a stand-up routine alongside an experienced actor, his taped performance was later consistently rated just half a point below the human on a scale of 1 to 7. Moreover, people were less disgusted by disparaging jokes if the robot told them. Nao "exceeded my expectations," says Taezoon Park, an industrial engineer then at Singapore's Nanyang Technological University and the study's lead author. Park says that in the future, scientists will optimize the robot's tone of voice, facial expressions and subtle gestures to fine-tune his comedy.

Robots still have a long way to go to fully understand human laughter, which can signify anything from happiness and amusement to sexual interest, embarrassment or anger. Also baffling to machines is the fact that laughter can vary: there is the classic ha-ha-ha laughter, speech laughter (when you speak while laughing) and smile speech (talking while smiling). Distinguishing among these types will be vital for better human-robot interactions. "Because laughter is such a crucial part of what it means to be human, we won't have convincing artificial intelligence until our machines can laugh along with us," says Gary McKeown, a psychologist at Queen's University Belfast who also works with Nao but was not involved with the new research.

Further, for robots to laugh convincingly with humans, they must be able to tell when a person wants such an interaction. "The inviting laugh is longer and louder and has a higher pitch than an isolated laugh," says Khiet Truong, a computer scientist at the University of Twente in the Netherlands who studies how people interact with virtual agents and robots. "Humans respond to an inviting laugh within half a second on average," Truong says. "We hypothesize that robots should do the same—otherwise it is no longer natural."

If these efforts succeed, we may soon have humorous robots and avatars that can assist the elderly, cheer up hospital patients, play with kids and help keep us amused.

—M.Z.

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Are You Blind to Faces of Other Races?

Some people are seriously impaired when it comes to recognizing individuals of another color

We tend to be worse at telling apart faces of other races than those of our own race, studies have found. Now research shows some people are completely blind to features that make other-race faces distinct. Such an impairment could have important implications for eyewitness testimony in situations involving other-race suspects.

The ability to distinguish among members of one's own race varies wildly: some people can tell strangers apart effortlessly, whereas others cannot even recognize the faces of their own family and friends (a condition known as prosopagnosia). Psychologist Lulu Wan of the Australian National University and her colleagues wanted to quantify the distribution of abilities for recognizing other-race faces. They asked 268 Caucasians born and raised in Australia to memorize a series of six Asian faces and conducted the same experiment, involving Caucasian faces, with a group of 176 Asians born and raised in Asia who moved to Australia to attend university. In 72 trials, every participant was then shown sets of three faces and had to point to the one he or she had learned in the memorization task.

The authors found that 26 Caucasian and 10 Asian participants—8 percent of the collective study population—did so badly on the test that they met the criteria for clinical-level impairment. "We know that we are poor at recognizing other-race faces," says Jim Tanaka, a professor of psychology at the University of Victoria in British Columbia, who was not involved in the research. "This study shows just how poor some people are." Those individuals "would be completely useless in terms of their legal value as an eyewitness," says study co-author Elinor McKone, a professor of psychology at the Australian National University. The world's legal systems do not, however, take into account individual differences in other-race face recognition, she notes.

One's lifetime level of exposure to other races could factor into a person's ability to recognize people of another color, according to the findings published in the January issue of the *Journal of Experimental Psychology: General.* Among 106 Asian participants born and raised in Australia, only about 3 percent were blind to Caucasian faces. In comparison, nearly 6 percent of the Asians born and raised in Asia had the impairment.

The effect extends to other races, too. In a study published in 2001 in *Psychology, Public Policy, and Law,* black people recruited in South African shopping malls, who had average levels of interracial contact, were better at recognizing faces of their own race than of others.

—Agata Blaszczak-Boxe

Once Dependable, Always Dependable?

Some aspects of personality may be subject to change throughout life

Many studies suggest that our personalities remain fairly stable, even over the course of decades. Yet a small but long-running study finds that traits related to dependability differ substantially between adolescence and late life. The findings raise new questions and highlight the challenges inherent in trying to track a person's defining characteristics over many years.

In the new research, published in December 2016 in *Psychology and Aging,* researchers in the U.K. reached out to a group of 635 77-year-olds from Scotland who had taken part in a study when they were 14. Back then, their teachers had rated them on six personality characteristics related to dependability: self-confidence, perseverance, mood stability, conscientiousness, originality and desire to excel. Some 60 years later a total of 174 participants from the original cohort rated themselves on the same six traits and had a close friend or relative rate them as well.

Lead author Ian Deary, a psychologist at the University of Edinburgh, expected, based on earlier findings, that dependability scores might remain stable over time. In fact, he and his colleagues found no relation between ratings for dependability-related traits over the 63-year span studied. (Deary emphasizes that his findings apply only to these six traits—not overall personality.)

One of the study's strengths is that it covers such a long period, but this characteristic also makes the research challenging. Nate Hudson, a social psychologist at Michigan State University who was not involved in the study, points out that the lack of personality stability could be an artifact of having different people rate the participants. Ideally, the same person would rate a subject's personality at both time points when assessments were made.

In decades-spanning studies, many subjects go missing, die or choose not to participate in follow-up assessments. Deary and his colleagues enrolled only 174 of the original participants, a number that makes it tough to find subtle, but real, correlations in sets of data. "It is difficult to know from their study alone whether there is truly zero stability in personality from age 14 to 77," Hudson says. Deary's work moves the field forward—but more research is needed to get a full picture of how personality evolves throughout a lifetime.

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—Melinda Wenner Moyer

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ANIMAL BEHAVIOR

Why Do Orcas Go through Menopause?

Evidence suggests it is for the greater social good

Humans and killer whales parted ways millions of years ago, evolutionarily speaking, yet the stately cetaceans have a lot in common with us: complex brains, close-knit family groups and, not least of all, grandmothers. Even though orca grannies may not sport white hair and glasses, they, too, go through menopause—a rarity in the animal kingdom known to affect only two nonhuman species: orcas and pilot whales. The question for biologists is, Why would a species live long past reproductive viability?

In an attempt to solve what he calls "a big evolutionary puzzle," behavioral ecologist and author Darren Croft and his colleagues delved into 40 years of data on births and deaths among two groups of Pacific Northwest killer whales—data collected by surveying the same ocean spots every year and identifying individual whales by their markings and scars. Female orcas stop reproducing in their 30s or 40s but can live into their 90s, and offspring stay in the same group as their mother. Previously the team established that post-reproductive females help their adult offspring survive and are important group leaders. "These old females actually act as repositories for ecological knowledge of when and where to find food," Croft explains.

These findings mesh with the grandmother hypothesis, which states that evolution favored long-living grannies because they support their children in reproducing and help to ensure their grandchildren's survival. The researchers suspected, though, that the value of having older females around was not sufficient to drive the evolution of menopause (older female elephants, for example, are matriarchs yet reproduce until death).

They decided to test the reproductive-conflict hypothesis, originally developed for ancestral humans, which suggests menopause evolved because older females were related to more members of the group but were less able to compete reproductively with younger females. When the researchers tested this hypothesis with killer whales, they found that older females do indeed have more relatives in the group, and when grandmothers and their daughters breed simultaneously, the grandmothers are less likely to have offspring that survive. As a result, older females switch from reproductive competition to cooperation for the benefit of their relatives, the team reported in January in *Current Biology*. Croft says, however, that the findings do not negate the grandmother hypothesis—rather they add to it, offering a concrete mechanism that may have driven the evolution of menopause.

Lori Marino, a neuroscientist and expert in animal intelligence who heads the Whale Sanctuary Project and was not involved in the study, agrees. "It's typically never a single explanation for complex behavior in complex animals," she says, adding that although humans and orcas inhabit very different environments, their similar social structures have caused their behavior to converge. Croft concurs: "The fact that we can draw these similarities between killer whales and humans—I just find that absolutely fascinating." —*Catherine Caruso*

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The Storybook Scientist

Researchers may have an overconfident view of their profession's objectivity

CHRIS WHETZEL

What's your mental image of a scientist? Chances are you picture not only a wild-haired, bespectacled, older man in a lab coat but also someone who is more rational, objective and intelligent than other people. Yet do scientists themselves subscribe to this stereotype?

That is the question researchers at Tilburg University in the Netherlands investigated in a study published this year in *Accountability in Research*. The team surveyed both scientists and highly educated nonscientists and asked them to rate the two categories of people in terms of objectivity, rationality, integrity, open-mindedness, intelligence and cooperativeness.

Both groups rated scientists higher on every one of these measures, yet scientists perceived bigger differences between the two groups than laypeople did. "That surprised us," says psychologist Coosje Veldkamp, the study's lead author. "We expected scientists to have a more realistic picture, but they see a larger difference," she says. (Some of these perceptions may be accurate, of course, but other research would be needed to determine that.)

The scientists' positive self-ratings may be partly explained by the human tendency to judge members of groups we belong to more favorably than others. Further investigation showed that established scientists judged their established peers more positively than those at earlier career stages, and female scientists rated researchers of their own gender more highly. "People who identify more strongly with their group display more in-group bias," Veldkamp explains. "Women are still a minority in science, and minority-group members have been found to identify more strongly with their group."

Organizational psychologist Michael Mumford of the University of Oklahoma, who was not involved in the study, cautions that surveys involve self-selecting participants who are "unlikely to be representative of scientists in general." He does not discount the results, however, given that they accord with previous research.

Veldkamp hopes that awareness of the findings may help scientists acknowledge their biases and fallibility. Scientists' overconfidence in their profession's intellectual rigor could, for instance, make them more resistant to efforts to improve the reproducibility of research. She notes that there are practices to reduce sources of bias in science—such as preregistering studies to prevent researchers from changing hypotheses and analyses midexperiment—"but we don't know how much support there is for them." Some scientists may resist such efforts, even if they agree with them, Veldkamp says, because they "may think it applies only to others." —*Simon Makin*

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Hiring by the Numbers

Interviews can be misleading

When employers are hiring, interviewing candidates is pretty much a given. Yet that practice may be overrated. Research has shown that unstructured interviews, in particular, do not inform an employer much and can actually hurt if one already has more objective data such as standardized test scores. A new study reports that interviews do not just make us less accurate at predicting how qualified a candidate will be, they increase overconfidence in predictions, compounding the problem.

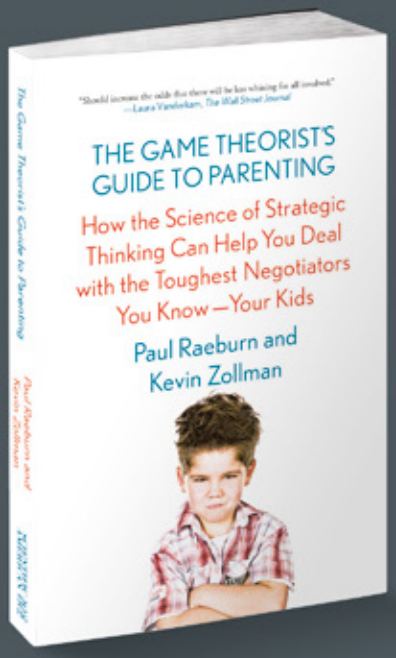
Edgar Kausel, a psychologist at the Pontifical Catholic University of Chile, once worked in retail and recalls that hiring managers did not ask consistent—or necessarily relevant—questions in interviews: "They might ask some people about their favorite celebrities to infer their personality and work ethic, then ask other people questions about their favorite color." Such unstructured interviews create noise and bias, diluting more useful information. In 2013 Jason Dana of Yale University and his colleagues reported that when people predicted college students' semester grades, interviewing them in addition to seeing their cumulative grade point averages reduced accuracy.

In the new study by Kausel and his collaborators, published in the November issue of *Organizational Behavior and Human Decision Processes,* hiring managers saw pairs of profiles based on actual airline employees and then attempted to select the better candidate. Everyone saw scores on tests of intelligence and conscientiousness, but some also saw interview scores. Surprisingly, when the raters' predictions were graded against actual job performance, managers with access to interview scores did worse.

In another experiment, undergraduates performed a similar task evaluating job candidates but could bet points on the accuracy of their forecasts. Students with access to interview scores were more overconfident in their judgments and lost more of their bets. In the real world, a human resources representative might select the wrong people, then bet big on them. "Managers generally perceive that their gut instinct is efficient and accurate when hiring," Kausel says.

Of course, these findings do not necessarily apply to all jobs or employees, nor are all interviews created equal. Kausel recommends using measures of actual performance, and when you do an interview, take a structured approach by asking everyone the same, job-specific questions and scoring answers individually rather than relying on a general impression. Then, trust the numbers.

—Matthew Hutson



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A GUIDE TO MASTERING YOUR WORLD

How to Be a Better news consumer

Lately I find myself feeling increasingly anxious, angry and demoralized after reading the news. Still, I refresh my phone's news app (my main news delivery device these days) multiple times a day, like a rat looking for one more drop of sugar water. I believe, as do most people, that citizens of a democracy have a responsibility to remain informed, but I fear this constant deluge of information has overwhelmed our ability to process it well. Regardless of your political leanings, we can all agree that the news cycle can feel relentless at times. So I dug into the research and talked to experts about some ways we can all become better consumers of news.

#1 Find the right dose. Psychiatrist M. Katherine Shear, director of the Center for Complicated Grief at Columbia University, says she has been hearing from many people that they're feeling bogged down by the news. Politically charged stories and tales of human suffering can cause sadness, anger, and even feelings of grief and loss, she says. One study done in 2015 by Pam Ramsden, who studies psychological resiliency at the University of Bradford in England, found that 22 percent of subjects experienced some symptoms of post-traumatic stress disorder (such as jitteriness or the belief that the world is extremely dangerous) after viewing violent news images on social media—and symptoms worsened with increased exposure. "We need to go there and contact that pain, and then we also need to set it aside," Shear says. When it comes to emotionally charged news, "you have to learn your own dose."

#2 Read past the headlines! Five or six words will never tell an entire story, yet people regularly share stories based solely on headlines, according to a study by Maksym Gabielkov and Arthi Ramachandran, both then at Columbia. For one month in 2016, they gathered all tweets, including links using Bitly—a Web app that shortens URLs—to a handful of major news stories and then collated them with Bitly's click logs. After crunching the data, the researchers extrapolated the fact that a majority (59 percent) of the shared links had never been clicked through and read. No wonder so many social media feeds are flooded with repetitive jabber. My friend Andrew DeVigal, a journalism professor at the University of Oregon, suggests a way to show friends you have done your due diligence: "When I share a link, I also share a piece of the content from the article so that people understand *why* I'm reacting to it and want to talk about it."

#3 Be your own fact-checker. Twenty-three percent of people admit to having shared a fake news story on Facebook, either accidentally or on purpose, according to a 2016 Pew Research Center survey. It's tempting for me, a journalist on her high horse, to chalk that up to people being willfully ignorant. Yet the news ecosystem has become so overcrowded and complicated that I can understand why navigating it is challenging. When in doubt, we need to cross-check story lines *ourselves.* DeVigal often consults AllSides, FactCheck.org and Snopes for a fuller picture of what's true or false, fact or opinion.

#4 Diversify your media diet. Because we are often connected with like-minded friends on social media, many of us have locked ourselves into echo chambers where most of the news we read or watch simply confirms what we already believe. Other aspects of our news diet are out of whack, too: a nationally representative survey done in 2014 by the Pew Research Center found that conservatives are far more likely than other ideological groups to rely on a single outlet—Fox News—for political and government news coverage. (The quick details: 47 percent of "consistent conservatives" say they get most of their info from Fox News; people with mixed political ideologies tend to rely on CNN and local television news; and "consistent liberals" are pretty evenly spread among CNN, NPR, MSNBC and the *New York Times.*)

The news landscape, like the world, is in flux. Organizations that have for decades been considered bastions of trusted reporting are regularly being called "biased" or "fake" by the president of the U.S., and some outlets truly are blurring the difference between reportage and opinionated audience bait. In this unprecedented time, I have started taking responsibility for my own information with this one small step: I have diversified my news app by seeding it with a rainbow of outlets, including the *Washington Post,* the *Washington Times,* the *Guardian,* NPR and Fox News.

These varied takes on current events help to ground me in what's really going on out there—and isn't that what news is supposed to be about? —*Sunny Sea Gold*

MAGOZ (*illustration*); PAUL PANTAZESCU © *iStock.com* (*globe*)

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Drunk Mice Get the Munchies

Alcohol activates brain cells linked to hunger

If you give a mouse a beer, he is going to want a cookie—and another, and another. If you give a person enough beer, she might find herself wolfing down a plate of greasy nachos or some other caloric snack. A study published in January in *Nature Communications* helps to explain why binge drinking, in both mice and humans, so often leads to binge eating even though alcohol is, itself, high in calories.

In the first part of the study, neuroscientists Craig Blomeley and Sarah Cains, both at the Francis Crick Institute Mill Hill Laboratory in London, injected mice with the equivalent of roughly two bottles of wine once a day for three consecutive days, mimicking a weekend of heavy drinking. Sure enough, the inebriated mice ate far more than sober mice in a control group.

To figure out why, the researchers then exposed thin-sliced postmortem mouse brains to alcohol and measured the resulting neural activity using fluorescent tags and electrodes. They found that ethanol exposure alters calcium exchange in the cells, causing specialized nerve cells called agouti-related protein (AgRP) neurons to fire more frequently and easily. These neurons normally fire when our body needs calories, and research has shown that activating them artificially will cause mice to chow down even when they are full.

The study results suggest that alcohol activates AgRP neurons in the brain, giving drunk mice the munchies. The same is likely true for humans because this brain circuitry has been highly conserved across mammal species, Cains says: "I don't doubt that AgRP neurons are activated in humans, and that's why you see this effect."

Scott Sternson, a neuroscientist at the Howard Hughes Medical Institute's Janelia Research Campus who was not involved in the research, says the work is the first to show how alcohol activates AgRP neurons and offers an "interesting and unexpected starting point" for further study.

Building on these results, Cains is interested in why alcohol seems to make us crave certain foods, such as those greasy nachos. After all, she says, "I've never had a drink and then really fancied a salad." —*Catherine Caruso*

GETTY IMAGES

A Conspiracy of Loneliness

What do conspiracy theorists really need?

Conspiracy theorists are often portrayed as nutjobs, but some may just be lonely, recent studies suggest. Separate research has shown that social exclusion creates a feeling of meaninglessness and that the search for meaning leads people to perceive patterns in randomness. A new study in the March issue of the *Journal of Experimental Social Psychology* connects the dots, reporting that ostracism enhances superstition and belief in conspiracies.

In one experiment, people wrote about a recent unpleasant interaction with friends, then rated their feelings of exclusion, their search for purpose in life, their belief in two conspiracies (that the government uses subliminal messages and that drug companies withhold cures), and their faith in paranormal activity in the Bermuda Triangle. The more excluded people felt, the greater their desire for meaning and the more likely they were to harbor suspicions.

In a second experiment, college students were made to feel excluded or included by their peers, then read two scenarios suggestive of conspiracies (price-fixing, office sabotage) and one about a made-up good-luck ritual (stomping one's feet before a meeting). Those who were excluded reported greater connection between behaviors and outcomes in the stories compared with those who were included.

"People think of conspiracy theorists as these weirdos," says psychologist Alin Coman of Princeton University, the paper's senior author, but even college students at a prestigious university can harbor these views. Coman adds, "Anybody could become entrenched in that kind of thinking if the right circumstances arise."

—Matthew Hutson

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Who Stole the Cookie from the Cookie Jar?

A small study finds older kids are more likely to confess to a bad deed

Parents of toddlers know the routine: You catch your child red-handed and sticky-fingered—the evidence of a candy raid literally written on his or her face. But instead of a confession, you get a wide-eyed denial: "I didn't do it!"

Learning to tell the truth, even at the risk of punishment, is an important part of moral development, and new evidence suggests it can take seven or more years for kids to get there.

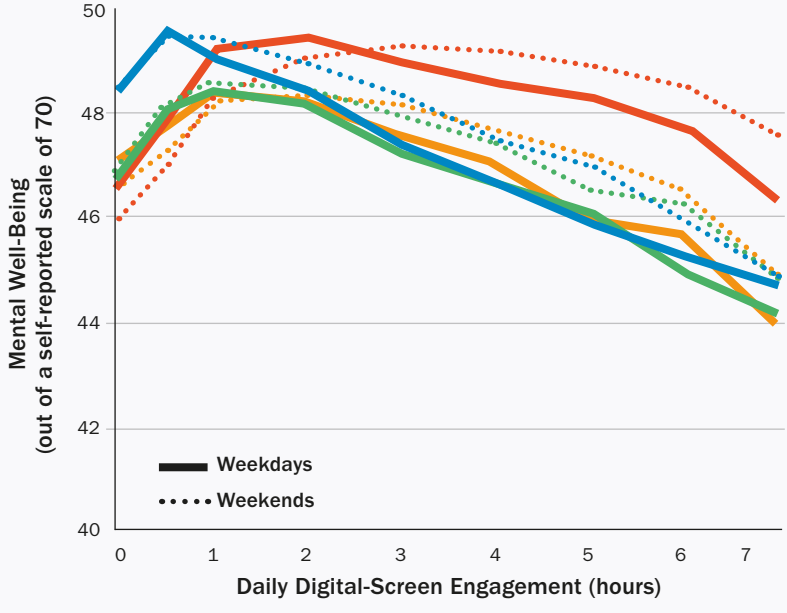
For a study published in 2017 in the *Journal of Experimental Child Psychology,* University of Michigan developmental psychologist Craig E. Smith and his colleagues recruited 48 children between four and nine years of age. They told the kids a story about a boy or girl doing something wrong, such as taking a classmate's toy or candy, and then either lying about the misdeed to a parent or confessing it. In each case, they asked the children, How would the child feel? How would the mother feel?

The children's answers were generally distributed according to age, which is in line with previous research showing a gradual growth of moral understanding and emotional complexity in early childhood. More of the four- to five-year-olds reported thinking the child in the story would feel better keeping the stolen candy, lying and escaping punishment. They imagined the parent in the study would be angry with the child who confessed. In contrast, the seven- to nine-year-olds were more likely to think the child would feel better owning up to the crime and that the parent would have positive feelings toward a confessor.

Moreover, the results of the storytelling exercise matched real-life behavior. Parents reported that regardless of age, children in the study who associated positive emotions with confessing in the story had a better history of honesty about their own transgressions.

This study dovetails nicely with past research, says developmental psychologist Angela Evans of Brock University in Ontario, whose own work suggests that children's literature can help shape moral development. In 2014 she and her colleagues found that children who were told classic stories about honesty, such as the story of George Washington and the cherry tree, in which he is praised for admitting he cut it down, were more likely to confess to ignoring researcher instructions than the children who heard stories in which bad things happened to kids who lie, as in *Pinocchio* or "The Boy Who Cried Wolf."

What parents can learn from these studies, Smith says, is to listen calmly when their child confesses rather than expressing anger. Reward the honesty even if you feel you must punish the offense. Evans adds, "Both these studies support the idea that parents need to show the positive aspects of confession because focusing on the negative consequences of lying does not improve behavior." —*Francine Russo*



THE "GOLDILOCKS" LEVEL OF TEEN SCREEN USE

It's a familiar lament: teenagers are spending all their time on digital devices, and it's wreaking havoc on their physical and mental health. But a study published in January in *Psychological Science* suggests a moderate level of use is not necessarily harmful—and may even be beneficial. The effect on well-being varies depending the type of medium or device: **TV and movies**, **video games**, **computers** and **smartphones**, as well as the day of the week (weekday versus weekend). The optimal amount of exposure peaks at around one to two hours daily during the week and longer on weekends. Limiting your teen's screen time is fine, but consider the benefits before you pull the plug entirely. —*Tanya Lewis*

DORIANGRAY *Getty Images (top)*; SOURCE: "A LARGE-SCALE TEST OF THE GOLDILOCKS HYPOTHESIS: QUANTIFYING THE RELATIONS BETWEEN DIGITAL-SCREEN USE AND THE MENTAL WELL-BEING OF ADOLESCENTS," BY ANDREW K. PRZYBYLSKI AND NETTA WEINSTEIN, IN *PSYCHOLOGICAL SCIENCE*, VOL. 28, NO. 2; JANUARY 13, 2017 *(bottom)*

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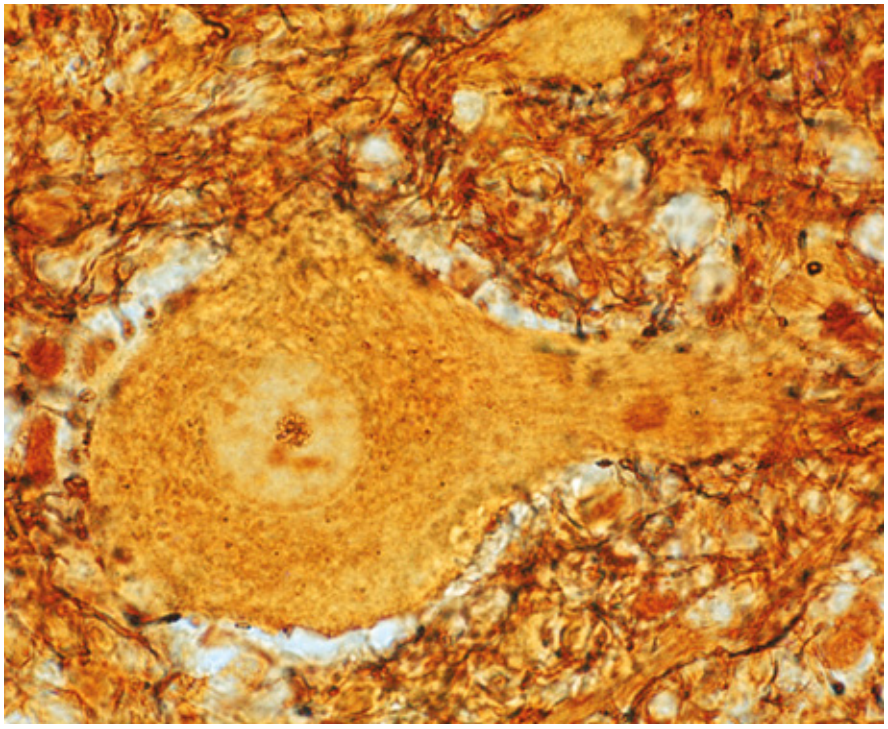

BIOPHOTO ASSOCIATES *Science Source* (*left*); © ISTOCK.COM (*right*)

Sleep Shrinks the Brain

The process keeps the attic of your mind well organized

Every day you wake up with a slightly less connected brain than the night before. New research in mice reveals that during sleep the connections between brain cells, which hold information learned throughout the day, undergo massive shrinkage. The process makes room for learning new memories while shedding weak ones. As author Marie Kondo would put it, this is the brain's very own "life-changing magic of tidying up."

"When we are awake, learning and adapting to the environment, synapses—or the connections between neurons—get strengthened and grow," says neuroscientist Chiara Cirelli of the University of Wisconsin–Madison. "But you can't keep growing the synapses. At some point, you will saturate them."

After more than a decade of study, Cirelli and her colleagues have finally found direct evidence that synapses reset at night. They reported their findings in February in *Science*. Using electron microscopy to look at thousands of ultrathin brain slices taken from awake and sleeping mice, they found that after sleep, the size of most synapses—specifically, the surface area where two neurons touch each other—shrank by about 18 percent.

Although the findings were in mice, Cirelli suspects this synaptic resetting also occurs in people. Indirect evidence, for example, from electrophysiological recordings of the human brain before and after sleep, is consistent with this idea, she says.

This shrinkage appears to spare important memories. About 20 percent of synapses, which were the largest and may hold well-established memories, did not shrink. Less important memories may not get entirely axed but merely pared down—although each synapse shrinks, the overall pattern of connections that constitute a memory remains.

The brain needs to be off-line for this shrinking to occur, Cirelli says, which could be one reason we sleep: "It's the price we have to pay to be able to learn new things." Yet the primary purpose of snoozing remains debated. Some suggest sleep's central function is to repair worn-out cellular machinery, and numerous studies have shown sleep's critical role in consolidating memories. Together with previous research in flies, "these findings strongly support the idea that synaptic resetting is an evolutionarily old function of sleep," says Niels C. Rattenborg of the Max Planck Institute for Ornithology in Munich, who was not involved in the new study. In other words, forgetting nonessential information might be just as vital as learning new material.

—Bahar Gholipour

Ask in Person

People respond better to face-to-face requests than e-mails

When you need a favor, there's nothing more convenient than shooting off an e-mail or two. It also saves you the awkwardness of in-person pleading. Just don't expect the same results.

Two new studies show that people nonetheless believe e-mail requests are just as effective as asking face-to-face. In the first study, published in the March issue of the *Journal of Experimental Social Psychology,* 45 participants were told they would have to ask 10 strangers, either in person or via e-mail, to complete a survey for no pay. People in both groups said they expected one in two strangers to agree, and both were wildly wrong. More than 70 percent of people approached in person complied; among those who received e-mails, the response rate was just 2 percent.

In a second study, people were recruited to complete a paid survey via e-mail or in person. Before they began the paid survey, they were offered the chance to complete a second, unpaid one. Again, canvassers underestimated in-person compliance and overestimated e-mail responses to the unpaid task. The e-mailers had an inflated idea of how much people trusted them and how much empathy they garnered. "If people want to have more effective e-mail messages, they have to include more personal information to facilitate building initial trust," says Mahdi Roghanizad, a business professor at Western University in Ontario, Canada, who co-wrote the paper.

What about soliciting a friend or colleague? Face-to-face is still best, preliminary data suggest. "When a friend comes to you and asks in person," Roghanizad says, "it means they are in serious need or respect you enough to pay a visit."

—Matthew Hutson

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Through a Glass, Darkly

Most of us really don't understand how mirrors work, which makes for some fun reflective deception

We are surrounded by mirrors all day, every day—when we drive, brush our teeth, check our hair while heading out the door. Yet for all their ubiquity, mirrors remain somewhat mysterious. In folktales and fiction at least, they can be conduits to spiritual, magical or supernatural realms: mirrors can out the soulless vampires in our midst. They can summon the legendary hook-handed murderer known as Candyman. And the Mirror of Erised—of Harry Potter fame—holds the remarkable power to lay bare its viewer's deepest desire.

Our enchantment with mirrors may stem in part from the fact that they often defy expectations. Not only do we find the right-left reversal of reflecting surfaces discomfiting, but many of our hard-won intuitions about how mirrors work are dead wrong. Psychologist Marco Bertamini of the University of Liverpool in England and his colleagues have identified three false beliefs we typically have about mirrors: First, people usually predict that they will see themselves in a mirror before they arrive in front of it. In other words, they overestimate what is visible in a mirror. This miscalculation is called the "early error." Second, most people assume that their projection on a mirror (the outline they could trace with a pen on its surface) is the same size as their body. In reality, that projection, as they see it, is half the physical size of their body. Third, people tend to think that the mirror projection of their own image will shrink with distance, so they will see their full body in a small mirror if they move far enough away from it. But in fact, distance does not affect the size of a body's projection. Moreover, some research indicates that people see objects in a mirror as somehow less real than nonreflected ones. The illusions we present here all take advantage of how little we grasp about the looking glass. M

VCG WILSON *Getty Images (painting)*; SEAN McCABE (*Martinez-Conde and Macknik*)

THE FAIREST OF ALL?

Bertamini and his colleagues Richard Latto and Alice Spooner, both then at Liverpool, coined the term "Venus effect" to describe a curious phenomenon that is exemplified by artistic depictions of the Roman goddess of love. Such portrayals were all the rage in the Renaissance. In some paintings, Venus appears with a small mirror—held by Venus herself or someone close to her—which reflects her face.

Asked to describe paintings such as Titian's *Venus with a Mirror* or Diego Velázquez's *Rokeby Venus* (*above*), most people say the goddess is looking at herself in the mirror. The problem, though, is that the mirror is not placed in Venus's line of sight. According to the laws of optics, if we can see Venus's face in the mirror, then she is watching us, too, rather than admiring her own image. This kind of illusion is not constrained to paintings: it also occurs in photographs and in real life, and television and film productions often take advantage of it.

One reason for the Venus effect is that we are notoriously bad at estimating the view from someone else's vantage point. Researchers have not ascertained whether the Old Masters included the Venus effect in their works unintentionally or as the result of conscious artistic choices. We may never know, but it seems likely that Velázquez—the creator of the intricate game of mirrors that is the painting *Las Meninas*—might have known mirrors well, along with our inability to truly grasp them.

BY SUSANA MARTINEZ-CONDE AND STEPHEN L. MACKNIK

Susana Martinez-Conde and Stephen L. Macknik are professors of ophthalmology at SUNY Downstate Medical Center in Brooklyn, N.Y. They are the authors of *Sleights of Mind,* with Sandra Blakeslee, winner of a Prisma Prize for best science book of the year (http://sleightsofmind.com).

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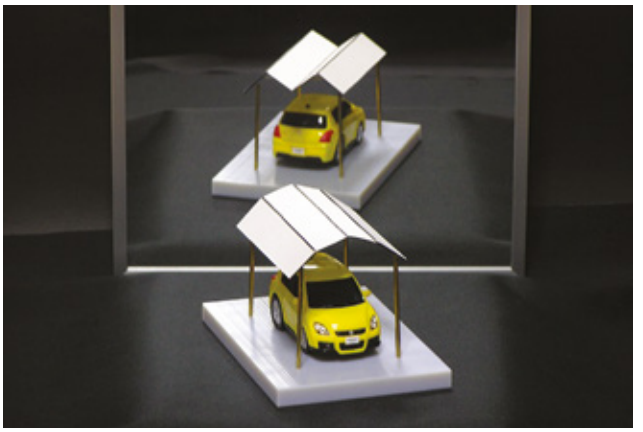
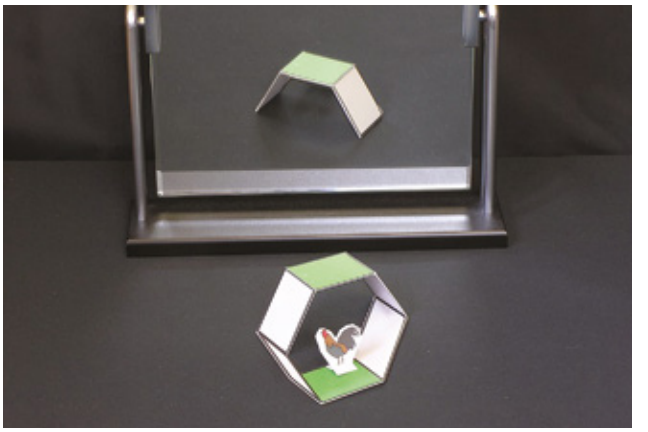
IT'S ALL DONE WITH MIRRORS





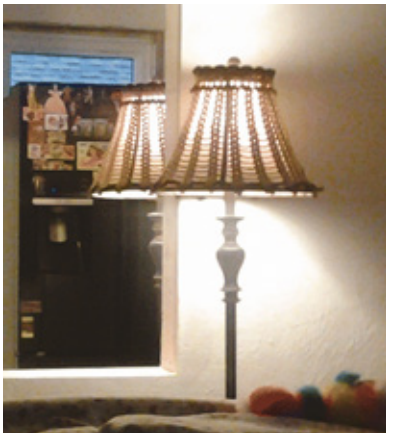
Kokichi Sugihara's interest in illusions grew out of what seemed at first like a software mishap. The mathematical engineer at Meiji University in Japan had developed a computer program to read building blueprints and other line drawings of three-dimensional objects. To test it, he fed his program images of impossible objects, such as Penrose steps (famously drawn by M. C. Escher), which look like they go up and down at the same time. To his surprise, the software did not always spit out an error message. Instead it interpreted many of these images as 3-D solids that only appeared impossible if viewed from a specific vantage point. Once he convinced himself that the software's interpretation was correct, he set out to construct "impossible solids," initially with cardboard and more recently with a 3-D printer. In the process, Sugihara also produced new kinds of impossible objects. His most recent illusions rely on mirrors and epitomize the axiom that things are not always as they seem. (For more details and templates to make some of these objects, visit Sugihara's Web site at http://home.mims.meiji.ac.jp/~sugihara/Welcomee.html.)

In the illusion on the left, a yellow toy car inside a tiny garage sits in front of a vertical mirror, but the reflection of the garage roof looks to be the wrong shape. Sugihara's trick requires two specific and simultaneous vantage points—seeing the car directly and through the mirror. Yet the actual shape of the roof does not match how it looks from either of these viewpoints. You can construct your own paper model of Sugihara's ambiguous garage roof by following the links at the home page of his Web site.

Sugihara's newest illusion showcases a mirror that fails to reflect half of a solid object sitting in front of it. Hold off on the garlic necklace and holy water, though: once again, it's a matter of perspective. The lower—and nonreflected—part of the image is a 2-D drawing that lies flat on the ground and appears to take up volume only from a particular vantage point. To make your own half-disappearing hexagon, follow the link labeled "Fourth Generation: Partly Invisible Objects" at Sugihara's Web site. To achieve the best effect, tilt the mirror slightly downward.

COURTESY OF KOKICHI SUGIHARA (*top*); FROM "TWO LAMPS OR ONE? AN ILLUSIONARY MIRROR," BY F. RICHARD FERRARO ET AL., IN *PERCEPTION*, VOL. 45, NO. 6; JUNE 2016 (*bottom*)

TWIN LAMPS?



Psychologist F. Richard Ferraro of the University of North Dakota and his wife, Jacqueline Lee Foster Ferraro, were remodeling their kitchen when they discovered an intriguing illusion. Look at the picture to the right. Do you see two separate lamps or one lamp reflected in a mirror? Richard Ferraro knew that there were two lamps because he had just moved one of them from the living room to the kitchen. But as he sat down on the living room couch, he could not shake the feeling that he was looking at a single lamp reflected in a mirror (in reality, a pass-through to the kitchen). The couple teamed up with then North Dakota student Cassidy Brougham and showed this same picture to 100 college undergraduates on campus. The team found that 72 people saw one lamp, and 28 saw two. Our visual system's preference for the simplest perceptual explanations for what we see around us, the so-called simplicity principle, may account for this skew.

MORE TO EXPLORE

- **The Venus Effect: People's Understanding of Mirror Reflections in Paintings.** Marco Bertamini et al. in *Perception,* Vol. 32, No. 5, pages 593–599; May 2003.
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- **Ambiguous Cylinders: A New Class of Impossible Objects.** Kokichi Sugihara in *Computer Aided Drafting, Design and Manufacturing,* Vol. 25, No. 4, pages 19–25; 2015.
- **Through the Looking-Glass: Objects in the Mirror Are Less Real.** Preeti Sareen et al. in *Psychonomic Bulletin & Review,* Vol. 22, No. 4, pages 980–986; August 2015.
- **Two Lamps or One? An Illusionary Mirror.** F. Richard Ferraro, J. L. Foster Ferraro and Cassidy Brougham in *Perception,* Vol. 45, No. 6, pages 684–686; June 2016.

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NEUROLOGY

Contacting Stranded Minds

Brain imaging can establish a two-way lifeline to some severely brain-damaged patients

> *"Solitude, isolation, are painful things, and beyond human endurance."*
> —From *The Mysterious Island,* by Jules Verne, 1874

Imagine you are an astronaut, untethered from your safety line, adrift in space. Your damaged radio lets you hear mission control's repeated attempts to contact you, but your increasingly desperate cries of "I'm here, I'm here" go unacknowledged—you are unable to signal that you're alive but injured. After days and weeks of fruitless pleas from your loved ones, their messages cease. You become lost to the world. How long do you keep your sanity when you are locked in your own echo chamber? Days? Months? Years?

This nightmarish scenario is vividly described by British neuroscientist Adrian Owen in his upcoming book *Into the Gray Zone* (Scribner). Taking my evening bath while dipping into its opening pages, I only put the book down after finishing hours later, with the water cold. The story of communicating with the most impaired neurological patients at a greater distance from us than an astronaut lost in space is told by Owen in a most captivating manner.

BY CHRISTOF KOCH

Christof Koch is president and chief scientific officer of the Allen institute for Brain Science in Seattle. He serves on *Scientific American Mind*'s board of advisers.

COMMUNICATING WITH THE MOST IMPAIRED NEUROLOGICAL PATIENTS IS AKIN TO **RADIOING AN ASTRONAUT LOST IN SPACE.**

A professor at Western University in Ontario, Canada, Owen pioneered brain-imaging technology to establish what islands of awareness persist in patients with severe disorders of consciousness. These people are bedridden and seriously disabled, unable to speak or otherwise articulate their mental state following traumatic brain injury, encephalitis, meningitis, stroke, or drug or alcohol intoxication. Two broad groups can be distinguished among those who do not quickly succumb to their injuries.

Vegetative state patients, in the first group, cycle in and out of sleep. When they are awake, their eyes are open, but attempts to establish bedside communications with them—"if you hear me, squeeze my hand or look down"—meet only with failure. These patients can move their eyes or head, swallow and yawn but never in an intentional manner. Nothing is left but surviving brain stem reflexes. With proper nursing care to avoid bedsores and infections, these individuals can live for years.

Consider Terri Schiavo, the woman in Florida who lingered for 15 years in a vegetative state until her medically induced death in 2005. Given the very public fight between her husband, who advocated discontinuing life support, and her parents, who believed that their daughter had some measure of awareness, the case caused a huge uproar. It was litigated up and down the judicial chain and eventually landed on the desk of then president George W. Bush. Despite continued legal wrangling to keep Schiavo alive, her husband ultimately prevailed in his wish to have his wife taken off life support.

Medically, her case was uncontroversial. She had brief episodes of automatisms: head turning, eye movements and the like but no reproducible or consistent, purposeful behavior. She showed no brain waves on electroencephalographic scans, indicating that her cerebral cortex had shut down, confirmed by her autopsy.

Given helicopters and modern emergency room medicine, her case is not an isolated one. With some rare exceptions, vegetative state patients are a modern phenomenon: these individuals depend on rapid, massive surgical and pharmacological intervention. Exact numbers are difficult to arrive at because there is no central registry and many of these patients are relegated to hospices and nursing homes or are cared for at home. Estimates of vegetative patients in the U.S. range from 15,000 to 40,000.

In a more ambiguous category are minimally conscious state (MCS) patients, who have some ability to communicate their internal state but usually only in a minimal or inconsistent manner. They may smile or cry in appropriate emotional situations, vocalize or gesture on occasion, track salient objects with their eyes, and so on.

SEAN McCABE

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JASU HU

Properly diagnosing vegetative patients remains a great challenge for clinicians. Unlike comatose patients, who may look dead to the naive viewer, vegetative patients are clearly alive. To loved ones desperately searching for any signs of recognition and recovery, they appear to be making an attempt to communicate. Who is to say that there may not be remnants of awareness of pain and distress in these patients living in a murky zone between fleeting consciousness and nothingness? Or, worse, maybe a full-blown stream of consciousness but an inability to cry out for help?

Enter modern neurotech, with its armamentarium of brain scanners. A slew of experiments had shown already in the late 1980s that brain activity could be reliably evoked in healthy volunteers by merely thinking—silently counting backward or imagining playing soccer. Such experiments are a spectacular confirmation of pure mind affecting matter; for example, thinking about kicking a soccer ball without moving a single muscle induces enhanced blood flow to that part of the brain involved in planning the bodily action.

Owen and his collaborators—in particular, Steven Laureys of the University of Liège in Belgium and Melanie Boly, now at the departments of neurology and psychiatry at the University of Wisconsin–Madison—developed two tasks that reliably evoke brain activity in two

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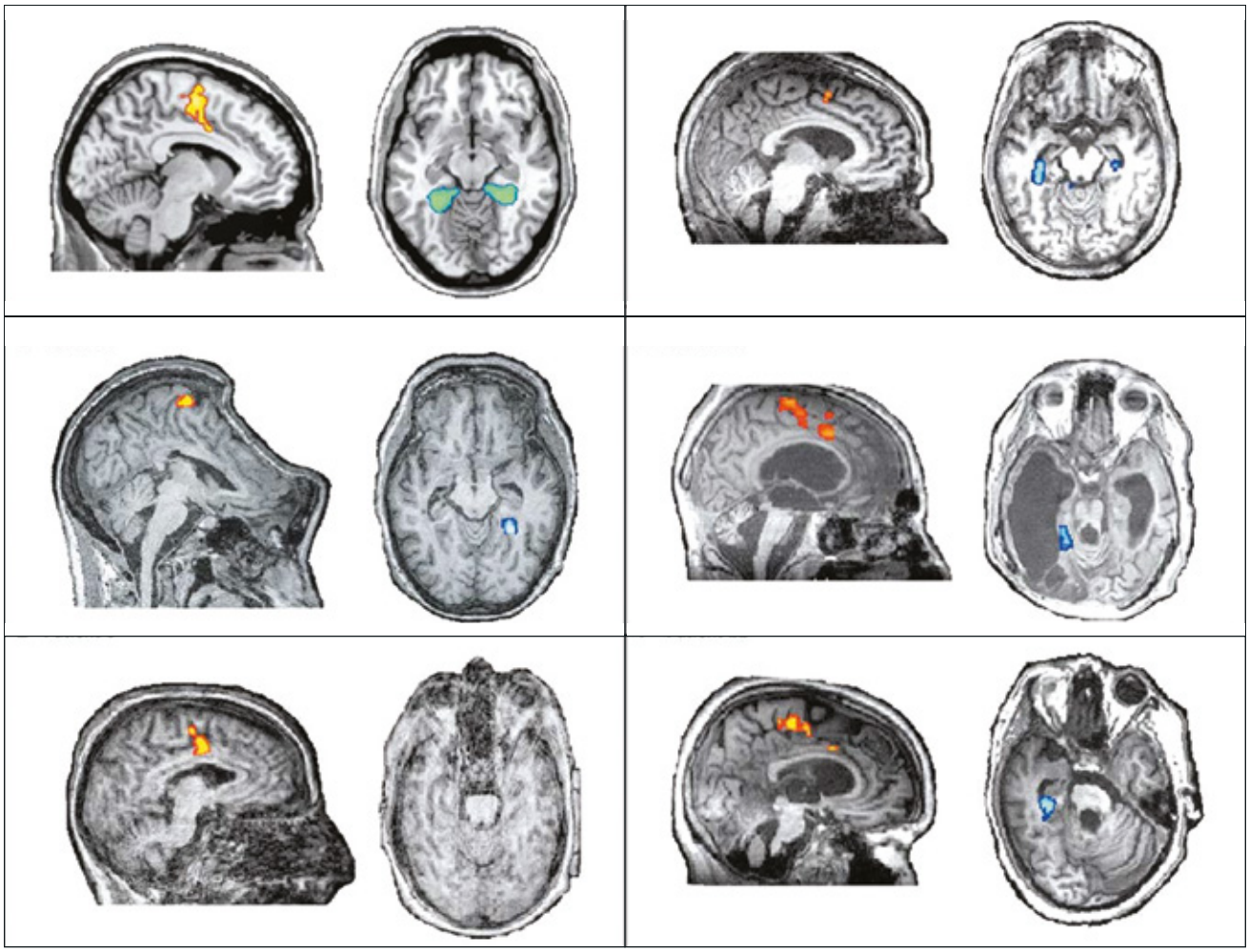

Is anybody in there? Seeking a way to reach consciousness-impaired patients, researchers tested two tasks with healthy volunteers in a functional MRI scanner. The first was to imagine playing tennis. This evoked activity in an area on top of the brain (*orange* and *yellow*). A second task—taking a mental tour of one's home—sparked activity in the middle of the brain (*green* and *blue*). The top left panel shows pooled results for the volunteers. The other panels show that five patients with consciousness disorders (out of 54 tested) were able to generate similar responses.

FROM "WILLFUL MODULATION OF BRAIN ACTIVITY IN DISORDERS OF CONSCIOUSNESS," BY MARTIN M. MONTI ET AL., IN *NEW ENGLAND JOURNAL OF MEDICINE*, VOL. 362, NO. 7; FEBRUARY 18, 2010

distinct cortical regions that can be seen with functional MRI.

The first task for volunteers in the scanner was to think about playing tennis, hitting a fictitious ball back and forth across an imaginary net. The resulting scans showed increased hemodynamic activity (more cerebral blood flow and nutrient supply) to their supplementary motor area (SMA) at the top of the head. The second task—to mentally walk from room to room inside their house— increased activity in the parahippocampal gyrus (PHG), an area deep in the brain that encodes the representation of space and spatial relationships.

One activity could easily be distinguished from the other. Because this type of willful and sustained mental effort goes hand in hand with vivid conscious experience ("I can see my right hand gripping the racket and swinging it"), it is taken to be as good a marker of consciousness as any.

The question Owen and his team then effectively posed to minimally conscious patients was the extent to which these individuals, behaviorally unresponsive to most requests put to them, could regulate their brain activity when asked to carry out one or the other imagery task repeatedly for 30 seconds.

Carol, a 23-year-old woman hit by two cars while walking across a road talking on her cell phone, was diagnosed as being in a vegetative state, with substantial damage to her frontal lobes. Yet to the surprise of the clinical staff, she could carry out both mental tasks, willfully up-regulating activity in either her SMA or PHG, depending on which task was requested. Carol therefore appeared to have some level of consciousness and cognitive control left, even though none of it could be observed with standard clinical tests.

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Over the next several years a study of 54 patients with consciousness disorders at two clinical centers—in Cambridge, England, and in Liège—confirmed the basic finding. Five patients could willfully modulate their brain activity in a controlled manner. Of these, four were among the 23 study patients that had been labeled vegetative. This observation suggests that perhaps 20 percent of vegetative state patients are misdiagnosed—they are at least somewhat conscious, a finding that aligns with some previous estimates. Subsequent bedside testing confirmed that a few of the patients were indeed in a minimally conscious rather than a vegetative state. Given the hectic pace of modern hospital settings, it is easy for the overworked care staff to miss the occasional subtle life signs of somebody locked inside their damaged brain. (Such a case—the story of Maggie—was evocatively described by neurologists in the November/December 2016 issue of *Scientific American Mind*.)

> AROUND 20 PERCENT OF VEGETATIVE STATE PATIENTS APPEAR TO BE MISDIAGNOSED—THEY **ARE AT LEAST SOMEWHAT CONSCIOUS.**

Two of the five patients in the English and Belgian study who succeeded on the imaginary tasks in the scanner nonetheless remained behaviorally incommunicado. That is, from the outside, they appeared alive yet without a mind. Only their brain-imaged responses revealed that they retained a conscious voice.

Surprisingly, of the 31 minimally conscious patients in the study, only one could manage the imaginary tasks. An editorial accompanying the publication of the article reporting these results in the prestigious *New England Journal of Medicine* cautioned that such willful manipulation of brain activity was seen only in a few patients and does not imply the existence of an internal stream of thought of the kind you and I experience throughout the day. Fair enough. But what is remarkable and a potential game changer for those patients is that this technique was adapted by Owen and his colleagues—in particular, Martin M. Monti, now a psychology professor at the University of California, Los Angeles—to establish two-way communication. Patients could signal yes to a question by imagining playing tennis for repeated periods of half a minute. They could give a no answer by engaging in mental navigation through their home. This cumbersome technique works reliably in healthy volunteers—cumbersome because the brain scanning and associated computer processing take many minutes for a single yes or no to be transmitted. Answers can be decoded with perfect accuracy from the subject's hemodynamic activity in one of the two brain regions: SMA or PHG.

The team of scientists and neurologists tried this with one Serbian patient who had suffered massive brain injury five years earlier. Though considered to be in a clinically vegetative state, the young man correctly signaled that he had brothers but no sisters, that his dad's name was Alexander but not Thomas, and that his last vacation was in the U.S.

This finding is remarkable. What does it feel like if, after five years of utter silence, you can finally send a few sparse messages to the outside world and come back from that remote gray zone? The team asked the man one final question: "Do you want to die?" The answer, as read out from his brain activity, was hauntingly inconclusive, and the experiment then ended.

Owen successfully repeated this communication task a couple of years later with Scott, a young man involved in a traffic accident. Declared a vegetative state patient, Scott was able to answer questions put to him—"Are you in any pain?" was one, to which he replied no.

For a variety of practical, technical and scientific reasons, communicating via a string of yes or no queries in a magnetic scanner is not routine clinical practice for brain-injured patients. It is not only demanding of equipment, people and time but also prone to generating incorrect answers.

Many patients are unable to drive activity in the SMA and PHG or can do so only erratically. Procedures that work perfectly well in healthy research subjects fail when tested in those whose brains have undergone massive changes because of disease or trauma. Carrying out an imaginary motor or navigation task is cognitively less demanding than answering questions using one of these two tasks, which explains why only a handful of consciousness-impaired patients have successfully communicated in this manner. The majority remain sadly lost to the world. **M**

MORE TO EXPLORE

- **Willful Modulation of Brain Activity in Disorders of Consciousness.** Martin M. Monti et al. in *New England Journal of Medicine,* Vol. 362, No. 7, pages 579–589; February 18, 2010.
- **Dissociations between Behavioural and Functional Magnetic Resonance Imaging-Based Evaluations of Cognitive Function after Brain Injury.** Jonathan C. Bardin et al. in *Brain,* Vol. 134, No. 3, pages 769–782; March 2011.
- **Into the Gray Zone: A Neuroscientist Explores the Border between Life and Death.** Adrian Owen. Scribner, 2017.

From Our Archives

- **In Search of Hidden Minds.** Joseph J. Fins and Nicholas D. Schiff; November/December 2016.

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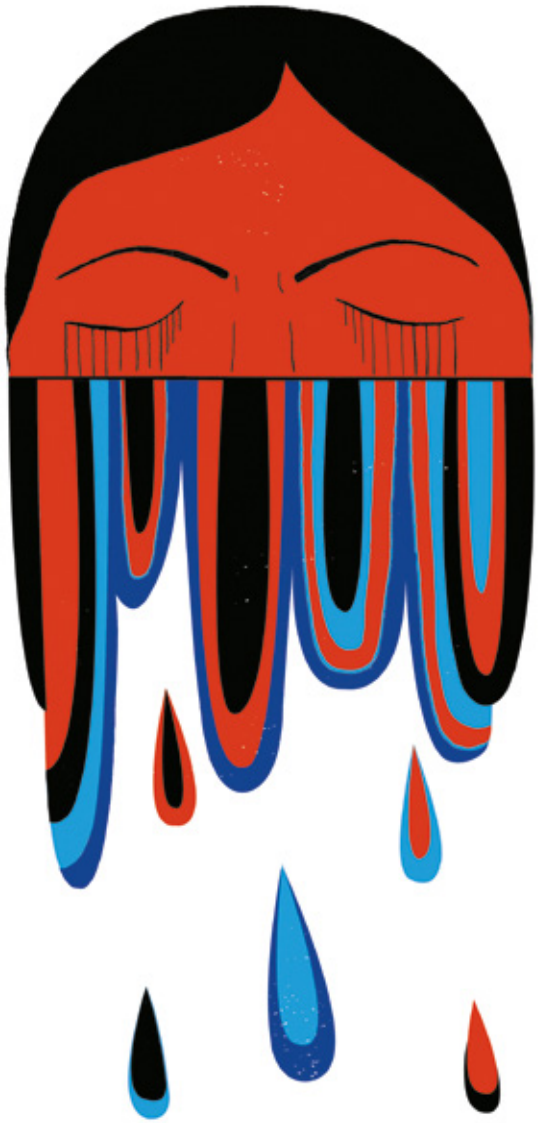
"Throughout our conversation, she would suddenly start sobbing. She spoke through the cracked refrain of her weeping, which seemed incongruous with the content of her speech."



ILLUSTRATIONS BY HANNA BARCZYK

Tears without End

The patient was not depressed. Her sobs stemmed from a brain disorder that few people have ever heard of

By Daniel Shalev

Maddie* couldn't stop crying. The first few days after her stroke, it had made sense. She had led a charmed retirement, with annual trips across the country, time with family and an active life. Now everything was in flux. A week before, Maddie, who was in her late 70s, had woken up unable to use half of her body. Her husband called an ambulance, and a diagnosis was reached within hours. Maddie had suffered a blockage in the blood vessels supplying her brain stem, affecting the pons, a region that conducts messages from higher centers of control and consciousness down to her body. At the hospital, she began to undergo a rush of frightening tests to evaluate the cause of her stroke and the risk of

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**Not the patient's real name.*

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CRITERIA FOR DIAGNOSING PBA

The inappropriate tears and laughter of pseudobulbar affect are easily mistaken for various mental disorders. Doctors use criteria such as the following to diagnose it correctly:

The patient's feelings and affective response are not closely related.

The duration and severity of the episodes cannot be controlled by the patient.

Expression of the emotion does not lead to a feeling of relief.

having another. She figured it made sense to cry.

A few days later, when Maddie was transferred from the stroke unit to the rehabilitation service, she was feeling more hopeful. Her risk of further strokes had been minimized with drugs to regulate her blood pressure, cholesterol and clotting. She could hear that her speech, initially slurred, returning to clarity. On the stroke unit, the emphasis had been on stabilization, but in rehabilitation, the goal was improvement. Maddie felt ready to work on her recovery.

Even with the hope of rehabilitation, though, the tears continued. Maddie cried when her husband came in and when he left. She cried during therapy meetings and medical updates. She cried through eating and bathing. The only time she did not weep was while she slept. Most oddly, Maddie cried even when she did not feel sad.

On the stroke unit, the crying had been annoying. In rehabilitation, it was downright disruptive. Maddie's therapy sessions were impeded by bouts of sobbing that invariably led the befuddled therapists to cut short their work with her.

Was It Depression?

Maddie's doctors worried she was having a recurrence of depression, which had plagued her in the past but was well controlled by an antidepressant. About a third of stroke patients experience new or worsened depression, for reasons ranging from functional loss to metabolic changes in the brain. Maddie worried, too, remembering the bleakness of her depression. Because of the complexities of her case, doctors asked for a consultation from a resident psychiatrist. That is when I was called in.

During our first meeting, Maddie spoke eloquently about the progress she had made since her stroke. Her words resonated with hope, which is unlike patients with depression. Maddie believed she would get better and return to the life she had enjoyed. But throughout our conversation, she would suddenly start sobbing. She spoke through the cracked refrain of her weeping, which seemed incongruous with the content of her speech. She even bawled through a description of her grandchildren.

When I asked Maddie whether she felt depressed, she replied, "I'm confused about why this is happening. I don't think so." Additionally, she did not meet other criteria used to diagnose depression, such as loss of interest in usual activities, poor sleep and appetite, low energy and weak concentration. Maddie was experiencing extreme, uncontrollable expressions of sadness without the accompanying emotion. In a sense, this was the opposite of depression, in which a person may feel despair within but appear blank or detached to others.

An Underdiagnosed Disorder

I recognized Maddie's condition as a relatively common, though vastly underdiagnosed, disorder called pseudobulbar affect (PBA). PBA is characterized by involuntary bursts of emotional expression—most often crying or laughing—independent of actual emotion. It can occur in many neurological disorders, including amyotrophic lateral sclerosis (ALS, or Lou Gehrig's disease), multiple sclerosis, Parkinson's disease and stroke. All told, it affects an estimated two million to seven million people in the U.S., according to a 2011 study published in *Advances in Therapy*. In this

SOURCE: "PATHOPHYSIOLOGY OF EMOTIONAL DISORDERS ASSOCIATED WITH BRAIN DAMAGE," BY K. POECK, IN *HANDBOOK OF CLINICAL NEUROLOGY*, VOL. 3, EDITED BY P. J. VINKEN AND G. W. BRUYN. NORTH-HOLLAND PUBLISHING, 1969

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same study, the great majority of patients who tested positive for PBA received either no diagnosis or an alternative diagnosis from their clinicians. Only half of symptomatic patients received any treatment, and for many, their treatment was based on a mistaken diagnosis.

PBA is caused by the disruption of an emotional expression circuit spanning several brain regions. Cortical structures responsible for higher emotional-intellectual function, such as the frontal lobe, produce the emotional context for expression and send it to the brain stem and cerebellum. The cerebellum acts as a gatekeeper, inhibiting or allowing the impulses to pass to the pons, where they are executed as laughter or tears. When Maddie's stroke injured her pons, she lost the integrity of the inhibitory circuit from the cerebellum that allowed her brain to regulate emotional expression.

THIS VASTLY UNDERDIAGNOSED DISORDER **AFFECTS UP TO SEVEN MILLION AMERICANS.**

Because Maddie had been treated for depression earlier in life, her diagnosis had been confounded—a common situation. As the 2011 study showed, PBA is routinely unrecognized or mistaken for other psychiatric disorders. Adding to the confusion is the issue, confirmed by a 2010 study in the *Journal of Neurology,* that people with PBA experience decreased quality of life and social isolation, which may further muddle diagnosis by contributing to psychiatric symptoms such as depression and anxiety.

For Maddie, the diagnosis was liberating. PBA is one of the most profound examples of disjunction between emotion and expression, something universally relatable: nearly everyone has had the experience of a misconstrued facial expression or tone. For Maddie, these disconnects became so frequent and intense that she wondered whether she could still recognize her emotions. Understanding that her crying was the consequence of her stroke allowed Maddie to trust her thoughts and feelings again.

When I sat down with Maddie and her husband to explain her diagnosis, they quickly asked about treatment. In 2011 a failed ALS medication called Nuedexta won Food and Drug Administration approval for treating PBA. Nuedexta, the rebranded combination of the common cough medicine dextromethorphan and the malaria medicine quinidine, works by blocking glutamate, one of the major excitatory neurotransmitters in the brain, in a way that seems to regulate the aberrant signaling in the affected pathway. Unfortunately, because of potential drug interactions with antidepressants, Nuedexta was a risky choice for Maddie. Yet I felt there was another class of medications that might help her brain regulate itself: another antidepressant.

When I told Maddie and her husband that I hoped to try a second antidepressant, they were baffled. "I thought you told me that you *didn't* think I was depressed?" Maddie asked me, with obvious concern. I explained that before Nuedexta came to market, doctors often prescribed an off-label treatment for patients with PBA: selective serotonin reuptake inhibitors (SSRIs), which are antidepressants that work by increasing serotonin in the synapses between neurons. It just so happened that Maddie's antidepressant worked through another mechanism, involving the neurotransmitter norepinephrine. We agreed to leave her original medication alone to do its job and to try a low-dose SSRI aimed at her PBA.

Shutting Off the Waterworks

Although both PBA and depression may respond to medications that increase serotonin in the synapses, the responses are distinct. Depression takes weeks to respond, possibly because the increase in serotonin has a number of secondary effects that are responsible for the mood changes. In contrast, PBA can respond in days. After five days on medication, Maddie was experiencing crying jags fewer than one time a day.

Maddie completed several weeks of rehabilitation, constantly gaining strength. When I came to see her, she savored the chance to speak. Her clear consonant laugh erupted at just the right moments to make me smile. I saw Maddie cry once more in her final days in the hospital; she was gazing at her weak left arm and pondering what a day at home might now be like. The tears streaming down her face reflected the true sadness and fear of that moment. We sat together, sharing in her hardship, before she looked up and said, "At least I'll get to be with my grandchildren again," her tears drying, her lovely smile breaking through. **M**

MORE TO EXPLORE

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- **Beyond Laughter and Tears: A Journey of Hope.** PBA Film Project: **www.pbafilm.com**
- National Stroke Association's Web page on pseudobulbar affect: **www.stroke.org/we-can-help/survivors/stroke-recovery/post-stroke-conditions/emotional/pba**

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RETHINKING RELIEF

Doctors are breaking away from opioids to treat chronic pain with nondrug remedies and psychological interventions instead

By Stephani Sutherland

ILLUSTRATION BY GUYCO

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The United States is in the grip of an unprecedented public health crisis—

one in which well-meaning doctors have played a part. Between 1999 and 2014 sales of prescription opioid drugs nearly quadrupled. In 2012 alone, physicians issued 259 million opioid prescriptions—enough to give a bottle of pills to every adult in the country. And in 2015 more than half of all overdose deaths in the U.S. involved opioids—either pain medications, such as OxyContin and Vicodin, or illicit substances, such as opium and heroin. To put that statistic in perspective, opioids claimed roughly as many lives that year as car crashes.

Addiction is undoubtedly part of the problem, but experts now agree that the real driver behind the opioid epidemic is chronic pain. According to a landmark study published in 2011 by the Institute of Medicine, an estimated 100 million American adults live with persistent or chronic pain. Many rely on opioids just to keep moving.

Chronic pain is defined as lasting more than six months but involves thought, emotion, attention, sleep, memory and social interactions.

There is no question that these drugs provide the best defense against acute, short-term pain, which alerts us to an injury or disease and subsides during recovery. But chronic pain is fundamentally different. It lingers long after an injury has healed and can produce a variety of symptoms, from headaches to body aches to crippling fatigue. It may stem from an underlying condition, such as osteoarthritis or multiple sclerosis, or have no obvious source.

FAST FACTS

TELL ME WHERE IT HURTS

1. Opioid drugs work well for acute pain but not chronic pain, which is fundamentally different and requires a broader, multipronged treatment approach.
2. Complementary therapies—including yoga, mindfulness-based stress reduction, biofeedback and acupuncture—have all shown promise against chronic pain.
3. Psychological interventions targeting anxiety and the tendency to catastrophize are also helping people to reduce their experience of chronic pain.

For some, chronic pain begins with nerve damage from diabetes, chemotherapy, a virus, a car accident or some other insult. In these cases, injured nerve fibers mistakenly continue to send pain signals to the brain, causing what is known as neuropathic pain.

No matter how chronic pain starts, it often increases and spreads, leaving many people reaching for more pills. Unfortunately, higher doses of opioid drugs do not guarantee relief—and can actually make matters worse. For starters, patients build tolerance to these medications, so that over time, it takes more opioids to blunt the same levels of pain. Higher doses increase the risk of dangerous side effects, including addiction, coma and death [*see box on page 33*]. And recent research shows that even relatively low doses of opioids can also cause hyperalgesia, or an increased sensitivity to pain: sometimes these drugs intensify the very pain they are meant to suppress.

For these reasons, a significant number of chronic pain sufferers eventually find themselves caught in a delicate—and deadly—balancing act: They need to take more opioid medications to keep their disabling pain in check while somehow dodging the drugs' serious and life-threatening side effects. Some succeed for decades. But those who lose their footing are

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flooding emergency rooms and hospital beds, battling withdrawal, accidental overdose and a host of other opioid-related complications.

Last year medical authorities began to respond on several fronts. In March 2016 the Centers for Disease Control and Prevention issued stricter guidelines for prescribing opioids. Contrary to what has been common practice, it advised against treating chronic pain with these drugs unless the benefits clearly outweigh the risks. Surgeon General Vivek H. Murthy amplified that message five months later, when he wrote directly to all the nation's health care providers—the first time any surgeon general has done so—urging 2.3 million professionals to commit to "turn the tide on the opioid crisis." Around the same time, the Food and Drug Administration required stronger warning labels on all opioid medications. The Department of Health and Human Services joined the fray by issuing a new *National Pain Strategy*, emphasizing the need for greater prevention, safer drugs and broader approaches to treatment.

The message is being heard. At a handful of state-of-the-art pain centers around the country, clinicians are exploring a range of nondrug alternatives, from psychological interventions to complementary therapies. Researchers are also working on next-generation opioid drugs, along with new nonopioid painkillers [*see box on page 34*]. These initiatives represent the one upside to the opioid crisis: "It's forcing us to revisit how we care for people in pain," says Sean Mackey, who heads the Pain Management Center at Stanford University and co-chaired the committee of experts from multiple U.S. agencies that developed the new HHS strategy. "I'm not pro-opioid. I'm not anti-opioid. I'm pro-patient," he says. "There will be no magic bullet, no pill. Chronic pain requires multipronged treatment."

Many chronic pain sufferers are now caught in a delicate balancing act—taking higher doses of opioids to keep disabling pain in check while also dodging the drugs' serious and deadly side effects.

A Different Kind of Pain

In August 2016 David,* a former school worker, wheeled himself into pain psychologist Beth Darnall's office at the Stanford pain clinic, one of the nation's few multidisciplinary pain centers. He and his wife had traveled for three hours that morning from their home by medical transport. David had undergone minor surgery on his right foot just one day before and was still wearing a hospital-issued blue paper bootie, but nothing was going to stop him from keeping this appointment, which he had waited weeks to get.

Darnall started by taking a detailed medical history. David described ongoing pain in his back and body, which had started in 1995, the last time he had felt well enough to work full-time. That year had been devastating for him medically: he had contracted meningitis from a tick bite and was diagnosed with cancer. The diseases, plus chemotherapy, had ravaged his nerves, causing constant pain, which led to further challenges, both physical and psychological.

Many experts now view chronic pain as a disease in its own right. Over time it engages and changes patterns of activity in brain areas associated not only with physical sensations but with sleep, thought and emotion. No wonder that studies show that chronic pain is associated with higher rates of mortality, sleep disorders, depression and anxiety. For 20 years David had been taking ever escalating doses of opioid drugs, including methadone, a long-acting opioid painkiller, and fast-acting Dilaudid, occasionally supplemented with Demerol, yet another opioid. But in addition, he depended on Valium to tamper his anxiety and Ambien to help him sleep.

more than an enduring physical sensation. It can affect
It is also associated with higher rates of mortality.

For most people, this drug cocktail would be deadly. For David, it had become a daily routine. Darnall listened to David's story and then asked if anyone had ever spoken to him about how dangerous this drug combination was. "No," he replied, although he did have firsthand experience: on three separate occasions, he had been rushed to the hospital near death. "This is really the only tool you've

**The patients' names have been changed to protect their privacy.*

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ever been given to cope with the pain," Darnall explained. "And we need to replace it."

David is far from alone. According to a *Washington Post*/Kaiser Family Foundation survey conducted last fall, among people taking prescription painkillers for at least two months, about a third said they did not receive information about the dangers of opioids from their doctor. Only a third said their doctor had outlined a plan to wean them off the drugs. And another third reported that their doctor had never discussed any complementary treatments beyond medications. To treat people more effectively "will require an important shift in how we think about pain," says David Shurtleff, deputy director of the National Center for Complementary and Integrative Health (NCCIH), the part of the National Institutes of Health that studies nondrug therapies. "We now understand that pain is not just a sensation but a brain state," Shurtleff explains. "And mind-body interventions may be particularly helpful."

The team at Stanford brings together pain psychologists such as Darnall, pain-management physicians, psychiatrists, neurologists, anesthesiologists, physical and occupational therapists, and nurse practitioners, who collaborate to help patients safely reduce their use of opioids and replace them with nondrug alternatives. The team members meet every week to fine-tune evolving treatment plans that might incorporate cognitive-behavioral therapy (CBT), physical therapy, mindfulness training, yoga, biofeedback and acupuncture. Above all, it is a customized approach to suit the individual patient.

For David, the plan started with an inpatient stay to safely and significantly reduce his dependence on opioid medications. At the same time, Darnall homed in on his anxiety, referring David to a local psychologist for talk therapy after discharge and prescribing a guided relaxation regimen using a CD. "Your anxiety makes the pain worse," she explained at the conclusion of his initial visit. "If we can focus on tools to stop the anxiety, that can help shrink the pain."

Turning Within

Taking such a broad approach is neither simple nor cheap—and better insurance coverage of nondrug therapies will be needed to make it widely practical—but experts such as Mackey say the complexity of chronic pain warrants it. Perhaps the complementa-

Mindfulness, yoga, biofeedback and acupuncture may all help to ease chronic pain by changing a patient's relationship to pain rather than lowering the intensity of the physical sensation.

GETTY IMAGES

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ry therapy that has garnered the most attention in recent years is mindfulness-based stress reduction (MBSR), a clinical and secular adaptation of Buddhist meditation practices. Jon Kabat-Zinn, now a professor of medicine emeritus at the University of Massachusetts Medical School, developed MBSR in the 1970s. Since then, MBSR classes have cropped up in every U.S. state and in more than 30 countries. A growing body of evidence suggests that MBSR—which encourages nonjudgmental awareness of the present moment and fosters greater mind-body awareness—can mitigate a variety of ailments, from cancer and depression to drug addiction and chronic pain.

In 2016 senior investigator emeritus Daniel C. Cherkin of the Group Health Research Institute in Seattle and his colleagues tested three treatments for chronic low back pain in 342 young and middle-aged adults: MBSR, cognitive-behavioral therapy—designed to change pain-related thoughts and behaviors—and standard pain care. They found that compared with participants who received standard pain care, more patients receiving MBSR or CBT showed a significant drop in "pain bothersomeness" after 26 weeks. In addition, the MBSR and CBT groups improved more in their functional abilities.

Other chronic pain sufferers are making gains with biofeedback. Using sensors to monitor bodily signals such as muscle tension and heart rate, they build awareness of physiological processes and learn to modulate their own pain. A 2017 meta-analysis evaluated biofeedback for chronic back pain in 1,062 patients and found that it not only lowered pain intensity but also improved patients' coping abilities and reduced the incidence of pain-related depression. Mackey and others have also tested a more sophisticated technique called neurofeedback, which provides patients with images of their own brain activity using electroencephalography or functional MRI. This kind of training can teach patients to control brain regions associated with pain processing.

Additional evidence suggests that acupuncture might help ease chronic pain in some cases—perhaps, some scientists speculate, by stimulating anti-inflammatory signals in the skin or influencing activity deep in the brain. The practice remains controversial, in part because it is difficult to study. But a 2014 analysis of 29 clinical trials of acupuncture for chronic pain in nearly 18,000 patients showed that compared with treatment with no needles or misplaced needles, the traditional form—with needles placed according to centuries-old Chinese practice—produced greater pain relief. At the same time, a significant number of people in the control groups also saw benefits, suggesting a strong placebo effect.

That finding reinforces the idea that when it comes to pain, simply being under the care of a receptive health care professional can be palliative. Researchers are investigating how all these complementary treatments work, "but we are not waiting for basic science to tell us the optimal way to treat pain," Shurtleff says. There is broad agreement that mindfulness, yoga, biofeedback and acupuncture may succeed by changing patients' relationship to their pain rather than actually lowering the intensity of the physical sensation. At the NCCIH, Shurtleff and others are trying to figure out how to best apply ex-

Relief at a Cost

Opioids' Side Effects

Opioids work so well in the short run because they mimic our brain's own morphinelike molecules, called endogenous opioids, which are released to drown out incoming pain signals. Endogenous opioids are released only where they are needed, in the brain's pain circuitry, but opioid drugs go everywhere and activate receptors throughout the body. As a result, the drugs cause a range of side effects:

- **In the brain's pain circuits:** opioids dampen pain, but tolerance develops quickly, so higher doses are needed to achieve the same effect.
- **In the gut:** opioids slow movement in the digestive tract, leading to constipation.
- **In the spinal cord:** some people develop intense itching in response to opioids.
- **In the brain's reward pathway:** the drugs produce highly pleasurable sensations, often leading to addiction.
- **In the brain stem:** most dangerous of all, opioids can drown out signals from the neurons that control breathing, leading to death by respiratory depression.

THE AUTHOR

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Next-Generation Painkillers

Researchers are working to create opioids that can blunt pain without their nefarious side effects. For instance, extended-release opioids, which are already available, produce less reward than a single blast, reducing the likelihood of addiction. But more sophisticated efforts are also under way. It turns out that the activation of opioid receptors triggers two signaling pathways within cells. Broadly, one pathway leads to pain relief, and the other leads to side effects. Researchers are now focused on creating compounds that can selectively turn on one without the other.

For example, clinical trials are now being conducted to test oliceridine, or TRV130, an agent produced by Pennsylvania biopharmaceutical company Trevena. And in September 2016 researchers described another compound, called PZM21, that produced analgesia in mice without side effects. "The principal goal for both PZM21 and TRV130 is to reduce opioid respiratory depression, which has been shown to be possible both in preclinical [animal] studies and in clinical studies," says William Schmidt, a pharmaceutical consultant at NorthStar Consulting in Davis, Calif. "In addition, both [drugs] appear to show reduced abuse liability and reduced effects on the GI tract, hence less risk of constipation."

To find the new compound PZM21, researchers used computer modeling to test how three million different "virtual molecules" interacted with the structure of the opioid receptor. Based on those interactions, they zeroed in on 23 compounds, which they further tested in cells in a dish. In these cells, PZM21 strongly activated the pathway for pain relief but not the pathway that produces side effects. In mice, PZM21 was more effective than morphine at dampening pain. Future clinical trials of PZM21 and ongoing trials of TRV130 will determine whether these agents will deliver on their promise. —S.S.

isting complementary treatments. "Patients are suffering, and we want to find what really works. We take that pragmatic approach," he says.

The NCCIH recently conducted an extensive review of published clinical trials for a variety of complementary therapies with the aim of finding out which treatments might work best for which patients. It found that acupuncture and yoga benefited people with chronic back pain the most. Acupuncture and tai chi proved most helpful for those with chronic pain resulting from osteoarthritis. Massage therapy provided short-term benefits for neck pain, and relaxation techniques were most effective in those with severe headaches and migraines [see "Can Anything Stop My Migraine?" on page 36].

Feeling Your Pain

There is another reason why individualized care makes sense for chronic pain: different people can experience the same kind of pain in very different ways. In particular, researchers are discovering that how much chronic pain affects any one person depends heavily on so-called biopsychosocial factors—how someone reacts to pain emotionally, what other sources of stress exist, how much social support surrounds the person. Targeting these influences can not only reduce patients' experience of pain but dramatically improve their quality of life. Indeed, chronic pain–related disabilities often leave people isolated and cut off from friends, which can, in turn, make the pain more intense.

To identify biopsychosocial factors up front, patients at the Stanford clinic fill out an extensive online questionnaire, capturing everything from work histories and adverse childhood experiences to sleep habits and anger levels. Mackey believes that collecting this type of data holds the key to matching patients with effective treatments. The questionnaire is part of a free, open-source repository that he and his colleagues at Stanford have created, together with researchers at the NIH. The system, called the Collaborative Health Outcomes Information Registry (CHOIR), is now in use at medical centers around the U.S. and soon will be in several other countries. It contains data from more than 15,000 patients. Health care providers can use the system to track patients' progress over time and to compare their trajectories with similar cases.

This data set has revealed that one factor in particular—a mindset called catastrophizing—predicts

MILOSJOKIC *Getty Images*

the impact of chronic pain on a person's life far better than any other measure. At its core, catastrophizing is a tendency to exaggerate or magnify the threat of pain, to fear the worst and remain focused on the experience of pain. For people trapped in this way of thinking, their pain feels overwhelming. They hold little hope that they will ever be well again. "That leads to a very strong desire to escape the pain, and they reach for the meds," Darnall says. Because catastrophizing is such a powerful force on the experience of pain, she says, "it seems like a stroke of genius to target it."

Darnall took exactly this approach with Angela,* a patient who scored very high on CHOIR's catastrophizing scale when she first came to the Stanford clinic. After a traumatic brain injury, Angela had endured years of severe headaches, neck pain and fibromyalgia, a poorly understood syndrome that includes all-over body pain and fatigue. She was taking opioid painkillers, as well as various potent migraine medications. Still, her pain often left her in a wheelchair. It interfered with her ability to care for her children, run her business, and maintain healthy relationships with her husband and parents. Like many chronic pain patients, Angela also mourned the loss of her life before the pain. She used to enjoy a variety of fast-paced sports—activities that now, she says, exasperated, "I can't even imagine!"

Angela's sense of powerlessness is common—and doctors who dismiss chronic pain because they cannot explain it only compound that feeling. When surgeries or other treatments fail to help, patients learn to expect failure. "Patients come to us so demoralized—they have been through the mill," Darnall says. "Our job is to 'remoralize' them first." The initial step is giving patients back a sense of control, no matter how small. "People need to know that their pain is real, it's not their fault, and here are some ways that we can address it," Darnall says.

As with all her patients, Darnall invited Angela—along with her family—to a free two-hour educational seminar to learn about how pain and biopsychosocial factors interact. Angela also received a relaxation CD like the one David was given. Darnall explains to patients in her care that the auditory experience recorded on the CD works to calm the nervous system and that they should think of listening to it as taking a dose of mind-body medicine. "Do it regularly—establish a new pattern," she emphasizes. "Even if you can't do 20 minutes, do five. Doing something is better than nothing. Always, always."

Angela started using the CD right away. She also took up yoga, began regular massage therapy and pursued a specialized pain-focused talk therapy with Darnall. Now, several months later, she has made measurable gains. She has learned to keep her emotions in check during stressful times, which has improved her relationships. Her catastrophizing score is way down. She no longer takes opioids but instead only a very low dose of naltrexone, a drug that blocks opioid receptors and is thought to reduce inflammation. And she can walk again for several miles at a time, pain-free. Perhaps most significant, she has started to set goals for her future. "I can't dance like I used to, but I can move a little bit," she says with a sly smile. For Angela, who spent years in a wheelchair, thinking she would never move freely again, to dream of dancing is a triumph. M

One factor—a mindset called catastrophizing—predicts the impact of chronic pain on a person's life far better than any other measure. It is the tendency to magnify the threat of pain, fear the worst and remain focused on the experience of pain.

MORE TO EXPLORE

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From Our Archives

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CAN ANYTHING STOP MY MIGRAINE?

After a long drought, neuroscientists are readying a host of new treatments that may not only knock out the debilitating headaches but also prevent them

By R. Allan Purdy and David W. Dodick

ILLUSTRATIONS BY GUYCO

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The attacks began in her early 20s; for two years now Stephanie* has been living under the pall of migraine. It usually starts with a visual disturbance called an aura—shimmering zigzag lines that move across her field of vision and gradually expand into blackness, blotting out her sight. Then comes pounding pain mainly on the left side of her head. Adding to her misery is an exquisite sensitivity to light, sound and smell that makes ordinary stimuli—even perfume—unbearable and the headache even worse.

When she arrived at the neurology clinic in Halifax, Nova Scotia, where one of us (Purdy) practices, she said she had tried numerous medications, but all had either failed or triggered intolerable side effects. Meanwhile, over the past year, her symptoms have become more extreme and frightening. Now as her vision blurs, a tingling sensation slowly moves upward from her right hand through her arm and sometimes into her face and tongue—a sign that blinding head pain is about to strike. At the same time, she begins to have trouble finding her words and making herself intelligible to others. She worries that migraine will lead to a stroke, which can be a genuine risk.

For some people, migraine is an occasional bother; for others, a persistent scourge. For people such as Stephanie, the attacks can involve bizarre alterations in perception and sensation. But in its various forms, migraine is one of the most common of neurological conditions, affecting an estimated 39 million people in the U.S.—about one in five women and one in 16 men.

It is a malady that often defies treatment and prevention. According to population studies in the U.S., only one quarter of those with episodic migraine (fewer than 15 days of headache a month) and fewer than 5 percent of those with chronic migraine (15 or more days a month) have seen a health care provider and received an accurate diagnosis and appropriate therapy. The newest class of drugs on the market dates back to the early 1990s. Taken after an attack has started, these medications resolve the pain in fewer than a third of those who use them, and they have potential side effects that rule them out for many.

Now, though, people with migraine have reason to hope that their misery may soon be behind them. Breakthroughs in understanding brain networks and the chemical messengers that cause migraine symptoms have spawned a number of sophisticated new treatments that halt attacks or prevent them from beginning. And just as new insights into the brain are generating novel ways to attack the disorder, the study of migraine is revealing some of the brain's secrets.

FAST FACTS

HEADING OFF A SCOURGE

1. About 39 million people in the U.S. have migraine, but fewer than 30 percent have received a proper diagnosis and treatment.
2. Triptans, the newest class of migraine drugs on the market, date back to the early 1990s; they work for only a third of those who take them, and many people cannot because of cardiovascular risks.
3. Now in clinical trials, monoclonal antibodies might prevent headaches from starting by blocking substances that carry pain signals to cranial nerves.
4. Other new drugs might knock out headaches after they start without constricting the blood vessels, making them safe for patients at risk of stroke.

An Ancient Affliction

Migraine is rivaled only by epilepsy for the title of oldest-known neurological disorder. The Egyptians described it in medical documents in 1200 B.C., although credit for its discovery as a distinct condition usually goes to Aretaeus of Cappadocia, whose second-century writings gave accounts of individuals with repeated attacks of severe, one-sided headaches and vomiting.

The severity of migraine varies widely. The lucky might have a very bad headache a few times a year, treat it with an over-the-counter painkiller and never bother to seek a doctor's advice. For most, however, attacks occur once or twice a month, and for

**The patient's name has been changed, along with a few details of her case, to protect her privacy.*

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about a quarter of U.S. migraine sufferers, the attacks become more frequent, with symptoms eventually occurring daily or nearly so. For them, while the disease is not in itself life-threatening, it certainly is life-altering.

Although the most debilitating element of migraine is the pain, the most distinctive (and fascinating for neurologists like us) is the aura, which affects about a third of migraineurs. Most often the aura is a visual phenomenon consisting of jagged lines that produce an area of blurry or reduced vision, sometimes with a blind spot at the center. Imaging studies have revealed that this so-called classical aura originates in the visual cortex at the back of the brain and spreads forward over the course of several minutes—a phenomenon that is known as cortical spreading depression [*see box on next page*].

Most of those who have no visual aura will still experience premonitory symptoms—yawning, fatigue, mood changes, neck pain, sensitivity to light—that may serve as a warning of an imminent headache. Migraine is also linked to risks of other maladies, such as ischemic stroke, depression and epilepsy. The risk of stroke is especially high in women, particularly those who smoke or take medications containing estrogen, such as birth-control pills.

Clinicians have long observed that migraine tends to run in families. Recent research has identified more than three dozen genes that appear to be associated with the disorder. These include genes responsible for so-called channels and transporters that sit on the surface of neurons and other brain cells. These structures control the traffic of ions (such as sodium, potassium and calcium) in and out of the cells and neurotransmitters across the synapses—and thus the excitability of certain brain cells and brain networks. Other genes associated with migraine are responsible for generating pain and maintaining the health of blood vessels. Taken together, these genetic variations may explain the hyperexcitability of the brain and the extreme sensitivity to light, sound and odors, the pain, and the vascular disorders, including stroke, associated with migraine.

For some people migraine begins with a shimmering visual aura that can partially blot out vision. The effect is simulated here.

ANDREW TOO BOON TAN *Getty Images (bike in front of store)*; SCIENTIFIC AMERICAN MIND (*blur*)

The Quest for Relief

The earliest treatments for migraine were rooted in superstition and witchcraft, ranging from bloodletting to opening a hole in the skull to release evil spirits. In the 19th century, migraine was considered to be a psychosomatic illness, along with other afflictions suffered principally by women. That notion began to change in the middle of the 20th century. A series of elegant experiments in the 1940s by New York Hospital–Cornell Medical Center neurologist Harold Wolff led to the modern vascular theory of migraine—notably, that the pain of migraine is from dilation and distention of blood vessels outside and inside the skull. Wolff measured the amplitude of pulsations of blood vessels in the scalp during migraine attacks and after the administration of a drug that constricted the vessels. His findings led to the adoption of the first true migraine medicine: ergotamine tartrate, a powerful

Among the most common of all neurological disorders, migraine affects one in five women in the U.S. and one in 16 men. The majority are not helped by current drugs.

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The Long, Slow Wave

One of the enduring mysteries of migraine is the relation between the splitting headache and the strange sensory symptoms that sometimes precede it. A phenomenon known as cortical spreading depression, or CSD, may be responsible for both. CSD is characterized by a wave of electrical activity that spreads slowly over the cortex, followed by a wave of quietude, producing symptoms that are related to the part of the brain through which the wave is traveling.

After any of a number of factors set off an attack—stress, bright lights, hormone changes, lack of sleep—CSD typically starts in the visual cortex in the back of the brain, triggering the zigzag patterns and blurred vision characteristic of classic aura. The wave then may travel to the sensory strip in the parietal lobe, inducing a marching disturbance from the hand up to the face and tongue. For some sufferers, speech is stricken next, bringing on aphasia.

As it traverses the brain, CSD can also stimulate pain-detecting neurons either directly or through inflammation that excites fibers supplying the sensitive outer surface of the brain. These pain fibers subsequently release a variety of chemical or protein neurotransmitters—among them the peptide CGRP—that are capable of transmitting pain signals from the peripheral to the central nervous system.

Two thirds of people with migraine, however, do not have an aura. For them, the migraine trigger remains an active area of investigation. CSD might occur in cortical or subcortical brain tissue without giving rise to sensory symptoms. Or different mechanisms might generate an attack in subcortical brain structures that help to process light, sound and other sensory stimuli and influence pain-sensing neurons in the brain. Or both types of mechanisms might work together. In either case, CSD is an elegant bridge between migraine pain and its remarkable neurological symptoms.

—R.A.P. and D.W.D.

Starting in the visual cortex at the back of the brain (*left*), cortical spreading depression moves forward as a wave of electrical activity (*purple*) at about two to three millimeters a minute, setting off a visual aura. When it reaches the parietal and temporal cortices (*center*), speech difficulties may ensue, and then, at the sensory strip (*right, green*), tingling sensations may occur in a limb or the head.

vasoconstrictor derived from the ergot fungus; it brought pain relief that coincided with artery constriction in the scalp.

Then, in the 1970s and 1980s, investigators at the Erasmus University Rotterdam in the Netherlands and the University of New South Wales in Sydney, Australia, noted an association between migraine and serotonin: levels of the neurotransmitter went down in the blood and up in the urine during attacks. In other words, the body was losing serotonin. They also found that administering serotonin to people during an attack relieved pain, just as ergotamine did. The thinking at the time was that loss of serotonin caused blood vessels to lose tone and dilate, bringing on migraine pain.

As treatments, though, ergotamine and serotonin have serious problems. Both have troubling side effects, including nausea, vomiting and cramping—which can already be problems for migraine sufferers. Ergotamine can also cause dangerous reductions in blood flow.

In the 1970s Patrick Humphrey, a pharmacologist then at British pharmaceutical company Glaxo, began to look for a way to reproduce the beneficial effects of serotonin without the harmful ones. Humphrey was working under the assumption that the dilation of the blood vessels inside and outside the skull was responsible for migraine headaches and that drugs that could bind to serotonin receptors might provide relief. So he set out to design a drug that did just that. The result, after a decade of work, was sumatriptan, which, like ergotamine, both eased pain and constricted blood vessels. It would be the first in the triptan family of drugs.

Triptans, too, have their limitations. They bring complete pain relief to only about 30 percent of migraine sufferers, and for many of them, the head-

COURTESY OF ROBERT HARGREAVES

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ache returns the same day. Triptans may also trigger a number of unpleasant side effects, including sleepiness, dizziness, tingling, tightness in the chest, and a reddish flushing of the face and neck. And because these drugs can constrict blood vessels throughout the body, people with heart disease or a history of stroke cannot use them.

But the triptans were a major breakthrough for millions of sufferers who could now take a pill or injection and stop a debilitating headache within 30 minutes. They were also a triumph in the science of drug design—except that the understanding of the underlying neurobiology was not altogether right. As further research would soon reveal, the primary cause of migraine pain is not dilation of blood vessels in the head, and the primary factor by which triptans help is not by constricting those vessels. Something else was going on, and the design of better drugs would depend on figuring out what that was.

Guided Missiles for Migraine

In the 1980s, at around the same time that Humphrey was working on triptans, neuroscientist Lars Edvinsson of Lund University in Sweden found a compound known as calcitonin gene–related peptide (CGRP) in the nerves that surround the blood vessels inside the skull. The compound had only recently been discovered in the central and peripheral nervous system, and evidence suggested that it served as a chemical messenger of pain. CGRP is also a potent vasodilator, and Edvinsson, a specialist in the brain's blood supply, hypothesized that it may contribute to the development of migraine headache.

Over the next two decades experiments by numerous investigators confirmed that idea. Researchers found, for instance, that blood levels of CGRP rose during migraine attacks and returned to normal after a dose of sumatriptan relieved the headache. Especially convincing, CGRP consistently triggered a migraine attack when infused into the bloodstream of migraine sufferers. Studies in both animals and humans showed that CGRP and its receptors are found in brain structures such as the hypothalamus and cerebellum, which were long thought to play a role in generating migraine attacks. They are also present in the trigeminal nerve, a key cranial nerve involved in processing sensory signals that was also implicated in migraine. Furthermore, CGRP turns out to be one of the chemical substances released during cortical spreading depression, the putative mechanism of migraine aura.

In the early 2000s scientists at pharmaceutical company Boehringer Ingelheim in Germany synthesized a small molecule designed to bind to the receptor for CGRP and block its activity—a category of substances known as receptor antagonists. A study involving 126 patients published in the *New England Journal of Medicine* in 2004 confirmed that this molecule, given intravenously, halted migraine headaches in some patients, and it did so without constricting blood vessels in the head. This was a crucial discovery: it demonstrated that the long-reigning vascular model of migraine was not wholly correct and that constriction of blood vessels was not essential to bringing relief.

The earliest treatments for migraine were rooted in superstition and witchcraft, ranging from bloodletting to opening a hole in the skull to release evil spirits.

Despite the promising results, progress in developing CGRP receptor antagonists faltered because of a serious side effect: liver toxicity that arose in trials of three of these drugs. Researchers would have to find another way forward.

Some decided to target CGRP or its receptor with a monoclonal antibody. Antibodies are large proteins that can be directed with precision to a single target much like a laser-guided missile. Drug developers typically produce them from clones of a single parent immune cell, which is why they are described as monoclonal. Like other proteins, they are metabolized into amino acids by tissues throughout the body rather than taxing the kidneys or liver. Thus, although they may have side effects associated with blocking their specific target (such as CGRP), they should not cause "off-target" side effects or toxicity such as kidney damage.

Antibodies are too large to pass through the

THE AUTHORS

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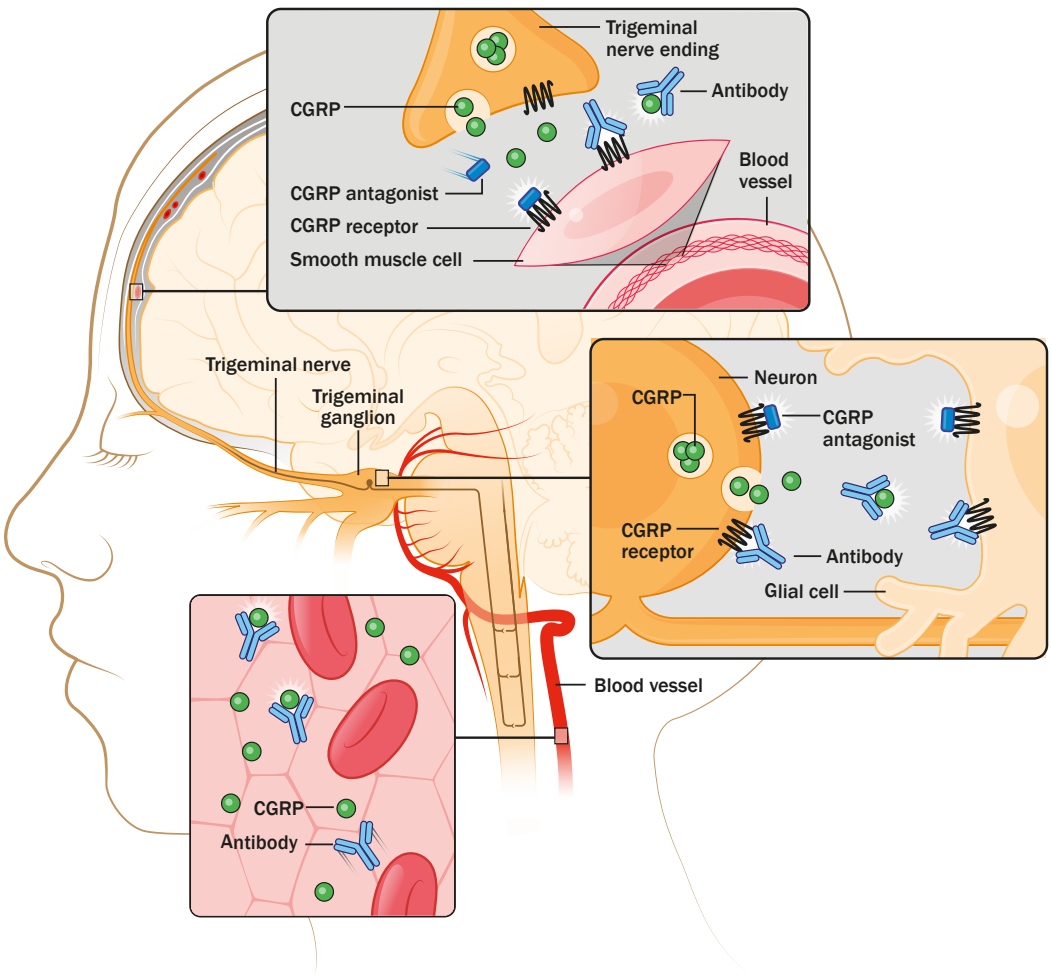
blood-brain barrier, and yet these new drugs have performed impressively in preventing migraines in preliminary studies. One possible mechanism: by blocking CGRP in trigeminal nerve pathways outside the brain, the antibodies may reduce signaling between the peripheral and central nervous systems, decreasing pain signals entering the brain.

Since 2012, numerous researchers—including one of us (Dodick)—have conducted placebo-controlled clinical trials involving a total of more than 10,000 patients. A large proportion of the trial patients have used the treatment for more than a year, without side effects, aside from some redness at the injection site. For up to 70 percent of them, the number of days with headache dropped by more than half, and up to one in six patients became completely migraine-free while the treatment lasted. The improvement appeared as soon as three days after administration of the antibody began. Pharmaceutical company Amgen recently completed its pivotal phase III studies and will soon file for FDA clearance. Three other companies—Alder BioPharmaceuticals, Eli Lilly and Teva Pharmaceutical Industries—are in the midst of their phase III trials. Barring unforeseen issues, the first of these antibodies will become available in late 2017 or early 2018.

The monoclonal antibodies will be a leap forward from currently available preventive treatments, which include beta blockers such as propranolol and a variety of blood pressure medications. The older drugs have similar response rates, but a noticeable effect might take weeks or months to appear. Their dose often needs to be increased over time, and the side effects, such as weight gain, hair loss, cognitive dysfunction and sedation, may deter patients from reaching an effective dose or continuing with the drug at all. In fact, more than 85 percent of patients who start treatment with today's

How New Agents Will Arrest Migraine

New drugs target the pain-bearing molecule CGRP (*green circles*) as it dilates blood vessels (*top*), irritates nerve centers (*middle*) and courses through the blood (*bottom*). Taken when a headache begins, CGRP receptor antagonists (*blue cylinders*) block CGRP from binding to receptors in the head, thereby halting the pain. In contrast, monoclonal antibodies (*blue Y shapes*) are taken continuously to prevent migraines. They do so by binding to CGRP receptors on nerves and blood vessels and devouring CGRP there and in the bloodstream.



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preventive drugs stop taking them within a year.

Still, monoclonal antibody treatment will not be for everyone. Patients will need to take them either intravenously, requiring a trip to the doctor every three months, or via a monthly self-administered injection. And questions remain over the long-term safety of blocking a protein found throughout the body. This concern is particularly relevant to patients with cardiovascular disease and hypertension because CGRP is thought to be important in maintaining the tone of blood vessels and compensating for low blood supply to the brain and heart during strokes and heart attacks. Nor is it at all clear that the drugs would be safe for use during pregnancy—an important consideration because most migraineurs seen in clinical practice are women of child-bearing age. (Migraines often abate at menopause.)

For patients who cannot use the antibodies or are not adequately helped by them and for the many who would prefer to treat migraines only when they arise, there remains a need for safe and effective on-demand treatment for acute attacks. Ideally such pain relievers would be in pill form and would not constrict blood vessels, as triptans do. Two classes of medication now under development show promise on all these counts. Clinical trials of newer CGRP receptor antagonists have demonstrated them to be about as effective as triptans but without the toxic effects. The liver toxicity seen in earlier trials appears to have been specific to the drugs and not to blocking CGRP.

And a new family of drugs called ditans, which target serotonin receptors, is showing great promise. Lasmiditan, under development by CoLucid Pharmaceuticals, is selective for serotonin receptors located only on neurons and not blood vessels, which means it should be safe for the 20 percent of migraine patients who have cardiovascular risk factors. In a recent clinical trial of lasmiditan by CoLucid involving 2,231 subjects who received treatment for a single migraine, a third of patients were pain-free within two hours. (Dodick helped to design the trial and analyze the results.) This success rate is similar to that of triptans but without the risks associated with constriction of blood vessels. In fact, more than 80 percent of the patients in the study had one or more cardiovascular risk factors, and no safety issues arose.

Hope on the Horizon

The new treatments making their way to market reflect tremendous strides in identifying the sites in the brain where migraine arises and the mechanisms that generate it. The result is medication with greater specificity and fewer side effects than older remedies. The creation of a successful drug often leads to a virtuous cycle of further insights into disease mechanisms and the next generation of treatments. This was true of the triptans and will almost certainly be true for the drugs in development today. The mere fact that a large molecule such as an antibody with no likely access to the brain can prevent attacks originating there is already transforming how we think not only about migraine but the very way in which the brain works.

In studies with new antibody drugs, up to 70 percent of patients found their number of days with headaches dropped by more than half. Up to one in six became migraine-free.

Most important, patients such as Stephanie who have been unable to find relief with current meds will—if all goes well—finally get the attention and treatment they deserve. Stephanie has tried at least 10 medications to control her migraines, as well as numerous alternative therapies, from acupuncture to yoga to special diets—without effect. As someone whose symptoms place her at risk of a stroke, she was excited to hear that potentially safer drugs are on the horizon. "That sounds wonderful," she said. "I can't wait!" As clinicians who see far too many patients whose migraines resist current treatments, we feel the same way. M

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Laughing MATTERS

AN INFANT'S LAUGHTER CAN REVEAL NOT ONLY HOW BABIES THINK BUT ALSO THE SERIOUS REASONS FOR THIS EXPRESSION OF JOY

BY GINA C. MIREAULT

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My son was three months old when he uttered his first laugh. That he did so at a funeral was more than ironic; it was compelling. Surrounded as we were by mourners, his tiny laugh was so powerful as to provoke his audience to go from sadness to joy—together and almost instantaneously.

This observation launched my empirical investigations into the early appearance and dramatic power of that simple phenomenon: infant laughter. As a developmental psychologist, I have studied the giggles and glee of babies for nearly a decade now in my laboratory at Johnson State College in Vermont. Psychologists such as myself are intrigued by why laughter appears so early and what, if anything, it can reveal about infants.

Laughter is universal. It is a hardwired response that comes online early—in the first four months of life—regardless of culture or native language. Whether a child is raised in Canada or Korea, Peru or Pakistan, her first laugh will delight her parents at about 14 to 18 weeks of age. A baby's laugh is easily recognizable, partly because of its genuineness. Like crying, it is hard to fake and, like yawning, is contagious. Its authentic quality makes it hard for parents to ignore. Scientists, on the other hand, have only recently caught on to its significance.

Of course, laughter is not exclusively an expression of amusement. In adults, it can occur in many emotional contexts, including when people are nervous, as a response to others' laughter or more simply when in the company of other people. But why do *infants* laugh? It is not so much a question of *what* they find funny. There is no universal joke for infants. (The funeral laugh was prompted by someone's sneeze.) Instead we must consider *how* infants extract humor from their environment.

In contrast to crying, which clearly urges an infant's caregiver into action, laughter seems like an emotional luxury. The fact that a three-month-old can have access to this ability—long before other major milestones such as talking and walking—suggests that her chortles, sniggers and guffaws have an ancient and important origin. Laughter can reveal a considerable amount about infants' understanding of the physical and social world.

FAST FACTS
TINY GIGGLES

1. By 18 weeks of age infants can laugh. Two months later children can clearly extract humor from their environment.
2. Laughter can be elicited in a very young child by presenting an out-of-the-ordinary event that defies expectations for social rules.
3. The profoundly social nature of this expression suggests it plays an important role in how we interact and communicate with other people, which could explain why it emerges so early in life.

Baby Darwin

Laughter precedes language both in infancy and in the evolutionary chain, having been prioritized and preserved by nature. Indeed, several species, including chimpanzees, other apes and squirrel monkeys, engage in vocalizations during play that resemble laughter. These mammals—especially juveniles—display signature breathy and rhythmic sounds while frolicking together.

Evolutionary neuropsychologist Jaak Panksepp of Bowling Green State University and Washington State University has shown that the brains of all animals contain the neural circuitry engaged in human laughter. These areas include emotional and memory centers, such as the amygdala and hippocampus. Laughter seems to bubble up from below the surface of the cortex as an involuntary response while activating the pleasure systems in the brain. Famously, Panksepp has even documented, using technologies that allow humans to hear very high frequencies, that rats emit a rhythmic chirping sound when "tickled."

In humans, infant laughter has gained the attention of a few prominent scholars. In the fourth century B.C., Aristotle posited that the first laugh marked an infant's transition to humanness and served as primary evidence of that infant having acquired a soul. In 1872 Charles Darwin hypothesized that laughter, like other postural, facial and behavioral expressions of emotion, served as a social signal of "mere happiness or joy." In his landmark volume, *The Expression of the Emotions in Man and Animals,* Darwin meticulously described the laughter of his own infant son, writing: "At the age of 113 days these little noises, which were always made during expiration, assumed a slightly different character, and were more broken or interrupted, as in sobbing; and this was certainly incipient laughter."

Psychology, however, neglected the topic for decades. For most of its history, the discipline has primarily focused on negative emotions such as anger, depression, anxiety and major mental illness. This trend started to change about 40 years ago, when some psychologists began studying resilience to adversity, happiness and the psychology of well-being. A whole new subfield known as positive psychology was born.

Furthermore, it is only within the past 30 years that developmental psychologists have had methodologies for making inferences about infant cognition and emotion. One such method, the "gaze paradigm," involves timing the duration of an infant's stare. Several studies have demonstrated that babies will gaze longer at a novel object, which at its most basic level reveals that they can differentiate it from a familiar one.

In 1985 psychologists Elizabeth Spelke, now at Harvard University, and Renée Baillargeon of the University of Illinois

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at Urbana-Champaign coopted the gaze paradigm to study infants' conceptual knowledge. Spelke and Baillargeon began presenting infants with possible and impossible scenarios—for example, one object, in keeping with natural laws, would not penetrate a solid barrier, but a second, similar object would appear to do so. They found that babies gazed longer at unexpected events. These findings led researchers to deduce that infants come equipped with some simple expectations about how objects behave, which, when violated, results in their rapt attention. Such violations, it turns out, are powerful catalysts for humor.

Funny Business

Stand-up comedians often exploit expectations to make audiences laugh. They build suspense and push the boundaries of norms and acceptability to provoke our laughter, whether with puns, zingers or witty retorts. For something to be funny, the person telling a joke and the person hearing it need some common knowledge. Humor therefore requires at least some rudimentary understanding of the physical and social world. This understanding can be based on experience and observation, which provide the foundation for what is "ordinary." With that baseline, we can differentiate the ordinary from the absurd.

Babies can laugh before they master speech. This ability may have deep evolutionary roots; several species, including bonobos, engage in breathy, rhythmic vocalizations, much like laughter, during playful interactions.

Research from my lab shows that infants as young as five months, just a month after laughter comes online, can independently manage this basic perceptual difference. In 2014 my colleagues and I published findings from an experiment in which we presented 30 infants with ordinary and absurd events. For example, an experimenter might squish and roll a red foam ball as an ordinary scenario, then wear it as a nose in an absurd iteration of that event. Not only did infants distinguish between the two, they laughed at the latter. The key finding was that their laughter was not made in imitation; it occurred even when the experimenter and infants' parents were instructed to remain emotionally neutral.

Just a few months later, at about eight months of age, infants can be effective comedians and understand how to make others laugh without using any words. Psychologist Vasudevi Reddy of the University of Portsmouth in England calls this nonverbal form of humor "clowning." She has documented babies from eight to 12 months engaged in numerous forms of clowning—for example, exposing their naked tummy while shaking back and forth, attempting to put their toes in a caregiver's mouth while laying supine, or snatching a clean diaper and feigning disgust, followed by a smile.

Infants this age also engage in teasing, such as smiling coyly as they intentionally disobey a parent's directive not to climb the stairs or offering the dog a Cheerio, only to snatch it quickly back with a cheeky grin. Such "fake outs" have been reported even earlier by parents of six-month-olds, at which point infants can employ fake laughter (or tears) to draw attention to themselves or be included in an interaction that others are enjoying without them. Recall that laughter is difficult to fake, so these displays are easily detected.

Most important, infants *create* these novel interactions. They decide when and with whom to employ these techniques. As such, these types of playful, teasing exchanges can give us a window into infants' awareness. Teasing in particular requires

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When an event violates babies' expectations, they stare. But such circumstances may require a social context to be humorous. Truly improbable events may be more startling than funny.

at least a rudimentary understanding of others' minds, a desire to engage, and a guess or prediction as to how to provoke the mind of someone else. To trick someone else means to know that someone else can, in fact, be tricked. This knowledge, referred to as a theory of mind, is a mature insight that has traditionally been credited only to children at least four years old. Although infants do not have the mind theory sophistication of older children, their ability to effectively tease and provoke others suggests they have at least some level of awareness.

Great Expectations

Clowning and teasing reflect the primarily social nature of humor, but for something to make us laugh aloud in amusement, we need more than just the presence of other people. After all, infants spend most of their time *with* others, though little of their time laughing. This is because humor—whether for adults or infants—also requires a cognitive component: incongruity.

Incongruity refers to a situation that psychologist Elena Hoicka of the University of Sheffield in England describes as *mis*expected, meaning it creates a misalignment between what the infant expects and what she or he experiences. Misexpected events are slightly out of the ordinary. In contrast, truly unexpected happenings are completely shocking or surprising—and, as such, can be perceived as more disturbing or amazing than humorous. For example, when a cup is worn as a hat, it does not match the infant's prior experience with cups (or with hats). If the cup transformed into an antelope, the situation would be totally unexpected.

Adults, children and infants alike find unexpected events interesting but not necessarily funny. Multiple explanations arise from the research employing the violation of expectation paradigm. When infants are presented with violations of natural physical laws—such as gravity, solidity, inertia or quantity—they stare at these "magical" events, but they do not laugh. If we contextualize Hoicka's ideas into the larger research on infant gaze and interest, we can speculate that perhaps humor relates to misexpectations of social behavior. A toy flying through space and defying gravity is cause for wonderment. But Grandma wearing that toy on her head? Absolutely hilarious.

Humor theorists present one possible explanation through a phenomenon called incongruity resolution. To perceive an incongruity as humorous requires that the incongruity be resolved, which means understanding its cause or getting to the "punch line." The aha moment at which a listener decodes the nuance or double entendre of a verbal joke, for example, is the moment of resolution. It is the point at which the incongruous nature of why "a guy walks into a bar" becomes humorous, whether or not it is accompanied by overt laughter.

Forty years ago many cognitive psychologists argued that infants were not sophisticated enough to resolve incongruity. Psychologists Diana Pien and Mary Rothbart, both then at the University of Oregon, proposed that humor perception does not necessarily require advanced cognitive skills. In a study published in 2012 my students and I put that idea to the test.

When we asked 30 parents to "do whatever you normally do to get your baby to laugh or smile," they resorted to wildly exaggerated "clowning." Blowing raspberries, making odd faces and walking like a penguin. They are major permutations of ordinary daily interactions. At the very least, such behavior gets a baby's attention. Starting when the children were three and four months of age, we tracked these families through their first year and found that 40 percent of the youngest children laughed in response to their parents' antics; by five and six months, 60 percent of the infants laughed.

Infants need not do much to resolve these misexpectations to find them funny. In fact, there are at least three clues available to them. Social context is one example: these absurd acts are performed by a social partner, which may be enough to bias the infant toward interpreting the behavior as positive. My colleagues and I have observed that parents typically pair clowning with their own smiling or laughing about 65 percent of the time. This combination signals that the antics are safe, satisfying and joyful.

DIANE COLLINS AND JORDAN HOLLENDER *Getty Images (left)*; DANIELA SOLOMON *Getty Images (right)*

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A second factor is familiarity. Social partners often repeat silly actions over and over again until the infant laughs and then *because* she or he has laughed. It is possible that the caregiver's repetition allows the infant to either predict the action and its outcome—a resolution in itself—or infer the intentionality of the act. That Dad is balancing a spoon on his nose is not an accident if he repeats the act several times. Psychologist Amanda Woodward, now at the University of Chicago, has shown that, by their first birthdays, infants can infer intention from others' actions and speech.

A third element that may help babies differentiate between magical and humorous incongruities is that the latter are possible. Ultimately there is nothing magical about Mom wearing a cup as a hat. The nonmagical nature of humorous events may move infants, as well as children and adults, beyond that initial state of wonder to a final state of humor.

FROM EIGHT MONTHS OF AGE, INFANTS CAN BE EFFECTIVE COMEDIANS WITHOUT WORDS. BABIES ENGAGE IN CLOWNING, SUCH AS MISCHIEVOUS ATTEMPTS TO PUT THEIR TOES IN A PARENT'S MOUTH.

Whatever their strategy, experimental evidence shows that although infants begin to laugh at humorous events at about five months of age, they can detect such activities even earlier. Four-month-olds in our study gazed at humorous events with intense interest, registering a significant heart rate deceleration. This physiological response is exhibited when they display the same interest in a stimulus, as well as when they smile.

Psychologist Stephen Porges of the University of North Carolina at Chapel Hill proposes that heart rate deceleration does not necessarily reflect joy so much as prime the infant for it. When babies are confronted with something novel, they stare at it, a response that is accompanied by a heart rate deceleration. Porges suggests that this physiological calm acts as a kind of resource, allowing the infant to remain oriented toward a novel and nonthreatening stimulus. When this reaction is combined with their bias toward sociability, young infants may benefit from this calming response by finding pleasure in absurdity.

All Together Now

Our work suggests that infants truly can perceive and create humor. But not all laughter relates to amusement. Although there is no evidence of infants laughing in discomfort, we know that adults can and do laugh without mirth. That observation may provide insight into its deeper purpose.

No matter how it is deployed, laughter is social. Robert Kraut and the late Robert Johnston, both then at Cornell University, ushered in the field of evolutionary psychology with a landmark 1979 study demonstrating that—among other things—bowlers were more likely to smile not after achieving a strike but after facing the audience following a strike. Psychologist Robert Provine of the University of Maryland, Baltimore County, found that laughter is 30 times more likely to occur in the company of other people, regardless of whether anything amusing is happening. Provine's research shows that laughter usually follows banal comments such as, "I better be going!" or "Great to see you!" rather than comedic punch lines. In addition, people can be amused and not laugh at all.

For youngsters at play, laughter seems to signal both positive emotion and affiliation with one another. Evolutionary psychologists Robin Dunbar of the University of Oxford and Guillaume Dezecache of the University of Neuchâtel in Switzerland have proposed that laughter keeps us connected and in harmony as adults when we have long given up rough-and-tumble romps. This idea is especially supported by the contagious quality of laughter in groups of people, including strangers.

Laughter, therefore, serves as a kind of social glue, with many possible meanings. Someone's nervous giggle may prompt peers to provide comfort or assurance, and a mischievous chuckle can signal when roughhousing is meant purely in jest. Hoicka has described what she calls a "humorous frame," in which social partners can interact in such a way that both actors interpret an interaction—such as teasing—as positive.

Indeed, four- to six-month-old infants are poised for positive emotion. Not yet wary of strangers or of separation from primary caregivers, infants are ready for interaction with anyone, increasing their opportunities for play, smiling and laughter at just the moment when that new response is available to them. From an evolutionary perspective, this joint emergence of laughter and sociability is wise.

Laughter—it turns out—has a serious side. Its value as a social signal and mammalian superglue explains why it comes "factory-installed" as part of infants' native hardware. At four months of age, infants' laughter most likely is neurologically jump-started by their intense attention toward novelty and the salience of the broad social context. But within one month, babies have enough cognitive sophistication to detect and interpret new, nonthreatening social events as funny, all by themselves. A few months later they can produce such events, too, much to the joy of everyone. **M**

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POWER MOVES

SUCCESS CHANGES HOW PEOPLE THINK AND ACT—OFTEN, BUT NOT ALWAYS, FOR THE WORSE

BY THEODOR SCHAARSCHMIDT

ILLUSTRATIONS BY TAYLOR CALLERY

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Turkish president Recep Tayyip Erdoğan achieved a stunning ascent from humble origins to the pinnacle of power. As a working-class teen, he sold sesame bread along Istanbul's waterfront and dreamed of being a professional soccer player. By age 40, though, he had become the city's mayor. Less than a decade later he was elected prime minister of Turkey. And in 2014, when he was ineligible to run for a fourth term in that office, he campaigned for and won the country's presidency.

This past January the political party Erdoğan co-founded—the ruling Justice and Development Party (known as AKP)—took extraordinary steps to extend his influence even further. AKP lawmakers drafted amendments to Turkey's constitution that would eliminate the role of prime minister, make the 62-year-old president the sole executive head of state and afford him the opportunity to retain the position through 2029. A majority in the parliament backed the proposal, paving the way to a referendum on the matter on Sunday, April 16, 2017.

Critics attacked the move as a blatant and autocratic power grab. And it signaled just how bold Erdoğan had become since his political start. Initially Turks trusted him, the son of a Black Sea ship captain, as "one of them." Internationally he was seen as a reformer, who abolished the death penalty in Turkey, strengthened freedom of speech laws and made efforts to end conflict with the country's Kurdish minority.

For many, though, any favorable impressions of Erdoğan began to fade as he consolidated his grip on power. In answer to charges of corruption and conspiracy that began in 2013, he imprisoned hundreds of police officers, public prosecutors, journalists and generals. In the face of protests that year and a coup attempt last summer, Erdoğan's government responded with massive shows of force, using tanks, tear gas and water cannons against civilians. To stifle his opponents, he has intervened in the justice system and censored the media, blocking Twitter and calling for news blackouts.

Why did Erdoğan—like so many leaders catapulted onto the world stage—seem to change from a man of the people to a tyrant by many Turks' account? Historian John Dalberg Acton would have blamed the toxic effects of power itself. At the end of the 19th century he famously wrote, "Power tends to corrupt, and absolute power corrupts absolutely." But some theorists have argued for an alternative explanation: Maybe top-ranking politicians, CEOs and others who rise quickly in their fields harbor ruthless, authoritarian tendencies to begin with—and do those

President Recep Tayyip Erdoğan rose from humble beginnings to become the mayor of Istanbul, then prime minister and president of Turkey. As Erdoğan's influence has expanded, so have his authoritarian tendencies.

FAST FACTS

THE DARK SIDE OF SUCCESS

1. Whether in politics or business, those who have held high office for a significant length of time typically think and act differently than they did before.
2. Influential people tend to overestimate their abilities and ignore outside perspectives. On the other hand, they are above average in thinking abstractly.
3. Many factors, including personality traits and gender, determine whether a person will use power to their own advantage.

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very traits help them to take and wield power more easily?

Recent psychological research sheds some light on this age-old question. The headiness of power can indeed make people feel justified to use and misuse it, explains social psychologist Susan T. Fiske of Princeton University. "Power allows people to act freely," she says. Studies also show that as individuals grow in influence, they tend to lose empathy and an affinity for details. But of course, not all powerful people trend toward despotism. Scientists are discovering that how we rise to power and what we do with it when we get there varies, depending on personality, gender and a host of other factors.

The Last Cookie

You do not have to be a world leader to encounter power plays almost every day—at work, among friends, with partners and other family members. According to British philosopher and mathematician Bertrand Russell, power is to the social sciences what energy is to physics—the fundamental driving force of human behavior. In 2003 psychologist Adam D. Galinsky, now at Columbia Business School, and his colleagues explored how even slight shifts in our perception of power can dramatically change our actions.

In one experiment, they split 66 participants into two groups. They instructed half to write about an episode in which they exerted power over another person; the other half wrote about a time when someone else held power over them. Galinsky and his team used this writing exercise to "prime" the volunteers to feel either somewhat powerful or powerless. Next they brought the participants into another room to perform a task that involved allocating lottery tickets. While they worked, a fan blew directly—and annoyingly—at their face. The researchers observed that among participants primed for power, some two thirds simply pushed the unit aside. Among those made to feel "powerless," though, fewer than a third dared to do the same.

"High- and low-power individuals inhabit and, through their own actions, create strikingly different worlds," says social psychologist Dacher Keltner of the University of California, Berkeley, who has conducted similar investigations. When we feel powerless, he explains, our actions tend to be inhibited; we concentrate on the needs of others and are more sensitive to punishment. But as we gain influence, we become more receptive to rewards and allow ourselves more freedom. He has compared this disinhibition with acquired sociopathy, which affects some head trauma patients with damage to their frontal lobes.

As people gain influence, they become more receptive to rewards and—as the "Cookie Monster" study revealed—less likely to observe social norms, such as closing their mouth while they eat.

This sense of freedom has far-reaching consequences. For instance, in what has come to be known as the "Cookie Monster" study, Keltner and his colleagues randomly asked one volunteer in a group of three to rate the performance of the others while they worked on a boring task, such as drafting university policies. As soon as the group looked a little restless, the scientists offered them a plate of five chocolate chip cookies. They found that when it came down to the last cookie, the raters, who perceived themselves to be in a position of greater authority, were far more likely to nab it. What is more, a hidden camera revealed that the raters also ate like the blue-furred monster from Sesame Street—mouth open, lips smacking, crumbs flying. They did not care what "subordinates" thought of them.

The Path to Power

Additional studies have extended Keltner's finding well beyond table manners: the more power people accrue, the fewer social norms they typically observe. Some people who aspire to power, though, may get ahead simply because they are willing to break with convention in the first place. That was certainly the opinion of Renaissance political philosopher Niccolò Machiavelli. Today we use the term "Machiavellian" to describe leaders who pursue their goals without regard for moral or legal limits. They focus completely on status, always look to their own advantage and use others to their own end.

Psychologists include Machiavellianism as part of the so-called dark triad of personality traits, alongside narcissism and psychopathy. Psychologist Kibeom Lee of the University of Calgary in Alberta and his colleagues have shown that people who score high in all three of these traits also tend to score low in measures of honesty and humility. These individuals will do almost anything to achieve material wealth and social dominance.

But the Machiavellian path to power does not work for everyone—especially women. In 2008 Keltner and his team examined social hierarchies in an American college sorority. They found that members tended to gossip more about sisters who exerted their dominance over the group and threw their weight around. The subjects of gossip were also viewed as less likely to be competent in an office setting. In conclusion, Keltner and his team surmised that less powerful women may use the rumor mill as a kind of corrective mechanism for regulating power within their group. In fact, the

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young women in the study who showed greater social skills and tried to look out for the good of the entire sorority were the ones who tended to build influence over time. It is unclear to what extent this finding extends to men.

Several other studies have shown that women are more apt to be punished for dominant behavior than men are. For instance, in 2010 psychologists Tyler G. Okimoto and Victoria L. Brescoll, then both at Yale University, asked student volunteers to look at the Web sites of two fictitious senators and pick one to vote for. The descriptions were identical except that one politician was a woman and one was a man. In addition, the text sometimes mentioned that the candidate was extremely ambitious. When the profile included this extra detail, the study participants—men and women alike—were less likely to vote for the female candidate.

Powerful people tend to overestimate their abilities, take greater risks, think in terms of stereotypes and ignore outside viewpoints more often than people who see themselves as less powerful.

What seems to hold true regardless of sex is that people who rank high in extraversion and low in neuroticism—what are regarded as prosocial personality traits—tend to rise in any social group. Once there they often start to take on other characteristics. In particular, research has found that powerful people tend to overestimate their abilities, take greater risks, think in terms of stereotypes and ignore outside viewpoints more often than people who see themselves as powerless. "The skills most important to obtaining power and leading effectively," Keltner points out, "are the very skills that deteriorate once we have power."

Above It All

To be certain, being freed from others' opinions can help powerful people excel at big-picture thinking and bold decision making, but in sum, achieving authority appears to have a negative effect on how we think and act. By way of explanation, researchers have developed the "construal level theory," which features at its the core the notion of psychological distance. The basic idea is that objects, people or events will seem farther away or closer to us depending not only on their spatial and temporal distance but also on our level of personal involvement with them. The theory states that we think concretely about things we perceive as close but abstractly about things that seem distant. In this framework, the higher up the corporate ladder, the more abstractly an executive thinks.

Social psychologists Pamela K. Smith, now at the University of California, San Diego, and Yaacov Trope of New York University tested this proposition in a series of experiments in 2006. In one test, they used a priming technique akin to Galinsky's writing method to rouse feelings of power or powerlessness in 123 students. Then they asked them to memorize a series of terms and then try to recognize them again a few minutes later.

It was a classic memory test with a twist: all the words in the first series (for example, drapes, frame and pane) were closely associated with a missing term offered in the second series (window). Many participants tripped up during recall and flagged the missing word as an original one. Those who had been primed for power, though, made this mistake more often. They were quicker to jump at the missing abstraction.

Many other experiments have corroborated the idea that those in power tend to think more abstractly. When leaders see their subordinates as distant, abstract beings, it renders them less likely to consider their perspectives or desires. In fact, studies show that powerful individuals often become less altruistic and less empathetic toward others—and use their pull to benefit themselves instead of those below them on the organizational chart.

In 2015 economist Samuel Bendahan of the University of Lausanne in Switzerland and his colleagues measured these changes using the so-called dictator game. They divided nearly 500 subjects into small groups, putting some participants in charge of splitting a small amount of money with their group members. These select few could then give themselves a larger share of the money and shortchange the rest—or give themselves a smaller amount and leave a larger pot for everyone else. In different rounds of testing, they were also given varying degrees of authority. In some iterations, for example, they could determine the payment made to one other group member; in others, they could set the amount doled out to three people.

The infamous 1971 Stanford Prison Experiment attempted to re-create prison power dynamics among 24 undergraduates. Students randomly cast as "guards" quickly became abusive toward those cast as "prisoners," and the experiment was halted.

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The researchers found that the more

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Abu Ghraib prison guard Ivan Frederick was charged with abusing inmates. At his trial, experts debated if the prison environment corrupted him.

DAVID J. PHILLIP *AP Photo*

influence they gave the test subjects, the more unethical their decision making became. Among those with less discretionary power, fewer than half chose to keep more money for themselves. But that figure rose to almost 90 percent among those with greater authority in the game. The researchers also measured testosterone levels in about half of the subjects. They found that participants with high testosterone and the highest level of influence kept the most money for themselves. In fact, the hormone (and male gender) proved more important than power: men tended to disadvantage other group members far more often than women did.

Drawing the Line

Social position affects a wide range of moral judgments, as social psychologist Joris Lammers, now at the University of Cologne in Germany, and his colleagues demonstrated in a 2010 study. They, too, used priming to influence the sense of power their test subjects felt and then asked: Is it okay to take an abandoned bicycle? Cheat on your taxes? Drive over the speed limit? They asked half the participants to note how acceptable they thought these behaviors were for themselves. The others rated these acts when carried out by other people. As expected, they found that participants primed for power applied considerably less stringent criteria to their own behavior than to others. But those primed to feel powerless judged themselves and others by more or less the same standards. In some cases, these people even judged their own transgressions more severely.

Psychologist Philip Zimbardo of Stanford University has a deep appreciation of the treacherous aspects of power. He devised the infamous 1971 Stanford Prison Experiment that simulated prison power dynamics among 24 undergraduate volunteers. In his setup, a coin toss determined whether a student would act the part of a prison guard or a prisoner. As it turned out, the role-playing quickly degenerated into actual abuse, and the experiment had to be stopped. Although some researchers have since questioned the validity of Zimbardo's experiment, it remains one of the best known psychological studies ever done.

In 2004 Zimbardo was asked to testify at the trial of Abu Ghraib prison guard Ivan Frederick, who had been accused by the military court of physically and psychologically abusing inmates. In his statements, Zimbardo defended Frederick and made a case for a milder sentence. Very few people, he claimed, could have withstood the toxic atmosphere in Abu Ghraib and not been warped—much like the test subjects in his experiment. The Pentagon held that the prison's human-rights violations had been the work of a few "bad apples," but Zimbardo saw the problem as a "bad barrel" that had corrupted good people.

Did Zimbardo wrongly minimize the personal responsibility of the perpetrators? There is no question that power disinhibits and mobilizes people. It all too often puts them into situations in which their personalities shift in unexpected ways and may bring to the fore traits that previously lay dormant. But many experiments conducted since Zimbardo's have shown that the effects of power are not automatic. No one forced Frederick to do what he did. And although many people in power will exploit their team members, many others will use their authority to act altruistically. Frederick was ultimately sentenced to eight years in prison and served just under three.

Sociologist Max Weber viewed power as a chance for men or groups "to realize their own will in communal action, even against the resistance of others." Whether leaders use their influence for the good of their subordinates or for their own benefit depends on numerous factors—not only on the political situation or corporate culture but on the person himself or herself. Lord Acton was entirely correct that power can corrupt—and more often than not, it does—but modern research also reassures us that it does not have to. M

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Since an accident almost seven years ago, Ian Burkhart, now age 25, has had limited use of his arms and no use of his legs. He works intensively with researchers at Ohio State University to improve a brain-machine interface that could restore movement to people who are paralyzed.

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FORWARD MOTION

One man's journey to overcome spinal cord injury with the help of a cutting-edge brain-machine interface

By Yudhijit Bhattacharjee

PHOTOGRAPHS BY ANDY SPEARS

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The first thing Ian Burkhart did after he got to the Outer Banks in North Carolina one afternoon in 2010 was dive into the ocean. Nineteen years old, Burkhart had just completed his freshman year of college and come to the beach to vacation with friends. Joyously and with abandon, he pitched himself into the waters.

As he swam and bobbed in the surf, a wave flung his body onto a sand bar, jerking his neck with a force stronger than anything he had experienced before. Burkhart found himself lying face down on the seafloor, struggling to move. "Stay calm," he thought to himself. "Don't freak out." The water was only a few feet deep where he lay, and his friends pulled him out. Laid flat on the sand, Burkhart still could not move. He lost consciousness as he was being carried into a helicopter that airlifted him to a trauma hospital in Virginia.

In a surgery that lasted almost nine hours, doctors put two rods into Burkhart's spine to stabilize it. The next day they delivered a grim diagnosis: the accident had broken two of the vertebrae at the base of his neck, damaging that section of his spinal cord. He would never be able to walk and would barely be able to move his arms again. He would need help with nearly all the things he had previously done with his brain on autopilot as a healthy 19-year-old: eating, going to the bathroom, holding a toothbrush, turning the knob of his car radio.

A wave of devastation crashed over Burkhart. Even as a child, he had strived to become self-reliant. He had played lacrosse since third grade and had been a Boy Scout. At 13, he took up delivering newspapers to make money. In high school, he had started a lawn-mowing company with his brother. Now, a year after entering college, he was looking at spending the rest of his life under round-the-clock care. That is when the magnitude of his loss began to hit him. "I thought, 'Oh, crap, this is major,'" he says. "There was a lot of numbness because I didn't even know how to respond."

But last year Burkhart did something neither he nor his doctors could have imagined him doing. Seated in a wheelchair inside a laboratory at the Ohio State University Wexner Medical Center in Columbus, he maneuvered his hand to pour from a bottle, stir his coffee with a straw and swipe a credit card through a reader, simply by thinking those actions. He achieved these feats using a chip implanted in his brain that transmitted the neural signals of his thoughts to a sleeve wrapped around his right forearm. Dotted with buttons that deliver tiny jolts of electricity to various muscles, the sleeve stimulated his hand to execute the movements he envisioned.

Burkhart's accomplishment represents a milestone in a decades-long effort to develop brain-computer interfaces to restore movement and other functions to individuals with spinal cord injuries. "These demonstrations are very impressive," says Andrew Jackson, a neuroscientist at Newcastle University in England, who is not involved with the project. "This is a field where things are moving very quickly from monkey experiments to human experiments, and this was another study that showed that."

The brain implant, the software interface between the chip and the computer, and the sleeve Burkhart wore on his arm are the culmination of decades of research in neuroscience, rehabilitation science, computer science and sensor design, as well as a preview of the technological breakthroughs that lie ahead. Although Burkhart was able to make those simple hand motions only within a lab, researchers hope the technology will one day enable spinal cord injury patients to regain the use of their limbs permanently, restoring their sense of normalcy and autonomy.

The advance, reported last year in *Nature* by researchers at Ohio State and the Battelle Memorial Institute, represents a triumph of both science and the human spirit. Burkhart has spent several hours each week over the past three years to help engineers perfect the algorithms that translate his brain signals into action. "Ian's the hero here," says Ali Rezai, director of Ohio State's Neurological Institute and a member of the research team. "He has tremendous resilience and dedication. It's because of him that we are making these strides."

Mind over Machine

After his surgery, Burkhart moved back home to Columbus and signed up for an outpatient rehabilitation program at Ohio State. He had always been optimistic by nature, and as he adjusted to

FAST FACTS

BRIDGING THE GAP IN PARALYSIS

1. Devices that translate signals from the brain into commands of the muscles have come a long way to enable a paralyzed person to move his or her own limbs.
2. Advances in neural-recording techniques and decoding algorithms make it possible to execute fine-motor movements such as holding a cup or swiping a credit card.
3. Brain-computer interfaces still face many obstacles before they can be used outside research settings and provide near-natural dexterity.

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life in a wheelchair, he concluded his only option was "to make the best of my situation." His doctor was Jerry Mysiw, chair of the department of physical medicine and rehabilitation, who had spent more than 20 years working with spinal cord injury patients. Burkhart wanted to stay informed about research advances that could help patients like him. He had high hopes for "an advancement of some sort in my lifetime that would improve my daily life."

Around the same time Burkhart was going to his rehab sessions, researchers at Ohio State were embarking on a collaboration with engineers at Battelle to translate neural signals from the brain into movements via a brain-computer interface. The idea of connecting the brain to a computer and converting the brain's electrical activity into actions had been around for more than half a century, but only in the past two decades have researchers landed on a workable approach, beginning with studies in lab animals.

In 1998 a chip developed by neuroscientist Philip Kennedy was implanted in a human patient for the first time, enabling the person to slowly move a cursor to spell out words on a computer screen. Starting in the late 1990s, Miguel Nicolelis and his colleagues at Duke University performed a series of experiments in which monkeys hooked up to an interface could, with training, control a robotic arm with their neural signals.

In the ensuing years, researchers were able to record signals from individual neurons or small groups of cells rather than a broad cacophony. This, together with improved machine-learning algorithms for interpreting the signals, made it possible to direct more intricate movements. A consortium of researchers led by neuroscientists John Donoghue and Leigh Hochberg of Brown University developed an interface called BrainGate that enables patients to move a cursor on a computer screen with their thoughts alone. In 2008 Andrew Schwartz of the University of Pittsburgh and his colleagues trained a monkey with an implant to mentally manipulate a robotic arm to feed itself marshmallows and fruit, demonstrating impressive dexterity. Both groups have since shown that humans with brain implants could control a robotic arm to perform similarly exacting feats.

Burkhart is hooked up to a computer at Ohio State's Wexner Medical Center. His hours in the laboratory helped engineers perfect algorithms that translate brain signals into action.

But for patients, moving a robotic arm does not compare with the dream of regaining motion in one's own paralyzed limb. The Ohio State–Battelle team set its sights on achieving that dream by developing an arm-stimulating device that could communicate with a brain-computer interface. Mysiw asked Burkhart if he would participate in a study to test the sleeve, which Burkhart was glad to do. Every week at the lab beginning in September 2013, researchers slipped the stimulator onto his arm and hooked it up by wire to a computer. "We were able to get really good results as far as what type of movements we could make my hand do—such as flexing my fingers or making a fist—something that was very exciting and promising to me," Burkhart says.

But these movements were the computer's, not his own. When the stimulator study was wrapping up, Mysiw sat down with Burkhart to explain the broader idea of the project: implanting a device in the brain that could control the stimulator directly. Would he like to volunteer for the procedure? Mysiw went over the implications with Burkhart. He

Burkhart was able to do what had seemed unimaginable: pour from a bottle, stir his coffee with a straw and swipe a credit card through a reader, simply by thinking those actions.

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"Ian's the hero here. He has tremendous resilience and dedication. It's because of him that we are making these strides," says Ohio State's Ali Rezai.

would have to undergo at least two elective brain surgeries—one to insert the implant, another to take it out—with the inherent risk of infection. He would be exposing his brain to further damage, and even if the study were successful, he would not benefit from it personally, because the researchers would not be allowed to leave the implant in his brain permanently.

Burkhart felt the positives outweighed the negatives, however. He told Mysiw he felt it would be irresponsible to pass up such an opportunity to help others like him. In addition, Mysiw recalls, "he wanted to be able to scratch his nose [and] brush his teeth." Even though Burkhart understood that the research would likely take a long time to yield a usable neural prosthesis, the prospect—however remote—was appealing. "Knowing there's a chance that I could use this in my everyday life, coupled with being able to make a big impact, really made me want to do it," he says.

On April 22, 2014, Rezai and his fellow surgeons implanted a chip the size of a baby aspirin into Burkhart's motor cortex, in an area responsible for controlling his right hand. The chip is equipped with 96 tiny electrodes, each of which records the aggregate electrical activity of hundreds of nearby neurons. It is connected to a wire that sticks out of Burkhart's scalp, whose tip sits inside a nickel-sized disk screwed onto his crown. The structure resembles a small bottle cap and functions as the port through which researchers hook up Burkhart's brain to a computer in the lab. Learning to live with a metallic protrusion on his head took a while. "At first I had to really position my pillow just right so I wasn't putting any pressure on it," he says. Over time, it came to feel less obtrusive.

Decoding the Language of Movement

In the years since undergoing the surgery, Burkhart has followed a demanding routine: spending several hours in the lab twice or three times a week to focus on making his hand do things it had lost the ability to do naturally. Every session starts the same way. A cable hooked up to his port relays the neural signals from his brain to a computer while researchers have him think about performing specific movements with his right hand—such as flexing a finger or clenching his fist. To focus on the tasks, he uses visual feedback from a virtual hand on a screen that is controlled by his brain signals.

The key challenge is to ensure that the computer correctly interprets the pattern of neural signals generated by Burkhart's thoughts. While millions of neurons are firing in his motor cortex every time he

Members of the research team prepare Burkhart for a round of tests. To participate in the studies, he agreed to undergo potentially risky surgery to place an implant in his brain and later remove it. Getting used to life with a metal disk on his head was another challenge.

THE AUTHOR

YUDHIJIT BHATTACHARJEE is an award-winning writer whose features and essays on science, medicine, espionage and cybercrime have appeared in the *New Yorker,* the *New York Times Magazine, National Geographic, Wired, Science* and other U.S. magazines. He is also author of a nonfiction book, *The Spy Who Couldn't Spell,* which was published by Berkley in November 2016.

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A Firmer Grasp

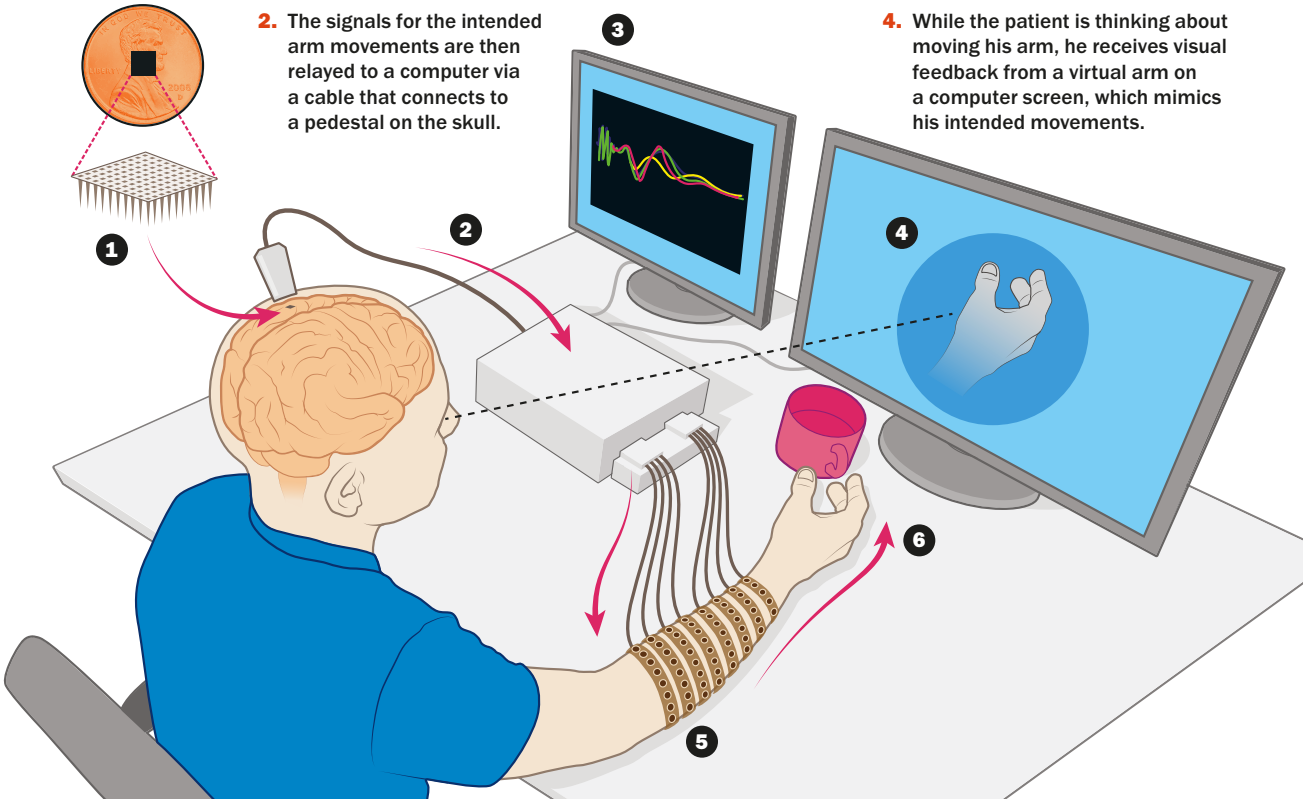
Brain-computer interfaces are making it possible to restore control of paralyzed limbs by recording signals from the motor cortex and relaying them to a computer that translates them into electrical stimulation of the damaged limb.

1. A 96-channel array the size of a small pea is implanted in the patient's motor cortex in a region that controls arm movements, where it picks up signals from individual neurons or small groups of brain cells.

2. The signals for the intended arm movements are then relayed to a computer via a cable that connects to a pedestal on the skull.

3. A computer algorithm filters and decodes the brain signals to determine the most likely intended movement. It then sends commands to an electrode cuff on the patient's arm.

4. While the patient is thinking about moving his arm, he receives visual feedback from a virtual arm on a computer screen, which mimics his intended movements.



5. The electrode cuff on the surface of the patient's arm stimulates his muscles to produce the desired hand motion.

6. Using the device, the patient is able to make movements as basic as picking up a glass of water or swiping a credit card or as sophisticated as playing the video game Guitar Hero.

TAMI TOLPA

thinks of an action, the chip in his brain picks up and transmits only a tiny sample of those signals. At 30,000 samples per second for each of the 96 microelectrodes, the data are still voluminous. The first step is to compress this information without stripping it of meaning. The processed signals are then fed into a set of algorithms that filter and convert them into electrical commands for the muscles.

The decoder—as these algorithms are collectively called—compares the pattern of activity received from Burkhart's brain with previously recorded patterns corresponding to a variety of movements and resting states. By this process, the decoder determines what action Burkhart most likely intends to perform. The decoder then receives feedback on whether it judged the pattern correctly or not, helping it do better over successive trials.

The firing patterns corresponding to the same movement can look quite different from one session to another because of the natural day-to-day variability in brain activity, according to Gaurav Sharma, a research scientist at Battelle and the nonprofit's lead investigator for the project. Shifting of the implant inside the brain also contributes to variability. "Ian might be happy or sad, he might be tired, he might be hungry, he might be hot or cold," Sharma says. And so, on any given

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Playing power chords: The pedestal on Burkhart's scalp provides access to the implant in his brain's motor cortex (*1*). A technician screws in the cable that connects the implant to an external computer (*2*). The brain-computer interface/electrode cuff is fitted to Burkhart's arm so that he will be able to move his hand (*3*). Burkhart grips the Guitar Hero instrument with the aid of the cuff (*4*). An image on a computer screen helps him focus on the buttons as he plays (*5*).

day, the decoder needs to learn anew "to recognize the patterns that are consistent with Ian thinking, 'I want to move my finger, I want to flex my wrist.' "

Burkhart went through a steep learning curve himself. When he began these sessions, a month after getting the implant, he did not know how he was supposed to mentally execute movements he had performed unconsciously before his accident. "The first few months of sessions, I would leave there being just completely mentally drained. I would feel like I [had] just sat through an all-day exam," he says.

One day in June 2014, less than six weeks after the sessions had begun, Burkhart was able to clench and unclench his hand around a spoon just by thinking it. The researchers who were there to witness the moment whooped and cheered. "There was just so much excitement out of everybody in the room," Burkhart says. Even before the cheers had died down, however, he was eager to hear what the next steps would be. "Now it's time to get to work," he thought, "because this thing does work, but how much can we do with it?"

Rezai and his colleagues wanted to graduate to more complex and finer movements. Burkhart proposed attempting actions he wished he could perform in daily life, such as using a credit card. "I can be fairly independent when I go out to stores, but I can't hold a credit card well enough to swipe it through a reader," Burkhart says. "Then we started working on all types of objects. Can we pick up a telephone and hold it to my ear? Can we pick up a spoon and scoop something out of a bowl and bring it to my mouth?" The researchers began working with Burkhart on a diverse range of grips and movements. The difference between a basic action such as flexing a finger and a complex task such as picking up a spoon and putting it down 10 inches away became quickly evident. "What would happen is, I would pick the spoon up, and then as soon as I would start to move my arm, it would drop out," Burkhart says. "Being able to sustain that grip through the motion was really challenging."

Enabling these higher-order movements required a unique kind of teamwork between human and machine. Like two people from different cultures, Burkhart's motor cortex and the decoder were learning to communicate through a process of trial and error he described as a "back-and-forth game of me learning the system and the system learning me." By early 2016 he was able to get his hand to execute acts of dexterity that months earlier had seemed out of reach: swiping a credit card, stirring a drink with a straw and even playing the video game Guitar Hero.

The Long Road Ahead

The publication of the *Nature* paper made headlines around the world. Weeks later Rezai and his colleagues got more good news. The U.S. Food and Drug Administration had given them permission to keep the implant in Burkhart's brain for another year. The researchers had estimated the chip would stop working

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properly after a year or so–the progressive scarring of brain tissue around the site was expected to gradually degrade the signal. "But it has been 700 days plus, and the signals can still be made sense of–that's unbelievable," Rezai said at the beginning of the study's third year, although he added that the signals had grown weaker.

Nobody was more pleased about the extension than Burkhart. "I am not ready to be done with the project," he said last October. He had driven to Ohio State's medical center–as he does two to three times a week–in a van modified for his needs. In addition to a wheelchair ramp, the vehicle has special levers that allow him to control the gas pedal, the brake and the steering wheel with his right arm, which he can still maneuver using his shoulder. (Burkhart retains the ability to use about two thirds of his shoulder muscles but has almost no functional control of either arm from the elbow down.) "I really enjoy seeing how much I can do," Burkhart says of the sessions. He found it rewarding that "now we can do seven different movements."

Still, the approach taken by Rezai's team has limitations. For one, Pittsburgh's Schwartz notes, the different muscles on Burkhart's arm are not controlled individually by his thoughts; rather the system selects a muscle-activation sequence from a menu of sequences, like "picking a particular tape for a player piano." In work done at Schwartz's own lab, he says, even though subjects move a robotic arm rather than their own, "our control is elaborate enough that our subjects [can separately] operate the arm, wrist and fingers." Burkhart's muscle control is limited, too, because the stimulating electrodes sit on the outside of his skin. In patients with a greater degree of paralysis, such external stimulation would be unlikely to work.

A group led by Robert Kirsch of Case Western Reserve University and Brown's Donoghue recently succeeded in inserting fine electrodes into the completely paralyzed arm of a patient with a brain implant, who was then able to make crude arm and hand movements.

Looking ahead, Rezai's group hopes to both expand the range of Burkhart's movements and make them more sophisticated. "When you're doing things in your day-to-day life, the strength is really important," says Battelle computer scientist David Friedenberg. He gave the example of picking up a paper cup. "If you grip it too hard and it's empty, you're going to crush the cup. Then once you fill it up, that light grip isn't even going to lift the cup off the table," he says. "As you're drinking it, you're constantly adjusting how much strength you're using."

The researchers are also working to improve the decoder so it can correctly identify signals associated with a specific action without extensive training. The stimulation technology is improving as well—in recent months engineers have equipped the sleeve with sensors to keep track of changes in the position of the electrodes on Burkhart's arm as he moves.

This summer, unless the FDA grants yet another extension, Burkhart will have the implant removed. But efforts to make the technology usable will continue. Rezai envisions an implant that relays signals wirelessly and a decoder that can run on a smartphone communicating with the stimulating sleeve. In fact, researchers at Brown have already developed a wireless implant. The ideal system would not only transmit Burkhart's thoughts to the decoder but also relay back tactile feedback—as a group at Pittsburgh demonstrated in 2016, when the researchers partially restored a paralyzed man's sense of touch by electrically stimulating his brain.

"We are far from where we need to be," Rezai says. "Ian needs to be able to take it home so that when he wakes up in the morning he can just wear a sleeve, like he wears a shirt, and he can pick up a croissant and a cup of coffee, go outside to the backyard and hang out." M

Like individuals from different cultures, Burkhart says, his motor cortex and the decoder were learning to communicate in a "back-and-forth game of me learning the system and the system learning me."

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THE SELF-COMPASSION SOLUTION

BUILDING ON A BUDDHIST PRINCIPLE, PSYCHOLOGISTS ARE LEARNING HOW BEING KIND TO YOURSELF CAN BOLSTER RESILIENCE, BUFFER AGAINST STRESS AND IMPROVE RELATIONSHIPS **BY MARINA KRAKOVSKY**

ILLUSTRATIONS BY MARINA MUUN

Two years ago Michelle Rapp, then a 28-year-old Cornell University graduate, experienced a series of unfortunate events. First, she lost her job in a mass layoff at a San Francisco start-up. Then, anxious to get back to work, she took a physically demanding job at a Chinatown tea shop—but weeks later she threw out her hip while carrying boxes up the store's steps.

Unable to walk and go on job interviews and feeling stressed and demoralized, she immersed herself in a cerebral and competitive card game, Magic: The Gathering. Yet even this diversion ended up causing anguish for Rapp. Her whole-hog approach to the game—joining tournaments and founding a local chapter—was only the latest act in a lifelong pattern of setting ambitious goals and then judging herself harshly for failing to meet them.

When she found herself on a losing streak, she could not stop beating herself up. "Looking

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back, it seems crazy," Rapp says. "Of course, I'm a good player. Yet I couldn't forgive myself for losing."

Rapp believes this self-destructive behavior stems from growing up with intense parental pressure to excel—pressure, she says, that often took the form of emotional and physical abuse. In recent years she has undergone treatment for anxiety and depression—but in her case, it was not therapy that broke her self-defeating pattern. Talking with her husband about her problems reminded Rapp of a book she had read on nonviolent communication that emphasized the importance of speaking with compassion—including compassion for yourself. That recollection was Rapp's aha moment.

Self-compassion, at its most basic level, means treating yourself with the same kindness and understanding that you would a friend. People who struggle with this concept, research shows, do not necessarily lack compassion toward others. Rather they hold themselves to higher standards than they would expect of anyone else. Developing self-compassion allows them to recognize and accept their own feelings rather than constantly challenging themselves to "do better."

Rapp is one of a growing number of people to discover that practicing self-compassion can be a surprisingly effective alternative to the crippling yet common habit of shame-laden self-criticism. Since the birth of self-compassion as a scientific construct—with the publication of a seminal paper by psychologist Kristin D. Neff of the University of Texas at Austin in 2003—the volume of academic publications investigating self-compassion has snowballed.

In the past few years self-compassion has gone mainstream, as some of its researchers and practitioners—including Neff—have written books and created workshops to popularize the concept. Untold numbers of life coaches, mindfulness teachers and psychotherapists now tout the benefits of self-compassion. Psychotherapists see it as a natural component of well-studied therapies that focus on accepting and gradually changing unhelpful thoughts or behavior patterns, such as cognitive-behavioral therapy and acceptance and commitment therapy.

Self-compassionate seniors reported a greater sense of well-being despite health issues and more willingness to use a walker if they needed one.

Yet many people resist self-compassion, fretting that being compassionate toward ourselves will make us egocentric, self-indulgent or weak. If we are easy on ourselves after a setback, we wonder, will we turn soft and complacent? This question is one of many self-compassion research has tried to answer. The conclusion: a resounding "no." As mounting evidence shows, self-compassion is typically a source of both personal and interpersonal strength, making self-compassionate individuals more emotionally stable, more motivated to improve themselves and generally better to be with.

Buddhist Roots

Neff, the pioneer in the scientific study of self-compassion, became interested in the topic in the 1990s. As a Ph.D. candidate struggling with the breakup of her first marriage, she was full of shame and self-loathing. She began attending meditation classes and exploring Buddhist thought.

Neff knew that compassion entails concern with another's pain and a desire to alleviate that person's suffering, but she had never thought about directing that energy toward herself until she read Buddhist teacher Sharon Salzberg's book *Lovingkindness*. She felt transformed by its message that showing kindness to oneself is essential for showing genuine love toward others. She soon began to lay the groundwork to study self-compassion scientifically.

Through her reading, Neff discerned three indispensable elements of self-compassion: kindness toward yourself in difficult times, paying attention to your suffering in a mindful, nonobsessive way, and common humanity, or the recognition that your suffering is part of the human experience rather than unique to you. These three components (along with their opposites) became the basis of the questions Neff used to develop a self-compassion scale [*see box on page 68*], an instrument she published in 2003 in the journal *Self and Identity* that is now widely used by other researchers in assessing a person's level of this trait.

Using this scale, Neff has shown that self-compassion correlates with important real-world outcomes. In particular, she found that people who score high in self-compassion are less prone to anxiety and depression.

Psychologist Juliana Breines first encountered Neff's work while she was an undergraduate at the University of Michigan. Breines suspected self-compassion could help people get off the roller coaster of "contingent self-esteem"—that is, the problem of tying your evaluation of yourself to fluctuating factors such as ac-

FAST FACTS

LOVE YOURSELF, TOO

1. Inspired by Buddhist practices, self-compassion involves treating oneself with the same kindness and understanding that someone would offer a friend.
2. This trait has been found to increase motivation required to persist in a task after failure and seems to enhance resilience to challenging or traumatic events.
3. By caring for themselves, individuals can also be more present in relationships and can sustain greater compassion for others.

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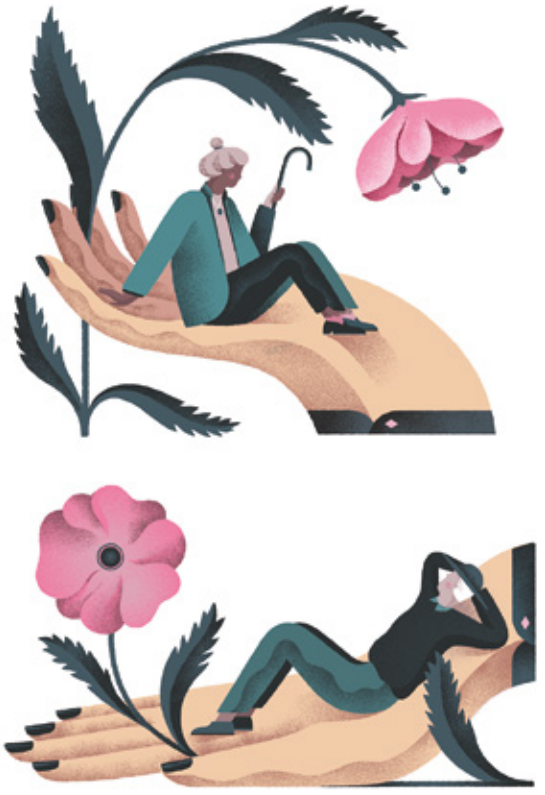
ademic achievement and others' approval. Many studies have demonstrated that this kind of thinking is not conducive to mental health or learning. But Breines worried self-compassion might also undermine motivation. As she puts it, "Self-compassion might be comforting, but does it let you off the hook too easily?"

Breines tested this question a few years later, as a graduate student at the University of California, Berkeley. In one of a series of experiments, she and her colleagues had 86 undergraduates take a tough vocabulary quiz. To see the effect of self-compassion on study behavior, they told one group that it was common to find the test difficult and urged subjects not to be too hard on themselves. A second group got a self-esteem message instead: "Try not to feel bad about yourself—you must be intelligent if you got into Berkeley." A third group received no additional statements.

Then the researchers measured how long the undergrads would study for a second, similar test. As they reported in 2012 in *Personality and Social Psychology Bulletin,* the self-compassion group went on to spend 33 percent more time studying for the subsequent quiz than the self-esteem group and 51 percent longer than the neutral control group—a sign that self-compassion bolsters motivation. Being kind to yourself can make it safe to fail, which encourages you to try again.

In a pair of 2012 studies led by social psychologist Ashley Batts Allen, then at Duke University, researchers investigating self-compassion in older adults found both psychological and practical benefits. In the first study, with 132 participants ranging from 67 to 90 years old, they found that people who were strongly self-compassionate reported a greater sense of well-being even when they were in poor health. In the second study, involving 71 seniors, self-compassion predicted how likely they were to be willing to use a walker if necessary. "The self-compassionate people were just less bothered by the fact that they needed help," explains Allen, now at the University of North Carolina at Pembroke.



Mark Leary, a Duke psychologist who collaborated with Allen, adds that if you are low in self-compassion, "you're using too much emotional energy thinking about the bad feelings" and not enough addressing the real issues. For example, denying one problem—insisting on not using a walker—can create further difficulties, such as a hip fracture. The mindfulness component of high self-compassion, in contrast, leads people to acknowledge and accept reality, without an emotional judgment. The common-humanity component helps, too, by, for example, allowing one to recognize that everyone has physical limitations with age.

In 2014 Leary and his colleagues studied 187 mainly African-American people living with HIV. Patients who were higher in self-compassion showed healthier reactions to life with the potentially deadly virus: they experienced less stress, felt less shame about their condition, and were more likely to express a willingness to disclose their HIV status and to adhere to medical treatment. And a 2015 meta-analysis of 15 studies with a total of 3,252 participants, published in *Health Psychology,* found links between self-compassion and health-promoting behaviors related to eating, exercise, sleep and stress management.

Bouncing Back to Normal

Research indicates that the self-compassionate are more psychologically resilient and better able to regain emotional well-being after adversity. People who used self-compassionate language after their divorce, for example, recovered more quickly than those who had a more self-critical or self-pitying ("Why me?") outlook on the relationship's failure, according to a 2012 study of 109 adults.

Caregivers, too, can benefit. Raising an autistic child, for instance, is more emotionally difficult than other forms of parenting, with levels of stress and hopelessness that tend to correspond to the severity of the child's symptoms. Yet a 2015 study of 51 parents of autistic children found that those mothers' and fathers' self-compassion was more important than the severity of the child's symptoms in predicting a caregiver's well-being.

Yet another example comes from 115 combat veterans of the wars in Iraq and Afghanistan. In a 2015 study in the *Journal of Traumatic Stress,* self-compassionate war veterans experienced much less

THE AUTHOR

MARINA KRAKOVSKY writes and speaks about the practical wisdom of the social sciences. Her most recent book is *The Middleman Economy: How Brokers, Agents, Dealers, and Everyday Matchmakers Create Value and Profit* (Palgrave Macmillan, 2015).

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Do You Have Self-Compassion?

The statements below are from an assessment created by psychologist Kristin D. Neff. In the full version (http://bit.ly/SlfCompassion), you would rate yourself on a scale of 1 to 5, where 1 is "almost never" and 5 is "almost always."

Statements associated with high self-compassion:

- I try to see my failings as part of the human condition.
- When I'm going through a very hard time, I try to keep my emotions in balance.
- I try to be understanding and patient toward those aspects of my personality that I don't like.

Statements linked to low self-compassion:

- When I fail at something important to me, I become consumed by feelings of inadequacy.
- When I'm feeling down, I tend to feel like most other people are probably happier than I am.
- I'm disapproving and judgmental about my own flaws and inadequacies.

severe post-traumatic stress disorder (PTSD) symptoms than those lower in self-compassion, even after accounting for the level of combat exposure. "It's a powerful testament to the idea that it's not *what* you face in life," Neff says, "it's how you relate to yourself when you face very hard times."

Recent studies of people with other psychiatric disorders, including binge eating and borderline personality disorder, suggest that self-compassion helps recovery. Allison Kelly, a psychologist at the University of Waterloo in Ontario who has studied the effect of a self-compassion intervention on binge-eating disorder, points out that recovery requires not only learning to tolerate urges to binge but also figuring out how to bounce back after giving in to those urges. "If, like a drill-sergeant coach or critical teacher, you're threatening yourself into change and beating yourself up whenever you slip up, it makes it hard to feel calm and confident," she says, "and often takes away the ability to reflect and learn from what you're going through."

Self-compassion might seem to go hand in hand with self-esteem. In fact, self-compassion can coexist with low self-esteem and can buffer against it. In a 2015 longitudinal study led by Sarah Marshall, a psychologist at Australian Catholic University, researchers tracked a group of 2,448 students as they moved from ninth to 10th grade. Marshall found that high self-esteem was a precursor to good mental health, regardless of the students' level of self-compassion. But self-compassionate kids who had low self-esteem *also* showed good mental health.

That news is good because it is usually easier to raise someone's self-compassion than his or her self-esteem, Duke's Leary says. "It's really hard to get someone with low self-esteem to like themselves until they develop more social skills or get a better job or something." By comparison, the bad habits of low self-compassion, such as denying a problem exists or beating yourself up, are easier to break.

Stronger Relationships

Recent research suggests that self-compassion is also good for relationships. Neff led a 2013 study of 104 couples that looked at how self-compassionate people treat their romantic partner—as rated by that partner. In general, men and women who scored high in self-compassion were seen as more caring and supportive (and less controlling and verbally aggressive) than individuals low in self-compassion.

Yet Neff has also found that most people have an easier time being compassionate to others than to themselves. A striking illustration is another 2013 study in which she measured both self-compassion and self-reported compassion for others among 384 college students. Neff found absolutely no correlation between the two forms of compassion; similar studies of practicing meditators and of ordinary adults showed only weak correlations. She has also noticed that practitioners of Buddhist metta, or loving-kindness, meditation—in which you start by wishing yourself well and go on to extend your goodwill toward an increasingly widening circle of empathy—give short shrift to the beginning section. Instead they focus on kindness to others.

But if people find it easier to show compassion to others than to themselves, how can we understand the results from the couples study? Neff believes that being kinder to others than to yourself, though possible, will not carry people through long-term relationships. "If you give your all to your partner and are hard on yourself, you can't sustain a healthy relationship," she says.

This interpretation dovetails with findings, published in 2013 in *Self and Identity,* that revealed how self-compassionate people handle interpersonal conflicts. The study, led by applied statistician Lisa Yarnell, involved 506 undergraduates. Yarnell, now at the American Institutes for Research, found that students high in self-compassion were better at balancing the needs of themselves and of others and felt better about a conflict's resolution than those low in self-compassion. The self-compassionate individuals reported lower levels of emotional turmoil and greater relational well-being.

These findings have implications for full-time caregivers, who have long been known to be at risk for burnout and "compassion fatigue," a deadening of compassion through overuse. In fact, a 2016 cross-sectional survey study of 280 registered nurses in Portugal suggested that although nurses with higher levels of empathy were at greater risk of compassion fatigue, empathy was not a risk factor if it was accompanied by self-compassion.

Teaching Self-Compassion

If being self-compassionate has so many positive outcomes, can people learn

SOURCE: "THE DEVELOPMENT AND VALIDATION OF A SCALE TO MEASURE SELF-COMPASSION," BY KRISTIN D. NEFF, IN *SELF AND IDENTITY*, VOL. 2, NO. 3, 2003

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to treat themselves more kindly? One promising intervention is mindful self-compassion, or MSC, an eight-week workshop that Neff developed with Christopher Germer, a clinical psychologist who teaches part-time at Harvard Medical School. The MSC program, designed for the general public, explains the research on self-compassion and introduces a variety of exercises, such as savoring pleasant experiences, touching yourself soothingly, using a warm and gentle voice, and writing a letter to yourself from a loving imaginary friend.

In a small study published in 2013, Neff and Germer reported that 25 people (mainly middle-aged women) who completed an MSC workshop reported higher gains in self-compassion and well-being than a similar group randomly assigned to the wait list for the workshop. Furthermore, the workshop participants maintained their gains a year later. Interestingly, people in the control group also showed some gains in self-compassion—the control group's self-compassion scores rose 6.5 percent between the pretest and the post-test phases, whereas the experimental group's self-compassion scores rose 42.6 percent. This result initially puzzled the researchers—until they discovered that the wait-listed group used the time to learn about self-compassion independently through books and Web sites.

It remains unclear how much the MSC participants' success is related to the training itself as opposed to, say, being in a group or having caring teachers, notes Julieta Galante, a research associate in psychiatry at the University of Cambridge. Last year Galante and her colleagues published the results of an online, four-week randomized controlled study of only the loving-kindness meditation—an exercise often used to cultivate compassion for yourself and others but not targeted specifically to relieve suffering. The team found no difference between the meditation group and a control group doing light physical exercise.

Give Yourself a Break

Expert tips for cultivating self-compassion:

- Realize that self-flagellation does not help you reach your goals but actually holds you back.
- If self-compassion scares you, perhaps because of past abuse, consider turning to a counselor trained in compassion-focused therapy.
- If you are a parent or teacher, strike a balance between celebrating children's achievements and helping them understand that struggles are normal, too.
- Everyone is different, so explore which self-compassion practices work for you. (You can find specific exercises on psychologist Kristin D. Neff's Web site: http://self-compassion.org/category/exercises)
- If you are struggling with self-compassion exercises, be patient and forgiving with yourself—even if that means *not* practicing self-compassion. —*M.K.*

Furthermore, many people dropped out of the intervention, some actually describing intense, troubling emotions—crying uncontrollably or realizing they had no uncomplicated relationships in their lives. Germer and Neff brace their workshop participants for this possibility, using the firefighting metaphor of "back draft" to explain the phenomenon: just as flames rush out of a room as oxygen returns, old pain can surface amid an influx of compassion in people starved of love. It is possible that before taking a course, some individuals may need to ease into self-compassion practice slowly, perhaps with the aid of a therapist.

Paul Gilbert, a professor of clinical psychology at the University of Derby in England, agrees. In his years of treating victims of childhood abuse or neglect, he has observed that kindness can backfire. Anything that stimulates fragile attachment systems can trigger memories of past trauma, particularly in cases of childhood abuse. "There are so many fears and resistances to compassion that it would just blow fuses" to start with exercises for the general public, Gilbert says.

The compassion-focused therapy (CFT) that he developed for such patients and tested through small-scale studies starts with psychoeducation and proceeds gradually. Gilbert explains to patients, for example, that self-criticism is not their fault and shows how it may have developed as a way to protect themselves from threatening parents. Once patients understand that neither their genes nor their early environment are their fault, they can begin to let go of shame—and start taking responsibility for their future.

That is what Michelle Rapp did. Although she came to practice self-compassion independently, earlier therapy likely laid the groundwork for her journey. She eventually came to accept her injury and other setbacks and overcame the shame she had often felt in asking for help. During her recovery, she stopped forcing herself to hobble to a bus stop on crutches and sprung for a cab. She knew she was worth it. M

MORE TO EXPLORE

- **The Compassionate Mind: A New Approach to Life's Challenges.** Paul Gilbert. New Harbinger Publications, 2009.
- **Self-Compassion: The Proven Power of Being Kind to Yourself.** Kristin Neff. William Morrow, 2011.
- **Self-Criticism and Self-Compassion: Risk and Resilience.** Ricks Warren, Elke Smeets and Kristin Neff in *Current Psychiatry,* Vol. 15, No. 12, pages 18–21, 24–28 and 32; December 2016.
- Metta Institute describes "Metta Meditation": **www.mettainstitute.org/mettameditation.html**

From Our Archives

- **Be Your Own Best Friend.** Marina Krakovsky; Head Lines, July/August 2012.
- **Letting Go of Self-Esteem.** Jennifer Crocker and Jessica J. Carnevale; September/October 2013.

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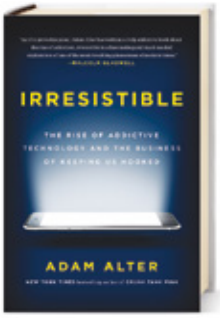
CONSUMED BY TECH

Irresistible: The Rise of Addictive Technology and the Business of Keeping Us Hooked

by Adam Alter. Penguin Press, 2017 ($27; 368 pages)



Confession: I can't stop checking my e-mail. I find myself reaching for my smartphone when I am in meetings, in the car, at the gym, at the beach. This impulse is surprisingly common. Studies suggest that the average worker checks his or her e-mail 36 times every hour and that as much as 40 percent of the U.S. population may suffer from some kind of Internet-based addiction. Modern technologies come with perks—such as the ability to connect with others and search for information on the go—but they can clearly intrude on our lives, too.

In *Irresistible,* Alter, a marketing professor at New York University, explores the rise of tech-based addictions—how unhealthy relationships with our devices get started, how we become hooked and how we can detach. The path to dependence and the consequences, he notes, mirror what happens with drug addicts. Both kinds of addictions "activate the same brain regions, and they're fueled by some of the same basic human needs: social engagement and social support, mental stimulation, and a sense of effectiveness," he writes.

Pinpointing exactly when normal tech reliance morphs into a psychological problem remains a challenge, in large part because technology is now all-pervasive in our daily lives in ways that drugs and alcohol are not. We can, and often do, carry smart devices and laptops wherever we go; we shop, date, house hunt and work at our screens. "Millions of recovering alcoholics manage to avoid bars altogether, but recovering Internet addicts are forced to use e-mail," Alter explains.

Yet the problem goes beyond access. Alter reveals how companies deliberately design devices and apps to capitalize on our most basic psychological needs for approval and success. So-called ludic loops—habit-forming circuits that influence dopamine levels in the brain—may explain, on a biological level at least, why we become obsessed, he says. These ludic loops drive Instagram users to chase the next stream of "likes" and Internet gamers to play for hours. They are strengthened every time we experience the high of posting a well-liked image or reaching a new level of Candy Crush.

So how can we unplug? Alter travels to a gaming and Internet addiction treatment center in Washington State to learn about various recovery strategies. For most users, simply taking a few moments of screen-free downtime every day can lessen tech's lure. That fact is prompting some experts and organizations to work toward developing novel ways to minimize people's exposure.

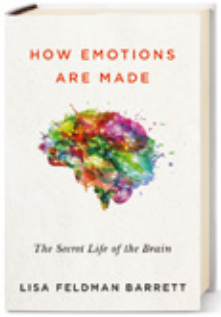
German car manufacturer Daimler, for example, allows employees to change the settings on their work e-mail accounts so that they automatically delete incoming messages during vacations. Similarly, one Web developer has created a browser add-on that makes it impossible to check how many likes or comments a Facebook post generates.

Alter's central argument is that technology has invaded our lives, and we need to keep it from completely consuming us. His book is an engrossing—albeit alarming—read that will make you want to chuck your smartphone out the window. *—Lindsey Konkel*

FEELING OUR WAY

How Emotions Are Made: The Secret Life of the Brain

by Lisa Feldman Barrett. Houghton Mifflin Harcourt, 2017 ($29; 448 pages)



In an essay in 1945, behavioral psychologist B. F. Skinner argued that our emotions are little more than social constructs: we think they exist only because the people around us tell us how to label our internal experiences. But in 1962 social psychologists Stanley Schachter and Jerome E. Singer showed just how tenuous this labeling scheme is. They jolted people's nervous systems with shots of adrenaline and found that how they described the effects depended on how the people around them behaved. In the presence of a euphoric person, the participants felt euphoria; when close to an angry person, anger.

Now Barrett, a psychology professor at Northeastern University, takes such thinking to a new level and, some might say, a new extreme. Drawing on extensive research that she and her students have been conducting for more than a decade, she argues that we create our own emotions based on how we learn to interpret both bodily sensations and our current circumstances. In other words, we do not experience the world directly but instead build mental models that help us predict and define what is happening to us. These states of mind are not very different from thoughts, which is why Barrett also rejects the common belief that emotions *cause* thoughts or behaviors (as in "she shouted and stamped her feet because she was angry").

How Emotions Are Made defends the author's "constructionist" view of emotion—and specifically the idea that, with little or no awareness, we generate our emotions on the fly. Barrett also rejects the more intuitive and traditional "essentialist" view that emotions such as anger and sadness have distinct essences, universal across cultures. She is especially dismissive of the pioneering work by psychologist Paul Ekman, whose painstaking cataloguing of emotion-correlated facial expressions has been supported by a huge number of studies. Barrett cites a fundamental design flaw: Ekman-type studies, she says, always suggest fixed emotion categories, a concept that her own studies reject.

Our mental models, she maintains, make it difficult for us to see the truth—and that, in a nutshell, is the problem with her ambitious book. Barrett views human functioning through a metaphor: We are all like research scientists, probing, predicting and constantly revising our theories. She cannot see mind and brain any other way. When it is "time to drink my own Kool-Aid," she does admit that most of the key concepts she proposes about emotion, mind and brain are speculative—and that is where the reader is left. Even so, Barrett's is a singular book, remarkable for the freshness of its ideas and the boldness and clarity with which they are presented. *—Robert Epstein*

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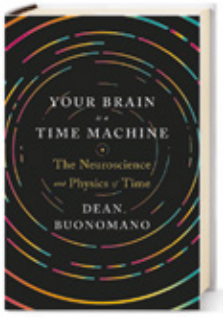
MIND TRAVEL

Your Brain Is a Time Machine: The Neuroscience and Physics of Time

by Dean Buonomano. W. W. Norton, 2017 ($26.95; 304 pages)



The idea of time travel is highly seductive. Cult classic movies such as *Back to the Future* and *Primer* imagine a reality in which we can physically hop among the past, present and future. In contrast, *Arrival* presents time travel in a more cerebral form: this 2016 film features four-dimensional beings—aliens who can control their placement in time and even perceive their birth and death simultaneously. Such diverse portrayals exist, in large part, because time itself—what it is and how we understand it—remains enigmatic.

In his new book, Buonomano, a neuroscientist at the University of California, Los Angeles, takes a stab at unraveling the complex nature of time. He begins by exploring the prevailing theories. According to physics, we live in what is called an eternalist universe, where time—like space—is a dimension and, as in *Arrival,* the past, present and future all exist simultaneously. One of the strongest pieces of evidence backing the eternalist theory comes from Einstein's theory of relativity, which revealed that space and time lie together on a continuum. Along this nonlinear timeline, we should be able to move physically between different periods.

But this eternalism clashes with how humans actually experience time. Our reality fits better with the theory known as presentism—in which we can imagine the future and remember the past, but only the present is real. How to reconcile the two ideas? Buonomano speculates that our brain must have adapted to understand time as something that moves forward in a linear way.

Perhaps, though, there is a middle ground. Studies suggest that space and time not only are threads along a single tapestry in the physical world, as Einstein showed, but may also be closely entwined in the brain. Researchers have found, for instance, that patients with spatial hemineglect—or an unawareness of objects on one side of the body—also have trouble remembering the timing of events. In addition, we often use spatial terms to describe time—"Boy, was that a long lecture" or "Let's move the meeting forward a week." Some scientists theorize that, as we evolved, the neural circuits recruited for perceiving time were co-opted by those used to comprehend space.

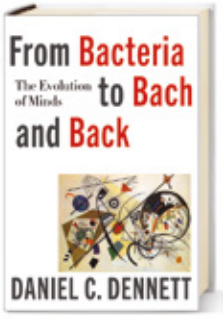
Theories of time aside, Buonomano's key argument is that the human brain itself already acts as a time machine of sorts. Timekeeping is built into our neural circuits, controlling everything from synaptic plasticity to circadian rhythms. Although we cannot physically travel to the past or future, to some extent our brain already does. We can learn, plan, build, prepare and even prevent disaster thanks to our ability to recall previous events and envision what could be. "The brain is a product of natural selection, and was thus 'designed' to survive a harsh and continuously changing world," he writes. "As it turns out, one of the best ways to prosper in such a world is to be able to predict *what* will happen in the future, and *when* it will happen."

Buonomano lays out a wealth of complex concepts in an entertaining, digestible way. He admits that both physics and neuroscience are still far from understanding the true nature of time, but his book will make you question your own perceptions and marvel at the fact that your brain is probably "the best time machine you will ever own." —*Diana Kwon*

INSIDE CONSCIOUSNESS

From Bacteria to Bach and Back: The Evolution of Minds

by Daniel C. Dennett. W. W. Norton, 2017 ($28.95; 496 pages)



First, let me say that I felt some trepidation in approaching what is being touted as the "masterwork" of such a prolific philosopher, famous for pondering the complexities of consciousness and free will. But this work touches on themes that every curious person with an existential itch—or knowledge of psychology, psychiatry or neuroscience—has contemplated: What *is* the mind? How and why are humans "conscious" in a way that other animals are (probably) not?

In answer to the first question, Dennett adheres to a materialist view: He believes that our mental capabilities are nothing more than a by-product of the brain's physical processes. We simply evolved the *how* and *why* of human consciousness, which gave rise to thinking and the ability to *think* about thinking. Well, not simply. I wouldn't use "simple" to describe anything about this work.

Dennett's central argument is that all of the intricate "design" that went into building our conscious minds happened through processes that were *competent* (they worked) but lacked *comprehension* (no one planned it that way). The evolution from bacteria (competent) to Bach (comprehending) happened faster than gene-based natural selection would allow and relied instead on cultural evolution via memes—any idea or trend that we share as a way to expand our cognitive tool kit.

Although his theory about consciousness may be impossible to prove, Dennett convincingly builds his case that we developed consciousness from "a cascade of competences" using recent evidence, plus historical lessons from philosopher René Descartes, biologist Charles Darwin and computer scientist Alan Turing.

Dennett's writing is inviting and witty, but as he presents 50 years of his own learning in one fell swoop, the prose can ramble. He welcomes the reader to the last chapter by acknowledging, "It has been a long and complicated trek through difficult terrain." He's right, although there is a reward at the end: you come away feeling that the human mind is not *less* special because it was not hand-designed but perhaps more special—a singular creation of necessity. —*Sunny Sea Gold*

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SPEAKERS:

John D. Barrow, FRS

John D. Barrow, FRS is Professor of Mathematical Sciences at Cambridge University and Director of the Millennium Mathematics Project, an outreach program for students and the general public. He studies cosmology and the interface between particle physics and astronomy. He is well known for his work on the Anthropic Principles in cosmology as well as the study of the large-scale structure and early history of the universe, and studies of whether the constants of Nature might be changing in time. He has also written and lectured extensively on the applications of mathematics to sport and the arts. Dr. Barrow has received many awards; he is a Fellow of the Royal Society and a member of the Academia Europaea, and holds five honorary doctorates. He has written more than 500 scientific papers, and 22 books translated into 28 languages. His play, *Infinities*, won the Premi Ubu for best play in the Italian theatre in 2002 and the 2003 Italgas Prize.

Bernie Carlson, Ph.D.

Bernie Carlson is the Joseph L. Vaughan Professor of Humanities at the University of Virginia. He is also Chair of the Department of Engineering and Society and holds a joint appointment in UVa's History Department. As a historian of technology, Dr. Carlson has written widely on invention and entrepreneurship as well as on the role of technology in the rise and fall of civilizations. He has written numerous books, including *Tesla: Inventor of the Electrical Age*, which has been translated into nine languages and won several awards. Dr. Carlson has also filmed 36 lectures on *Understanding the Inventions that Changed the World* for The Great Courses. He directs Engineering Business Programs at UVa and teaches a course called Engineers as Entrepreneurs. For over a decade, he was a consultant on innovation to Corning Incorporated and has served on several governing boards. He recently finished a five-year term as Executive Secretary for the Society for the History of Technology.

Robert Garland, Ph.D.

Robert Garland is the Roy D. and Margaret B. Wooster Professor of the Classics at Colgate University. In addition to his 30 years teaching Classics at Colgate University, Robert Garland has taught English and Drama to secondary school students and lectured at universities throughout Britain and at the British School at Athens. Before beginning his Ph.D. he trained professionally as an actor and has directed a number of plays. His research focuses on the social, religious, political, and cultural history of both Greece and Rome. He has written 13 books and many articles in both academic and popular journals. His expertise has been featured in The History Channel's *The True Story of Troy*, and he has often served as a consultant for educational film companies. Dr. Garland has taught *Greece and Rome: An Integrated History of the Ancient Mediterranean*, *The Other Side of History*, and *Living History* for The Great Courses. He is an avid squash player and cyclist.

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- Evolution of the Catapult: Paradigm for Ancient Technological Development

Stephen Ressler, Ph.D.

Stephen Ressler is Professor Emeritus from the United States Military Academy at West Point and a Distinguished Member of the American Society of Civil Engineers (ASCE). He served for 34 years as a commissioned officer in the U.S. Army Corps of Engineers and retired at the rank of Brigadier General in 2013. In 2007, he deployed to Afghanistan to create a civil engineering program for the newly created National Military Academy of Afghanistan in Kabul. Dr. Ressler is passionate about communicating the joys of engineering to inquiring minds of all ages. His three video lecture series — *Understanding the World's Greatest Structures, Understanding Greek and Roman Technology*, and *Everyday Engineering* — are among the most highly-rated offerings in The Great Courses' catalog. Dr. Ressler has received numerous awards and his Bridge Designer software has been used by over two million students worldwide. He is also a developer and principal instructor for the ASCE Excellence in Civil Engineering Education Teaching Workshop.

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Does the brain use more energy during particular activities?

—Carlos Augusto Manacorda
Buenos Aires

Claude Messier, a psychology professor at the University of Ottawa in Ontario, and **Alexandria Béland-Millar,** a Ph.D. candidate in his laboratory, respond:

The short answer is yes: certain brain regions do indeed consume more energy when engaged in particular tasks. Yet the specific regions involved and the amount of energy each consumes depend on the person's experiences as well as each brain's individual properties.

Before we delve into the answer, it is important to understand how we measure a brain's energy expenditure. Picture the colorful brain images researchers use to display neural activity. The colors typically represent the amount of oxygen or glucose various brain regions use during a task. Our brain is always active on some level—even when we are not engaged in a task—but it requires more energy to accomplish something that demands concentration such as moving, seeing or thinking. A simple example is that our primary visual cortex lights up more in brain scans—consuming more energy—when our eyes are open than when they are closed. Similarly, our primary motor cortex uses more energy if we move our hands than if we keep them still.

Say you are learning a new skill—how to juggle or speak Spanish. Neuroscientists have made the fascinating observation that when we do something completely novel, a broad range of brain areas becomes active. As we become more skilled at the task, however, our brain becomes more focused: we require only the essential brain regions and need increasingly less energy to perform that task. Once we have mastered a skill—we become fluent in Spanish—only the brain areas directly involved remain active. Thus, learning a new skill requires more brainpower than a well-practiced activity.

But even here there are no hard-and-fast rules across individuals because every person has a variety of strengths and every brain is wired differently. In other words, no single activity will require the same amount of energy for everyone. One person may have a knack for singing, whereas another person may struggle to stay on key regardless of how much he or she practices. If a person is tone deaf, for instance, he or she will likely always expend more energy than a naturally good novice singer would.

Overall, though, on an individual level, our brain adapts and becomes more efficient as we gain mastery. We build new connections among neurons to keep pace with the greater demand on our neural resources. As our skill level grows in a particular area, our brain will inevitably require less energy to perform that task.

Is there a link between music and math?

—via e-mail

Nadine Gaab, an associate professor of pediatrics at Boston Children's Hospital and Harvard Medical School, and **Jennifer Zuk,** a doctoral student at Harvard University, answer:

Many of the skills musicians must master to play an instrument are also important for mathematical achievement. But the precise relation between music and math—whether talent in one area influences aptitude in the other or whether these skills simply develop in parallel—remains unclear.

Some research does indicate that music training influences mathematical achievement. Studies have found, for instance, that individuals who learn an instrument tend to have higher grades and standardized test scores in math compared with peers who have not studied music. Indeed, playing a musical instrument relies on understanding and using math-specific concepts such as fractions and ratios even though a person may not necessarily be consciously applying such math skills as they play.

But not all studies have found that these skills influence each other directly. Some suggest that aptitude in music and math may be driven by high-level cognitive processing skills that are necessary for both. Executive functions—cognitive processes that regulate our ability to learn, reason, remember and plan—are known to predict academic achievement in math. Studies have also suggested that we recruit these cognitive processes when we play a musical instrument because we must train the brain to adjust to subtle motor movements that involve varying tempos and key signatures.

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Why is synaptic pruning important for the developing brain?

—**Rowena Kong** via e-mail

Irwin Feinberg, professor emeritus of psychiatry and behavioral sciences at the University of California, Davis, replies:

One of the grand strategies nature uses to construct nervous systems is to overproduce neural elements, such as neurons, axons and synapses, and then prune the excess. In fact, this overproduction is so substantial that only about half of the neurons mammalian embryos generate will survive until birth.

Why do some neural connections persist, whereas others do not? A common misconception is that neurons that do not make the cut are defective. Although some may indeed be damaged, most simply fail to connect to their chemically defined targets. In a series of brilliant studies performed during the latter half of the 20th century, researchers discovered how pruning works. They found that newborn neurons migrate along chemically defined routes and that when the neurons arrive at their genetically assigned locations, they compete with their "sibling" neurons to connect with predetermined targets.

Victorious neurons receive trophic, or nourishing, factors that allow their survival; unsuccessful neurons fade away in a process called apoptosis, or cell death. The timing of cell death is genetically programmed and occurs at different points in the embryonic development of each species.

For decades neuroscientists believed that neural pruning ended shortly after birth. But in 1979 the late Peter Huttenlocher, a neurologist at the University of Chicago, demonstrated that this excess production and pruning strategy actually continues for synapses long after birth. Using electron microscopy to analyze carefully selected autopsied human brains, he showed that synapses—the tiny connections between neurons—proliferate after birth, reaching twice their neonatal levels by mid- to late childhood, and then decrease precipitously during adolescence.

These changes at the synapse level cause neural restructuring that very likely has important consequences for normal and abnormal brain function. Streamlining neural circuits could explain the boost in cognitive skills that occurs in our late teens or early 20s. The loss of redundant pathways could help elucidate why we have difficulty recovering from a traumatic brain injury: eliminating synaptic redundancies diminishes our ability to develop alternative pathways to bypass the damaged region.

In addition, many major mental illnesses start to emerge in adolescence, which may be caused by aberrant synaptic pruning. In 1982 I hypothesized that disordered synaptic pruning could explain the age of onset of schizophrenia, and in 2016 researchers published genetic and experimental evidence supporting this association in *Nature*.

> "Streamlining neural circuits could explain the boost in cognitive skills that occurs in our late teens or early 20s."

Although we are only beginning to unravel the ramifications of synaptic pruning in the human brain, this process clearly has significant consequences for normal human brain function and may provide key insights into the causes of some devastating and mysterious neuropsychiatric diseases. M

Other factors may contribute to a person's success in music and mathematics. It is possible that noncognitive variables—socioeconomics or education—are involved. If, for example, you grow up in a household with significant financial resources, you may be more likely to attend a top-rated school or be able to afford music lessons.

Although the precise connection between music and mathematics training has not yet been untangled, this line of inquiry raises intriguing questions about the relation between these two subjects. To determine whether music training influences aptitude in math, or vice versa, researchers would need to conduct long-term studies that measure one ability before and after studying the other. But regardless of how these skills are connected, it is clear that studying math and music provides a range of benefits, such as improving mood, memory and focus.

Do you have a question about the brain you would like an expert to answer?

Send it to editors@sciam.com

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MIND'S EYE

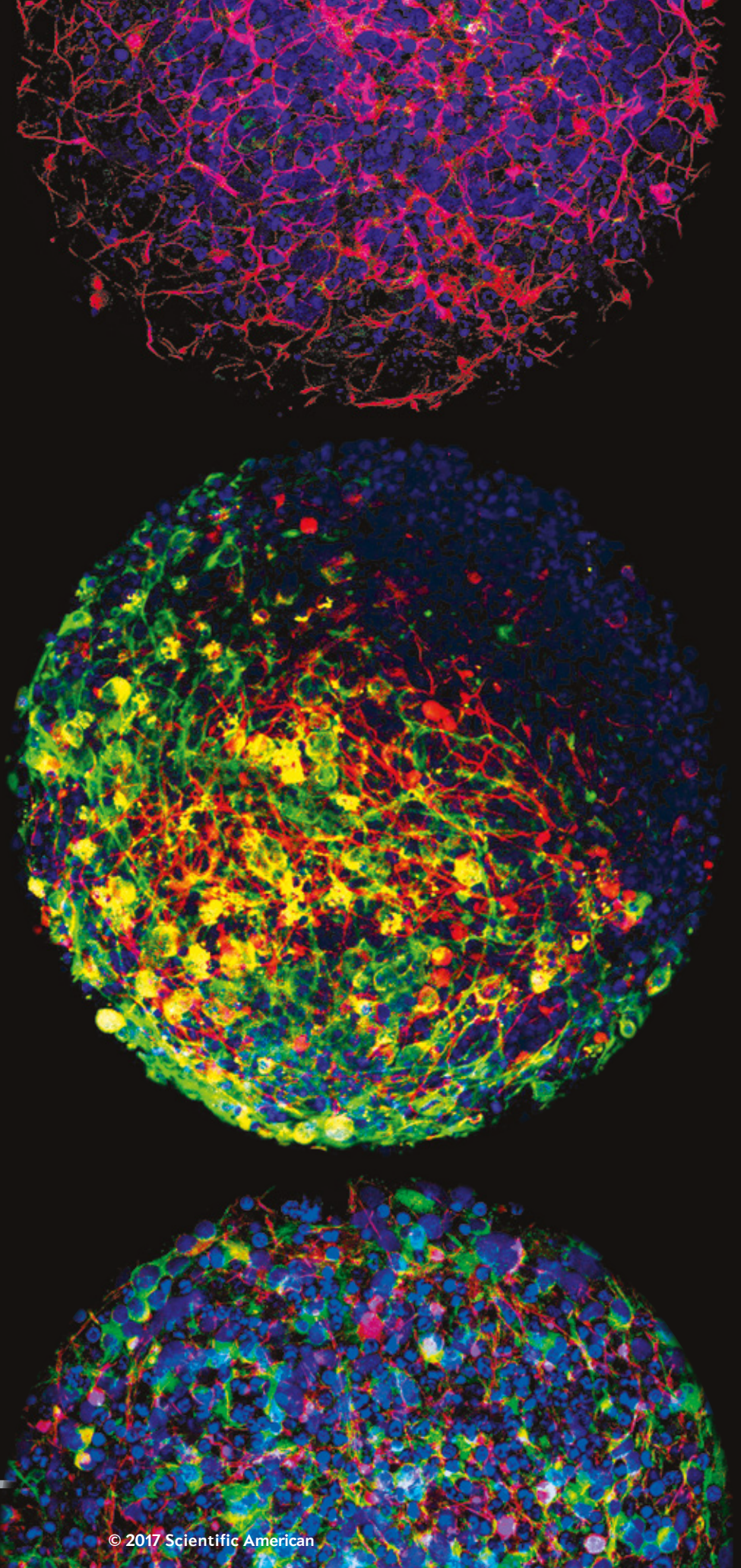
THE BEAUTY OF "MINI BRAINS"

Lab-grown miniature brains are poised to shake up drug testing for everything from Alzheimer's disease to Zika. Each bundle of human brain cells is so tiny that it could fit on the head of a pin. Researcher Thomas Hartung and his colleagues at Johns Hopkins University created these mini brains using stem cells that, over the course of two months, morph into supporting cells and various types of neurons, which quickly connect to one another and start communicating.

These three micrographs were taken with lasers to illuminate colorful fluorescent dyes. The cells' nuclei appear purple or blue. The mini brain at the top features a tangle of axons (*pink*)—extensions of neurons that send and receive signals. More axons (*red*) and neurons that produce the neurotransmitter dopamine (*green*) are highlighted in the middle brain. The bottom one shows nerve cell bodies and their projecting dendrites (*both green*), as well as supporting astrocytes (*red*).

The mini brains are highly uniform, freezer-proof and relatively cheap. Hartung's start-up, Organome, plans to market them soon as a substitute for lab animals in drug testing. "We are moving into cell culture for the 21st century," he says.

—Catherine Caruso



COURTESY OF THOMAS HARTUNG AND DAVID PAMIES *Johns Hopkins Center for Alternatives to Animal Testing and Organome, LLC,* AND PAULA BARRERAS AND CARLOS PARDO *Division of Neuroimmunology and Neurological Infections, Johns Hopkins Hospital*

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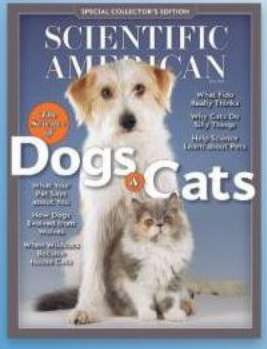

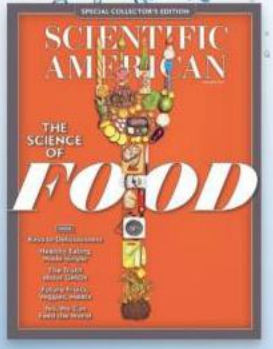

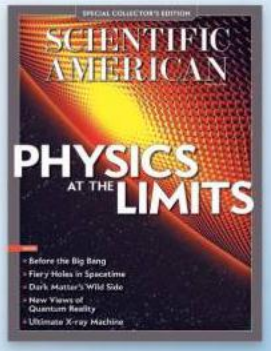

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