SENSITIVE KIDS: WHY VULNERABILITY CAN BE AN ADVANTAGE *page 40*

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September/October 2015
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CIRCADIAN RHYTHMS

How Your Inner Clock Controls Your Health

page 30

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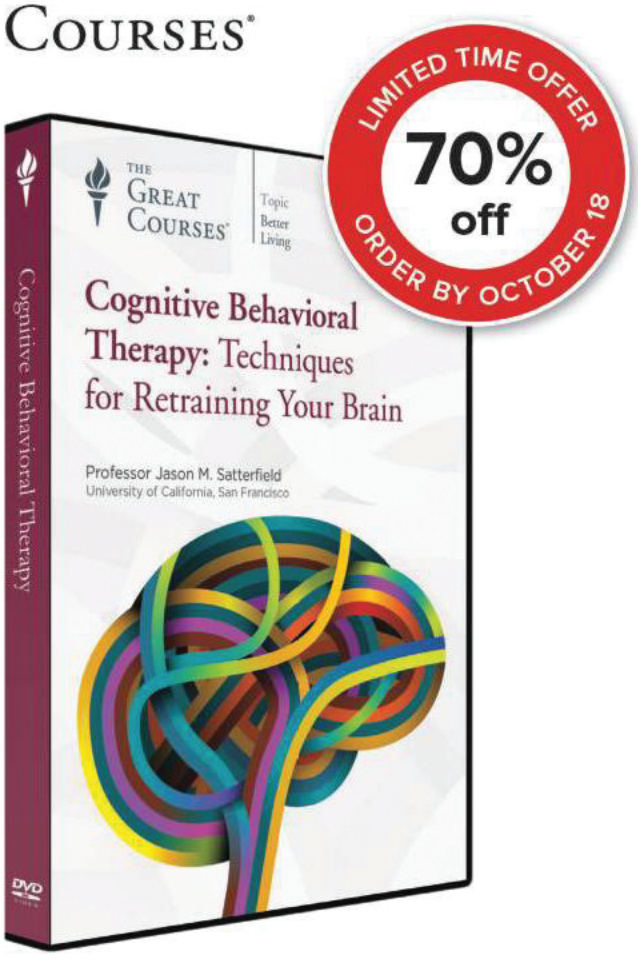

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Timing Is Everything

Insomniac readers (yes, you reading this at 3 A.M.), please don't hate me! I just happen to be one of those people who falls asleep minutes after my head hits the pillow and awakens cheery and refreshed when the sunlight filters through the window.

I have always counted this as a blessing (so much better than counting sheep) but never so much as I do in view of our special report on circadian rhythms. Now I find myself wondering if my reliable inner clock also deserves some credit for other aspects of my generally good health: blood pressure, metabolism, digestion, and more. Read "Out of Sync," by contributing editor Emily Laber-Warren (*page 30*), and you, too, will marvel at the pervasive role that these daily rhythms play in sickness and in health. And consider this astounding fact: timekeeping proteins rise and fall with such precision in our brain that by testing for them in an autopsy, you can pinpoint an individual's time of death.

Timing also plays a vital role in maintaining a healthy body weight. Make a habit of nighttime eating, and you are asking for trouble. In our cover story—"Don't Diet!"—Charlotte N. Markey, a Rutgers University psychologist and weight-loss investigator, dismantles many popular notions of how to shed pounds. Along the way she parses the research on the common psychological traps of dieting. Ironic processing is one example: You decide to give up carbs, and all you can think about is pasta. You cut red meat and obsess about a juicy steak, eventually yielding to temptation. Want to know more about these pitfalls and what weight-loss strategies actually work? Turn to page 46.

Many of us are familiar with the idea that some kids are like orchids—ultrasensitive to being damaged by an unfavorable environment. In "The Upside of Vulnerability" (*page 40*), developmental psychologist Jay Belsky of the University of California, Davis, shows us the other side of that coin with evidence that these delicate flowers have a surprising hidden strength: they blossom prodigiously when given enriched environments. Belsky calls it a "for better and for worse" pattern and raises provocative questions about what it means for policies aimed at poor and vulnerable children.

There are plenty more surprises blooming in *Scientific American Mind*'s autumn garden. Don't miss the medical detective story that begins on page 54: an excerpt from *Brain Storms*, Jon Palfreman's riveting new book about Parkinson's disease. Take a stroll through our pages and let us know what you think!

Claudia Wallis
Managing Editor
MindEditors@sciam.com

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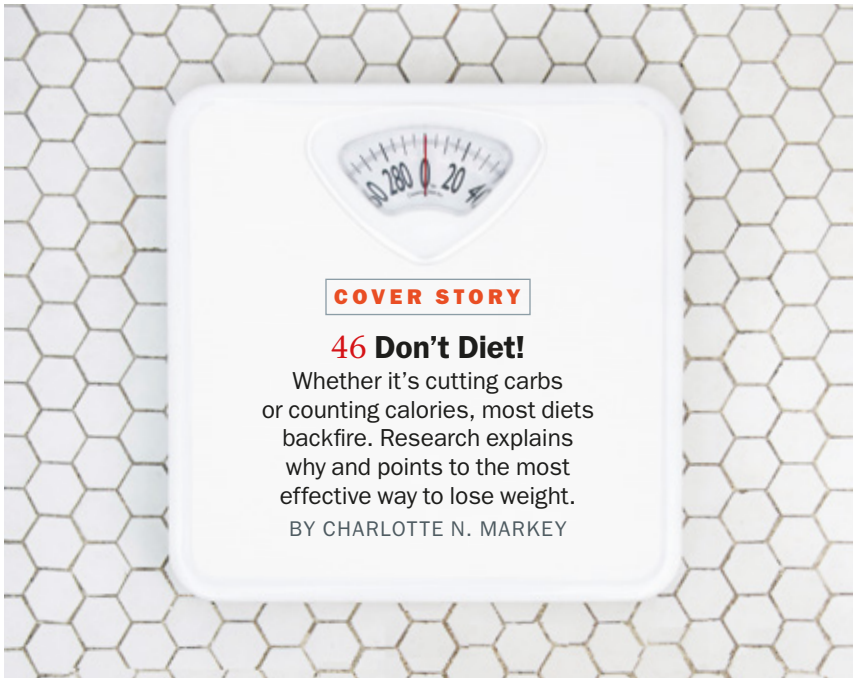
SCIENTIFIC AMERICAN MIND

CONTENTS

FEATURES



COVER STORY

SPECIAL REPORT

DEPARTMENTS

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PET THEORIES

I enjoyed the stories in "The Psychology of Pets" package very much. As a dog owner and dog lover, I have always tried to make the distinction between dogs genuinely picking up on human emotions and looking to help versus them relieving their own stress and anxiety. Either way, the relationship humans share with other animals is awesome!

Peter Stratakos
via e-mail

Plenty of people don't love pets. Thousands and thousands of pets are dumped at pounds or animal shelters every year.

By the way, it was a bad idea to feature a border collie on the cover. This breed is way too hyper and neurotic to be a suburban pet. It belongs on a sheep farm or ranch, herding livestock.

Clyde Mason
Tulsa, Okla.

The editors of *Scientific American Mind* should know better than to claim pets love us. Animals are incapable of this abstract emotion, be it platonic love, brotherly love or romantic love. In fact, pets view us as walking can openers.

People with low self-esteem flatter themselves with the notion that their schnauzer or tabby loves them. Pathetic.

Don Manning
Tacoma, Wash.

As science reveals more about the complexity of canine emotions, as discussed in "The Science of a Friendship," by Ádám Miklósi, one fact remains: humans will forever be changed by the impact that dogs continue to make in our society. It is because of their unique bond with us that we strive to understand them better. And although our language and DNA may differ, both species have found a way to build a friendship that illustrates the true power of the mind.

Michael Aaron Gallagher
Syracuse, N.Y.

CONSIDERING CONSCIOUSNESS

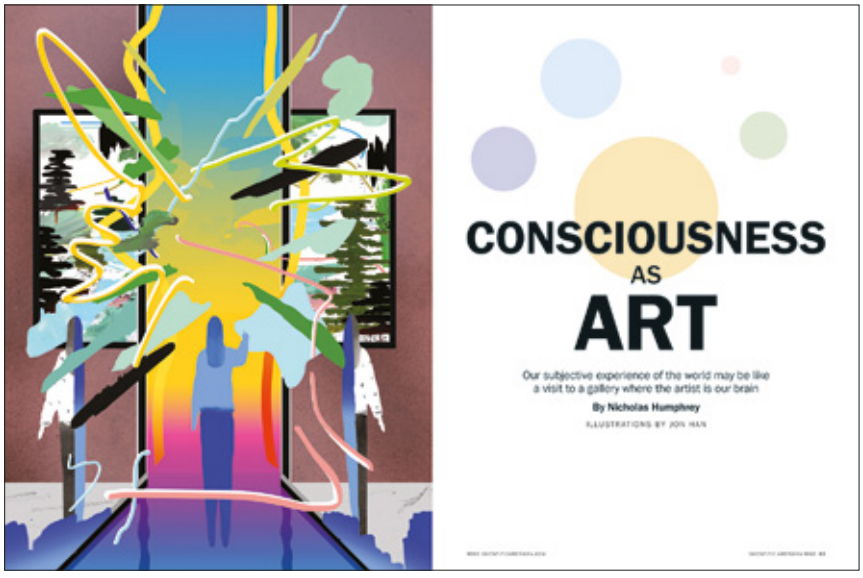
I liked Nicholas Humphrey's article, "Consciousness as Art," very much. It accords with the narrative theory of psychotherapy, in which your memories are a narrative that you tell yourself, which is another way of making your life into a work of art. Cognitive and psychoanalytic therapies make considerable use of the idea that changing your narrative can lead to significant changes in your life. I wonder if Humphrey's theory can be used in any such way to help people.

Naomi Goldblum
via e-mail

Humphrey's article is lots of fun to think about. In it, he looks for new supporters for the theory of illusionism by offering a "more palatable" conception of the theory. But I'm afraid that just makes the issue more complicated and illogical.

This should be obvious, but a thinking person doesn't sign on to a new theory merely because it's pleasant (that is, palatable) to believe in; the theory must be supported by evidence and reason.

And there are other problems. Consciousness is a natural phenomenon. A core concept underlying most accepted art theory is that for a thing to be art, it must be created through the intentional act of a being that itself has some level of consciousness. Humphrey's idea that the laws of natural selection are the "artist" in the equation doesn't fit, because natural laws don't have intention. A painting of a lake might be art; the lake itself is not.



Humphrey reaffirms his dogged belief in consciousness as illusion even while pitching the reader on consciousness as art. But let's assume someone takes the bait. If I were inclined to believe that consciousness is art, how and why do I have to reconcile that with consciousness as illusion? They aren't the same thing.

Daniel Culhane
Madison, Wis.

HUMPHREY REPLIES: *I'm glad Daniel Culhane found my essay fun. But I don't think he quite gets what I'm saying. To recap my argument, I suggested that although there are scientific grounds for believing that consciousness is in part an illusion, we would do well to think of it also as a work of art. First, doing so allows scientists to emphasize the positive, creative side of the illusion. Second, it opens up questions about what is the evolutionary payoff of "brain art."*

Human beings across the world and across history have tended to see consciousness as a door to an alternative, nonphysical reality. Modern science says that, in this belief, they are mistaken. Yet in my view, this tendency is not a mistake in human biological design. Rather natural selection has designed humans to make this mistake because, in several ways, it leads us to have more fulfilling and productive lives.

In relation to specific points Culhane raises, I'll offer three quick responses: (1) I was not asking him to sign up for illusionism simply because I've made it more palatable; I was asking him not to refuse to sign up because he finds it unpalatable. (2) I hardly think it matters whether natural selection intended to create consciousness as artwork; what's important is that what came out of the evolutionary mill does in fact have all the hallmarks of artistry. (3) Yes, of course, illusion and art are not the same thing. Not all illusion is art. But arguably, all art does involve illusion.

DETERRENTS FOR CRIME NEEDED

"Crime without Punishment?" by Oriel FeldmanHall and Peter Sokol-Hessner [Perspectives], focuses on the needs of victims, as opposed to the punishment of perpetrators. I believe that this idea is interesting, and it indeed merits further consideration.

The analysis of the findings from the study on the role of third parties, however, is incorrect when it leads to questions about the role of judges and juries. The role of these third parties is wider than that of only satisfying the needs of victims.

There has to be some form of deterrence for the perpetrators in addition to satisfying the victims' needs. Otherwise, what is to prevent the perpetrators from reoffending? That is why an impartial third party is required.

Frank Smyth
Dublin, Ireland

A HISTORICAL SLIGHT

I am a long-term subscriber and enthusiast for *Scientific American Mind*. I find your reporting to be thought-provoking and of extremely high quality.

I read with interest Bret Stetka's article "Did Affluence Spur the Rise of Modern Religions?" [Head Lines]. It presented a typically evenhanded assessment of Nicolas Baumard's paper on the subject in *Current Biology*.

What troubled me was the chart at the bottom ["The Beginnings of Moral Religion"], which was attributed to Victoria Stern. It listed five venerable schools of thought, showing their approximate inception and commenting on their contribution to moral religion. But in one, and only one, was there an editorial comment critical of one of the religions. Second Temple Judaism is accused of "exclusivity," and this alleged exclusivity is credited with why Christianity split from it.

This dogmatic myth, created by some early leaders of Christianity as a way to differentiate the new religion from its parent, was perpetuated for centuries and became one of the pillars of anti-Semitism. Like others of these pillars, it makes people more willing to accept attitudes about Judaism that they would not find acceptable in regard to other religions.

Including this "faith fact" strikes me as highly unscientific and hence inappropriate. The comment is also irrelevant to the arguments in the article.

Richard Berenson
via e-mail

THE EDITORS REPLY: *While working on the brief descriptions of the five religions in this chart, we sought to make the language historically accurate, neutral and inoffensive. At the time, we did not see "exclusivity" as a negatively charged word. Now that you have explained the historical context, we see your point and sincerely regret the oversight.*

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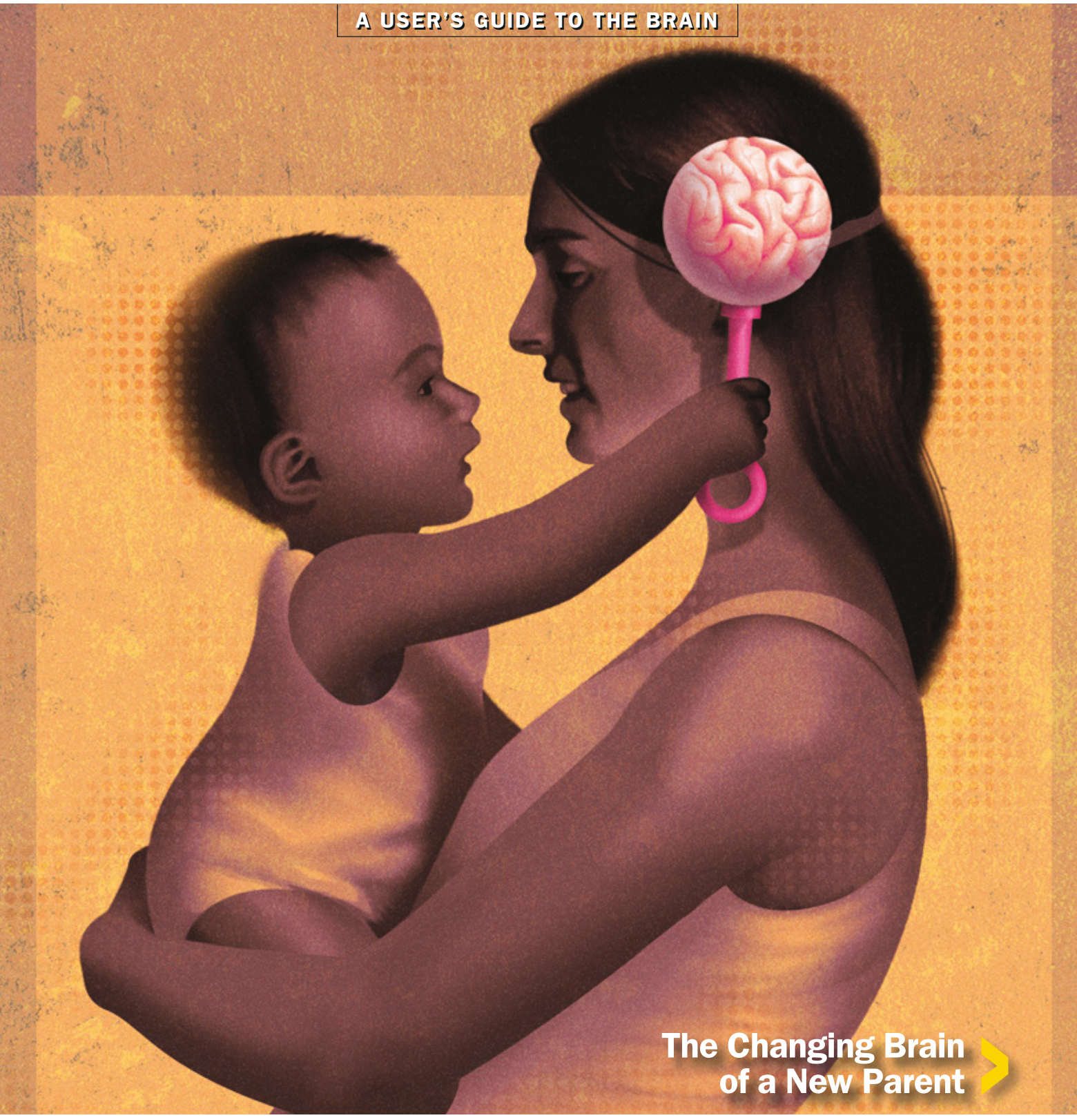
Head Lines

A USER'S GUIDE TO THE BRAIN



The Changing Brain of a New Parent

NEW-PARENT BRAIN

The arrival of a child brings big changes in the brains of moms and dads. Mothers experience a near-immediate shift, thanks in part to the hormones involved in giving birth and nursing. Fathers' brains tend to change in different and more subtle ways. New research reveals how the first months of parenting can affect mood and cognition.

ILLUSTRATIONS BY STUART BRIERS

Motherhood Can Be a Lonely Place

Without adequate social support, many new moms struggle to feel happy

Entering motherhood is a rite of passage for most women. For many new moms, however, the first months and years can be a lonely place. A new study finds that several types of social support are crucial for staving off negative feelings.

Although only 10 to 15 percent of mothers from Western nations will develop a full-blown case of postpartum depression (PPD), many more will experience some serious symptoms of depression, explains Patricia Leahy-Warren, a senior lecturer at the School of Nursing and Midwifery at University College Cork in Ireland. "Feelings of PPD are on a continuum, with PPD at the end," Leahy-Warren says. Even if PPD can be diagnosed clinically, there is no standard for measuring where the remaining 85 to 90 percent of mothers land on the scale. Yet she estimates that most first-time mothers are overwhelmed.

Becoming a mother is a major transition, points out clinical psychologist Ann Dunnewold, whose practice in Dallas, Tex., provides support for mothers. New mothers give up autonomy, sleep and relationships to tend to the relentless needs of a baby. On top of that, they are also expected to be in a constant state of bliss and fulfillment with their new role. "There's a lot of pressure to be the perfect mother, and women are afraid to say they're not coping," Leahy-Warren says.

Making matters worse, research that demonstrates the importance of early childhood experiences in determining future success and happiness puts additional pressure on moms to get it right. Also, for working mothers (57 percent of women are in the U.S. workforce), who are used to a productive mind-set and established social routines, it can be difficult to adapt to the repetitive life of meeting the basic daily needs of a baby. "A lot of women go back to work because of the loneliness," Dunnewold says.

According to Leahy-Warren's recent study published in the *Journal of Clinical Nursing,* mothers with strong social support who have confidence in their ability to parent were 75 percent less likely to be depressed than mothers who had neither advantage. There are four parts to social support, Leahy-Warren explains: hands-on, emotional, informational and appraisal, meaning affirmation that a mother is doing a good job.

Moms require a network of people to meet these four types of social needs. Generally they lean most on their partner, then their own mother, then sisters. Health professionals, other family and friends can be an important part of a mother's community. Good social support will also boost a mother's confidence and ability to parent, Leahy-Warren says, which has a significant positive influence on her mental well-being.

—Esther Hsieh

© ISTOCK.COM (*mother and baby*)

A World of Difference

A group of studies that looked at the best data available from more than 40 countries across the globe found that the incidence of postpartum depression in mothers ranges from 3 to 63 percent, with Malaysia and Pakistan at the bottom and top, respectively. The rate for U.S. mothers is 10 to 15 percent. Although mothers in all corners of the world agree that lack of social support or an unhelpful partner can make them feel depressed, there are also many factors they do not agree on. One mother's blessing is truly another's curse.

WEIGHT LOSS

In places where thin equals beautiful, such as France and the U.S., the struggle to return to prepregnancy weight is often a source of distress. Not so in Uganda, where weight loss and food scarcity are a cause for concern, and the weight gain is welcomed.

The Mind of the Father

Dad's mental shifts are more future-oriented than Mom's

The birth of a child leaves its mark on the brain. Most investigations of these changes have focused on mothers, but scientists have recently begun looking more closely at fathers. Neural circuits that support parental behaviors appear more robust in moms a few weeks after the baby is born, whereas in dads the growth can take several months.

A study in *Social Neuroscience* analyzed 16 dads several weeks after their baby's birth and again a few months later. At each check, the researchers administered a multiple-choice test to check for signs of depression and used MRI to image the brain. Compared with the earlier scans, MRI at three to four months postpartum showed growth in the hypothalamus, amygdala and other regions that regulate emotion, motivation and decision making. Furthermore, dads with more growth in these brain areas were less likely to show depressive symptoms, says first author Pilyoung Kim, who directs the Family and Child Neuroscience Lab at the University of Denver.

Although some physiological brain changes are similar in new moms and dads, other changes seem different and could relate to the roles of each parent, says senior author James Swain, a psychiatrist at the University of Michigan (*brain diagrams below*).

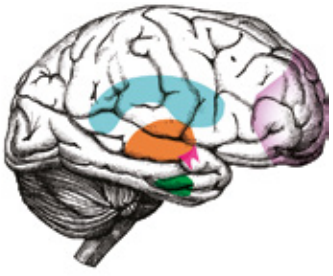
A 2014 behavioral study of expectant fathers showed that midpregnancy ultrasound imaging was a "magic moment" in the dads' emerging connection with their baby. Yet the emotional bond was different than it is in expectant moms. Instead of thinking about cuddling or feeding the baby, dads-to-be focused on the future: they imagined saving money for a college fund or walking down the aisle at their daughter's wedding.

"It was interesting how little dads' images

centered on an infant," says psychologist Tova Walsh of the University of Wisconsin–Madison, who led the study. "I didn't hear dads talk about putting the baby down for a nap or changing diapers." —*Esther Landhuis*

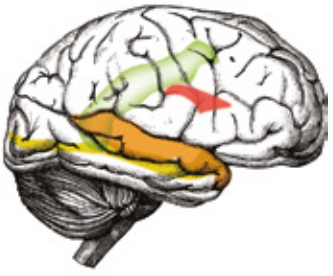
This Is Your Brain on Baby

Research is beginning to reveal the multiple ways that parenthood alters the brain. Some of these changes are immediate; others occur gradually over the course of many months, as parents settle into their new routines. The significance of changes in the volume of various brain structures is not yet well understood.



Areas That Increase in Volume in Both Parents

- **Hypothalamus:** Regulates the production of hormones, such as dopamine and oxytocin, involved in attachment
- **Amygdala:** Processes emotions; may drive parental motivation
- **Striatum:** Part of reward system; also involved in parental motivation
- **Thalamus:** Involved in sensory perception; may help parents understand their infants' movements and sounds
- **Prefrontal cortex:** Governs conscious decision making and higher-order behaviors



Sex-Specific Changes

- **Insula:** Processes threats and stress; in fathers, the volume decreases, perhaps reflecting an increased focus on family matters; in mothers, the volume increases, possibly reflecting heightened protectiveness
- **Superior temporal gyrus:** Important for perceiving emotions in faces and for auditory processing; the volume increases in fathers
- **Posterior cingulate cortex:** Related to our sense of self and self-related thinking; the volume decreases in fathers
- **Fusiform gyrus:** Involved in visual recognition; the volume decreases in fathers, and the change is linked to lower levels of depression, both for unknown reasons

THE MOTHER-IN-LAW
Mothers in all nations studied identified their mother-in-law as a source of friction, except in Sweden. This friction was more acute in Asian countries, where there is a strong tradition of postnatal rituals that may be imposed by the mother-in-law.

BREAST-FEEDING
In countries such as Ireland and the U.S., where there is a perception that "good" moms breast-feed, many are anxious about nursing. In countries such as Uganda and Botswana, where it is the norm, mothers do not consider it an issue.

HORMONES
It can take months or years for a woman's hormones to return to prepregnancy levels. One survey found that this was not a source of distress for moms in Japan or Uganda. In Europe, however, mothers felt a hormone imbalance contributed to sadness.

DEPRESSION TREATMENT
In one study that asked mothers from four continents what would help relieve their depression, all responded that hands-on help, emotional support and a confidant would help. Only in the U.S. did mothers mention antidepressants. —*E.H.*

Is "Pregnancy Brain" a Myth? ☛

Is "Pregnancy Brain" a Myth?

Research suggests that the mental fog is a matter of expectations

As many as four out of every five pregnant women say that they suffer from "pregnancy brain"—deficits in memory and cognitive ability that arise during pregnancy, making women more forgetful and slow-witted. Yet studies on the phenomenon have generally not supported these claims: although some have found evidence of problems on certain types of tasks, others, including a recent paper published by researchers in Utah, have found no signs of cognitive problems at all. Some experts believe that pregnancy brain and its postnatal cousin, "baby brain," could largely be a product of confirmation bias: pregnant women and new moms expect to experience brain fog and therefore believe they are actually affected. Others argue that the mental symptoms might simply be too difficult to confirm in a laboratory setting.

In the most recent study, researchers at Brigham Young University gave cognitive and neuropsychological tests to 21 women in their third trimester of pregnancy and then tested them again six months after they gave birth. They administered the same tests at similar intervals to 21 women who had never been pregnant. They found no differences between the groups no matter when they were tested, including before and after giving birth. These findings mesh with those from a 2003 study, which found that pregnant women did not score differently from nonpregnant women on tests of verbal memory, divided attention and focused attention.

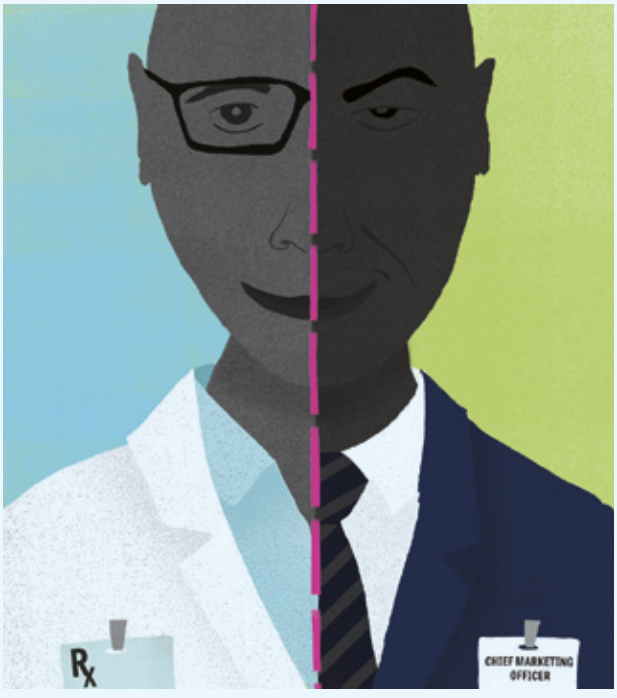
"There is variety in the results, but overall most studies suggest there are few to no memory impairments associated with pregnancy," says Michael Larson, a psychologist at Brigham Young and a co-author of the recent paper. He thinks the reason the myth persists may be that women selectively look for evidence that supports the cultural expectation. For example, when a pregnant woman loses her car keys, she might blame pregnancy brain—without recalling the times she lost her car keys before she was pregnant.

Joanna Workman, a psychologist at the University at Albany, agrees that confirmation bias may play a role, but she says there is another possibility, too. In a 2011 study, a team at the University of British Columbia found that although pregnant women did not display any problems on cognitive tests given in a lab, they were less likely than nonpregnant women to remember to call the lab when asked and to return a questionnaire on time. "It's possible that lab-based measures do not reveal differences, because labs are typically quiet environments with minimal distractions, in contrast with everyday life," she says. —*Melinda Wenner Moyer*

(PHARMA WATCH)

RAISING AWARENESS OR DRUMMING UP SALES?

Restless legs? Binge eating? Behind many disease-awareness campaigns are drug company dollars



In January the U.S. Food and Drug Administration approved the amphetamine Vyvanse as the first drug for binge-eating disorder (BED). Four days later former tennis star Monica Seles appeared on *Good Morning America* to discuss her long-time struggle with BED, and public service announcements (PSAs) began to run on national television to raise awareness about the disorder, urging concerned viewers to talk to their doctors. It soon came to light that Seles was a paid spokesperson for Shire, the drug company that makes Vyvanse, and that the company had also sponsored the television PSAs. "Shire was clearly aware that recommending doctor visits would increase prescriptions for the drug," says Jeffery Lacasse, a mental health researcher at Florida State University.

This is not the first time a pharmaceutical company has tried to educate the public about a condition for which it sells a treatment. "Promoting diseases to sell drugs is a common and venerable practice among drug companies," explains Marcia Angell, a senior lecturer on social medicine at Harvard Medical School and former editor in chief of the *New England*

STUART BRIERS (*left*); DAVID SENIOR (*right*); ©ISTOCK.COM (*pills*)

Journal of Medicine. "They try to expand the size of the market by implying that nearly everyone has the condition." Although some people may legitimately suffer from a particular disorder and require drug treatment, others might be diagnosed with a disorder they do not actually have or start taking medications that might not ultimately benefit them. As a drug-selling tactic, awareness campaigns are tried and true. Below are some other notable examples—and ways you can use this information as a consumer.

ADHD

Drug companies help to spread the word about attention-deficit/hyperactivity disorder—and the treatments they sell for it—by funding its high-profile patient advocacy group, Children and Adults with Attention-Deficit/Hyperactivity Disorder (CHADD). From 1991 to 1994 Ciba-Geigy, the company that then manufactured Ritalin (it subsequently merged with Sandoz to become Novartis), gave $748,000 to the patient organization, prompting the U.S. Drug Enforcement Administration to note that "the relationship between Ciba-Geigy and CHADD raises serious concerns about CHADD's motive in proselytizing the use of Ritalin." Yet the tradition continues: in 2014 CHADD received $345,000 in grants from drug companies.

SOCIAL ANXIETY DISORDER

In 1999 posters featuring pictures of glum individuals began appearing in U.S. bus stops and other public locations featuring the slogan "Imagine you are allergic to people." The posters were designed to raise awareness about social anxiety disorder, a condition characterized by overwhelming anxiety and excessive self-consciousness in everyday social situations, which the drug Paxil, then made by SmithKline Beecham (which would later merge into GlaxoSmithKline), had just been approved to treat. As reported in *Mother Jones* in 2002, the posters were sponsored by the Social Anxiety Disorder Coalition, a partnership between several nonprofit advocacy groups and SmithKline Beecham. The coalition also sponsored studies discussing the importance of "building public awareness" to improve "treatment access," according to one study author, and it sent press releases to journalists to inspire media coverage.

BIPOLAR DISORDER

In 2002 a series of TV advertisements aired to raise awareness about bipolar disorder, a condition that causes cyclic swings in mood and energy. The ads, which did not mention any drugs, urged viewers to log onto a Web site called the Bipolar Help Center and take a questionnaire that would help them track variations in their moods. Viewers were also told to bring the results of the questionnaire to their doctor because "getting a correct diagnosis is the first step in treating bipolar disorder. Help your doctor to help you." The ads were sponsored by Lilly, which had just been licensed to market its drug Zyprexa for mania. In the journal *PLOS Medicine,* David Healy, now at Bangor University in Wales, argued that these types of ads "reach beyond those suffering from a mood disorder to others who will as a consequence be more likely to see aspects of their personal experiences in a new way that will lead to medical consultations."

RESTLESS LEGS SYNDROME

GlaxoSmithKline made restless legs syndrome—a disorder characterized in part by the urge to move one's legs at night—a household term in 2003, when it ran a vigorous awareness campaign for the disorder. The company began by issuing press releases about presentations given at the 2003 annual meeting for the American Academy of Neurology, a professional society representing neurologists and neuroscientists. Two months later it distributed another press release, for a company-funded, as yet unpublished study, entitled "New Survey Reveals Common Yet Under Recognized Disorder—Restless Legs Syndrome—Is Keeping Americans Awake at Night." The press releases led to a slew of media coverage of the disorder; according to an analysis in 2006, one fifth of all articles written about it referred readers to the nonprofit Restless Legs Syndrome Foundation for more information, an organization that is heavily subsidized by GlaxoSmithKline. —*Melinda Wenner Moyer*

Staying Savvy

Awareness campaigns may help some people get useful support and treatment, but they might also prompt healthy people to start taking drugs they do not need. "Drug company sponsorship doesn't mean the information is bogus—but it does raise a red flag because companies do stand to benefit from increasing diagnoses, which leads to more treatment," says Steve Woloshin, a researcher at the Dartmouth College Institute for Health Policy and Clinical Practice. It can be difficult for consumers to know if a condition they are hearing about is part of a drug company awareness campaign—TV ads and Web sites do not always disclose company sponsorship—but consumers can look out for phrases such as "the disease your doctor has never heard of," which can be red flags. Most important, before starting a new treatment, is to always talk to your doctor about risks and benefits. "The key questions to ask about treatment are 'What is likely to happen to me if I am not treated? What is likely to happen to me if I am—including side effects?'" Woloshin says. —*M.W.M.*

Awestruck and Selfless

Awe shifts our focus toward the greater good

"Awesome" has become a common descriptor, yet genuine awe is a profound emotion: the intake of breath at a starry night sky, goose bumps during soaring music or tearing up at the sight of a vast crowd holding candles aloft. Can this feeling make us better people? A recent paper in the *Journal of Personality and Social Psychology* suggests that it does.

Philosophers long ago suggested that awe binds people together, explains lead author Paul Piff, an assistant professor of psychology and social behavior at the University of California, Irvine, who began his investigation of awe in Dacher Keltner's lab at the University of California, Berkeley. This new research, he says, proves that awe can make people less self-involved and more attuned to the needs of the larger group.

In the first of five studies, the researchers ascertained, through a representative national survey, that people who report feeling awe more often are, in fact, more generous. When given raffle tickets and offered the chance to donate some, those who frequently felt awe gave away more tickets.

Then the researchers conducted four other experiments in which they induced awe in some participants and other emotions such as pride or amusement in others. They evoked awe through videos of breathtaking natural scenes and by taking subjects outside to gaze upward at towering eucalyptus trees.

In every case, those who experienced awe behaved in what psychologists call a more "prosocial" way, being more helpful or making more ethical decisions. The participants who had gazed up at the trees, for example, picked up more pens that were "accidentally" dropped by an undercover researcher than other subjects outside who had gazed at a building.

By making us feel like a small part of something grander, the authors suggest, awe shifts our attention from our own needs to those of the greater good. Some researchers have speculated that awe might have evolved as the response to a powerful leader. Maintaining social hierarchies and ensuring membership in a group can boost odds of survival.

Not surprisingly, some studies suggest that awe can increase religiosity. "I'd guess," Piff says, "that religion is one of those cultural institutions that ritualizes awe through architecture and music."

Piff suggests that people try keeping an "awe diary" for two weeks and every day soak up whatever evokes it—a sunset, a bird's feathers. Shifting your focus toward something vast is bound to put your problems in perspective, he observes, and open you to the greater world. —*Francine Russo*

GETTY IMAGES

… And Awe Might Make Us Healthier, Too

The feeling is linked to lower levels of an inflammation molecule

Negative emotions have been linked to poor health outcomes, such as heart disease and even a shorter life span. Research suggests inflammation may be responsible for this link, at least in part. The molecules involved in inflammation are essential for our body's response to infection and injury, but high levels over the long term have been linked to everything from diabetes to depression.

Few studies have assessed the health effect of positive emotions, so a team led by Jennifer Stellar of the University of Toronto (who also began studying awe in Keltner's lab at U.C. Berkeley) conducted two studies to investigate the link. In the first, 94 students completed a questionnaire to determine how often they had experienced various emotions during the past month. The scientists then took a saliva sample to assess levels of a molecule that promotes inflammation called interleukin-6 (IL-6). They found more positive emotion was associated with lower levels of IL-6.

In the second experiment, 105 students completed online questionnaires designed to assess their tendency to experience several specific positive emotions. They later visited the lab to provide saliva samples. Joy, contentment, pride and awe were all associated with lower levels of IL-6, but awe was the only emotion that significantly predicted levels using a strict statistical test.

These results do not establish whether awe actually causes changes in IL-6 levels. In fact, the authors caution that the relation probably operates in both directions: having a healthier, less stressful life may allow a person to experience more awe. They point out that awe is associated with curiosity and desire to explore, which they contrast with the social withdrawal that often accompanies illness or injury. "We know positive emotions are important for well-being, but our findings suggest they're also good for our body," Stellar says. —*Simon Makin*

A GUIDE TO MASTERING YOUR WORLD

How to Be a Better *listener*

During an argument a few months ago, my husband, John, accused me of being a bad listener. "Who, me?" I thought. "I interview people for a living—all I *do* is listen!" Later, after I calmed down, I remembered that John is actually a pretty reasonable and insightful guy—if he says he's not feeling listened to, maybe it really *is* me. So, for a second opinion, I texted someone who has known me for a really long time: "John says I don't listen. Am I hard to talk to?" Her response: "You can be, yes. Love, Mom." And there you have it. I quit arguing and asked some experts for help. Here's the advice that has really resonated with me. Think you don't need it? Read on anyhow—you may be surprised.

#1 Check your assumptions. If you're already certain that you know what's going on in someone's head, your brain is primed to accept only information that agrees with your preconceived notions. Yet if you can cultivate a sense of genuine interest about where the other person is coming from and what he or she might say, you create an environment in which whoever you're talking to feels heard and you can actually *hear.* "I don't think it's possible to not make any assumptions—it's just in everybody's hardwiring," says psychology researcher John Stewart, author of *U&Me: Communicating in Moments That Matter* and other seminal texts on interpersonal communication. Still, it is possible, he says, to check your assumptions out loud, with the person you're listening to. Try asking "so you mean …" or "so you're thinking that …" and let the person confirm or correct.

#2 Get curious. The amazing thing about being genuinely curious is that it keeps you from being defensive, Stewart says. Seriously—try it! "Hmmm, I wonder why my partner hates it so much when I leave my clothes on the floor?" instead of "Ugh, he's such a neat freak and thinks I'm lazy." You might find out, as I did, that the piles of clothes make your partner feel stressed and disorganized, as if our lives are out of control. I'd *much* rather just pick up my yoga pants than do that to him. A good way to exercise curiosity is to ask open-ended questions such as "say more about…," one of Stewart's favorites. "Can you say a bit more about how that makes you feel?" or "Can you say more about that to help me understand?"

#3 Suspend judgment. Sometimes we become so entrenched in our own beliefs and opinions that we close down and don't want to hear *anything* else from *anyone* else, even those closest to us. "But if we close down, we're going to miss important messages," says Philip Tirpak, an instructor of communication studies at Northern Virginia Community College and president of the International Listening Association, which supports research and teaching on effective listening. "The first thing to do is suspend your judgment. Try really hard to let the other person talk," he says. "Take in the entire message, no interruptions allowed. Just listen." When you do that, you'll often find that even if you do disagree there is at least some shared ground or goals, which makes it easier to put yourself in the other person's shoes—that phenomenon known as empathy. "Empathy deals with shared experiences—sometimes we don't have many, but in the big picture we're all really more the same than we are different," Tirpak says.

#4 Know when to tap out. "Genuine listening requires humility and curiosity—and neither can be successfully faked," Stewart says. If you're not feeling well, if you're hurried, rushed or overly stressed, you're not going to be able to be truly present and curious during a conversation, especially a tough one. In those moments, Tirpak says, "there's nothing wrong with just saying, 'I can hear that this is really important to you, and I want to give you my full, undivided attention. Can we wait for a bit? I need some time.'"

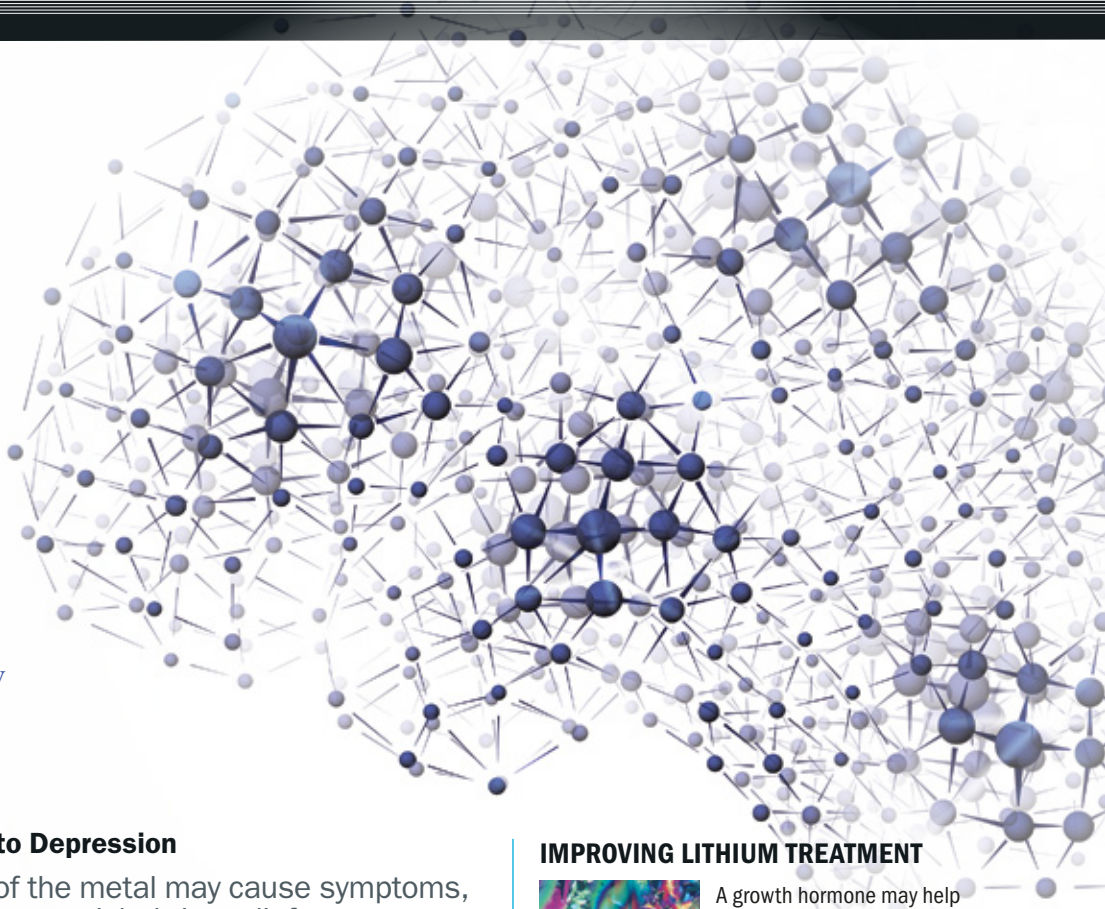
After talking with story sources all day at work and listening to the near-constant chatter of our two little girls at home, I sometimes feel as if I can't listen to one more word. Even from the mouth of the one I love most. But the next time I find myself there, I'll be honest about my intentions *and* my limitations. Instead of trying to fake it, we'll just try again later.

—*Sunny Sea Gold*

MÁGOZ (*listener*); PAUL PANTAZESCU © *iStock.com* (*globe*)

An Elemental Effect on Mental Health

Zinc, copper, iron—these and many other elements play a crucial role in health and sickness. Beyond the well-known toxic effects of lead, it can be difficult to determine the precise impacts of these metals because they interact with one another and with many types of molecules found in our body. Recent research has led to some key insights, however, which may lead to new treatments for mental illnesses.



Linking Zinc to Depression

A deficiency of the metal may cause symptoms, and supplements might bring relief

Depression is tricky to treat because many patients do not respond to antidepressant medications. A growing body of evidence suggests that zinc deficiency may be a factor underlying depression in some cases—and zinc supplements can be an effective treatment for people whose levels are low.

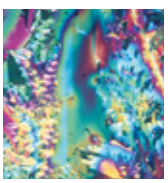
A meta-analysis published in December 2013 in *Biological Psychiatry* analyzed 17 studies and found that depressed people tended to have about 14 percent less zinc in their blood than most people do on average, and the deficiency was greater among those with more severe depression. In the brain, zinc is concentrated in glutamatergic neurons, which increase brain activity and play a role in neuroplasticity, explains one of the paper's co-authors, Krista L. Lanctôt, a professor of psychiatry and pharmacology at the University of Toronto. "Those neurons feed into the mood and cognition circuitry," she says.

Newer results increasingly point to a causal relation. Last September researchers at the University of Newcastle in Australia reported findings of two longitudinal studies that demonstrated an inverse relation between depression risk and dietary zinc intake. After adjusting for all known potential confounders, they found that the odds of developing depression among men and women with the highest zinc intake was about 30 to 50 percent lower than those with the lowest intake. Although previous studies have shown that zinc supplementation can augment the effects of antidepressant medications, research published in May in *Nutritional Neuroscience* is the first to investigate the effects of zinc alone on depressive symptoms. In the double-blind, randomized, placebo-controlled trial, researchers assigned participants to one of two groups: every day for 12 weeks, one group received 30 milligrams of zinc; the other group received a placebo. At the end of the study period, the zinc group showed a steeper decline in its scores on a rigorous inventory of depression symptoms.

"The future treatment of depression is zinc sulfate," says Atish Prakash, a postdoctoral fellow in the department of pharmacy at the MARA University of Technology in Malaysia, who co-authored a thorough review of studies on the role of zinc in brain disorders, published in April in *Fundamental and Clinical Pharmacology.* Researchers strongly caution against people trying zinc supplements on their own, however—when levels are too high, zinc can cause other complications. Working with a doctor is essential, and in most cases, eating a healthier diet is probably a better way to ensure optimal zinc levels than supplementation. Yet for those with depression who are also at high risk for zinc deficiency, including vegetarians, people with alcoholism, gastrointestinal issues or diabetes, and pregnant or lactating women, zinc may be just what the doctor ordered.

—Tori Rodriguez

IMPROVING LITHIUM TREATMENT



A growth hormone may help people with treatment-resistant bipolar disorder respond to lithium

Lithium has been providing relief to patients with bipolar disorder for decades. Although it is considered the standard treatment for the illness, how it works—and why it does not work for at least half of patients who try it—remains largely a mystery. Recent study findings suggest that a hormonal mechanism may be a factor.

In research published in July in the *Journal of Molecular Neuroscience,* scientists from several universities expanded on earlier work investigating the role of insulinlike growth factor (IGF1) in lithium sensitivity. (*Scientific American* is part of Springer Nature.) A 2013 paper by some of the authors of the newer study had found higher levels of the hormone in blood cells of bipolar patients who were responsive to lithium treatment, as compared with nonresponders. In the current study, researchers tested the effects of administering IGF1 to the blood cells of those same patients.

Adding the hormone increased lithium sensitivity only in cells of nonresponders, which "proves that indeed IGF1 is strongly implicated in determining clinical response or resistance to lithium," says study co-author Elena Milanesi, a postdoctoral fellow at the Sackler Faculty of Medicine at Tel Aviv University in Israel. Further research will be needed to discern treatment possibilities, including supplemental use of the hormone or a similarly acting drug in lithium-resistant patients. Synthetic human IGF1 is already FDA-approved for human use in other kinds of disorders, Milanesi says, so she hopes clinical trials can get under way quickly. ***—T.R.***

Other Metals and the Mind

Many studies find that high or low levels of certain elements are linked to mental health. Here are some associations that are well supported by research:

IRON. Iron deficiency impedes neurotransmission and cell metabolism, and research findings have linked it with cognitive deficits in children and adults.

MAGNESIUM. Low magnesium intake has been implicated in anxiety and depression in studies of humans and rodents, and new research published in *Acta Neuropsychiatrica* suggests the relation is mediated by altered gut microbes, which have previously been linked with depression. In the study, mice fed a magnesium-deficient diet displayed an increase in depressive behavior and alterations in gut microbiota that were positively associated with neuroinflammation in the hippocampus.

MANGANESE. In research reported in the *Journal of Alzheimer's Disease,* scientists from China and Japan investigated the role of manganese—a known neurotoxin at high levels—in the progression of cognitive decline. In 40 older adults, they found that manganese levels were significantly correlated with scores on assessments of cognitive function and dementia and that levels of the characteristic protein tangles of Alzheimer's disease increased as manganese levels did. Excessive manganese is usually caused by airborne pollutants or pesticides, but eating too little iron can increase manganese absorption—so a healthy diet is key here, too. *—T.R.*

Beware of Supplements

That headline may sound alarmist—if your doctor advises you to take a supplement, by all means, you should take it. Yet we cannot emphasize enough the importance of consulting a health care provider before starting any kind of supplement regimen, especially one that includes the trace elements discussed in this overview. Many of these elements can cause serious complications at high levels as well as low levels, and it is easy to accidentally go overboard. In addition, it can be hard to tell whether a person truly needs supplements—zinc, for example, cannot be reliably measured in blood or urine. Researchers use a complex variety of measurements and indicators to determine patients' zinc levels—something the average doctor's office cannot replicate.

In addition, most researchers and physicians believe that improving a person's diet is a far better way to reach healthy levels of these elements. Eating whole foods such as fresh meats, vegetables, fruits, nuts and seeds will give most people the nutrients they need. Avoiding highly processed foods with added sugars and fats is key, too, because those types of foods can impede your body's absorption of nutrients. In other words, that spinach salad is actually rendered less healthy if you chase it with a candy bar. *—T.R.*

SCIENCE SOURCE (*elements*); RON CHAPPLE *Thinkstock* (*vitamins*); FROM "SELF-ORGANIZATION OF POLARIZED CEREBELLAR TISSUE IN 3D CULTURE OF HUMAN PLURIPOTENT STEM CELLS," BY KEIKO MUGURUMA ET AL., IN *CELL REPORTS*, VOL. 10, NO. 4; FEBRUARY 3, 2015 (*Purkinje cells*); SCOTT DUNLOP © *iStock.com* (*sun icon*)

ON THE HORIZON

LAB-GROWN SPARE PARTS FOR BRAINS

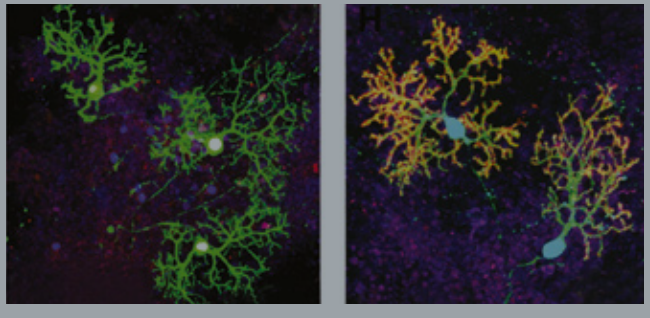
The "brain in a vat" has long been a staple of philosophical thought experiments and science fiction. Now scientists are one step closer to creating the real thing, which could enable groundbreaking experiments of a much more empirical kind. Research teams at Stanford University and the RIKEN Center for Developmental Biology in Japan have each discovered methods for coaxing human stem cells to form three-dimensional neural structures that display activity associated with that of an adult brain.

By applying a variety of chemical growth factors, the RIKEN researchers transformed human embryonic stem cells into neurons that self-organized in patterns unique to the cerebellum, a region of the brain that coordinates movement. The Stanford team worked with induced pluripotent stem cells derived from skin cells and chemically nudged them to become neurons that spontaneously wired up into networks of 3-D circuits, much like the ones found in the cerebral cortex—the wrinkled gray matter of the brain that supports attention, memory and self-awareness in humans.

"For years people have used mouse embryonic stem cells to generate teratomas—things that look like they could be organs," says David Panchision, a neuroscientist at the National Institutes of Health, which supported the Stanford research. "But it's not organized and systematic, the way a developing brain needs to be to function." In contrast, the Stanford team's neural structures not only self-assembled as cortexlike tissue, the neurons also sent signals to one another in coordinated patterns—just as they would in a brain. The cerebellar tissue generated by the Japanese scientists did, too.

So what could one do with a working chunk of lab-grown brain? Using it to someday grow neural spare parts for diseased or aging patients "is not impossible," says RIKEN's Keiko Muguruma. But the near-term goal is to subject these living mini brains, dubbed "organoids" by scientists, to medical research that is otherwise impossible or unethical. "You can do detailed, mechanistic experiments that are directly relevant to human disease," Panchision explains. "If you're looking for very specific molecular targets or pathways in the brain, and how drugs might act on them, the difference between human cells and mouse cells is significant."

Panchision foresees organoids being used in virtual clinical safety trials for new psychiatric medications. "Most brain disorders aren't understood at the circuit level," he says. So whereas growing spare parts for your brain remains a fantasy for now, having these neural crash-test dummies for research purposes could be the next best thing. *—John Pavlus*



Purkinje cells are a type of neuron found only in the cerebellum. The team at RIKEN in Japan confirmed that its embryonic stem cells had grown into mature Purkinje cells (*above*) by checking for molecules that occur at different stages of development.

Subliminal Messages Influence Pain

The brain can learn to associate certain images with more or less pain, even if the images never reach conscious awareness

Most people associate the term "subliminal conditioning" with dystopian sci-fi tales, but a recent study has used the technique to alter responses to pain. The findings suggest that information that does not register consciously teaches our brain more than scientists previously suspected. The results also offer a novel way to think about the placebo effect.

Our perception of pain can depend on expectations, which explains placebo pain relief—and placebo's evil twin, the nocebo effect (if we think something will really hurt, it can hurt more than it should). Researchers have studied these expectation effects using conditioning techniques: they train people to associate specific stimuli, such as certain images, with different levels of pain. The subjects' perception of pain can then be reduced or increased by seeing the images during something painful.

Most researchers assumed these pain-modifying effects required conscious expectations, but the new study, from a team at Harvard Medical School and the Karolinska Institute in Stockholm, led by Karin Jensen, shows that even subliminal input can modify pain—a more cognitively complex pro-

When researchers flashed an image of a brand-name drink, likely to choose that brand to quench their thirst but only if

TIMELINE

The Fall and Rise of Subliminal Messaging

The idea that people can be subliminally influenced is ancient—historical evidence suggests that in the fifth century B.C., Greek thinkers attempted to employ subtle yet persuasive language to sneakily influence people. In the mid-20th century the idea famously captured popular attention, but science has only recently begun to parse the actual effects of subliminal messages.

—Victoria Stern

1943: Subliminal messages were occasionally embedded in radio, film and television programs. In an animated short featuring Daffy Duck in 1943, for example, the words "BUY BONDS" appear briefly on screen. Nobody knew whether these messages would influence people, but they figured it couldn't hurt to try.

1957: James Vicary, a market researcher, claimed that by flashing the words "Eat Popcorn" and "Drink Coca-Cola" during a movie for a fraction of a second, he significantly increased the sale of these snacks. Five years later he admitted he had faked the study. By that time, however, the public had grown concerned—and advertisers and government agencies intrigued—about the manipulative power of these messages.

Late 1960s–1980s: Scientific studies throughout the 1960s, 1970s and 1980s tended to discredit the claims that subliminal messages could subtly influence behavior. One study, for instance, showed that flashing the words "Hershey's Chocolate" on a series of slides during a lecture did not influence whether students purchased Hershey's products during a 10-day period.

1990s: Although many studies continued to discredit the claim that subliminal messages carried any psychological weight, other research started to uncover subtle effects. In one such study from 1992, participants viewed images of a person engaged in a normal daily activity. After each image, researchers quickly flashed a photograph: half the viewers saw positive, uplifting content, and half saw negative content. Those who saw negative messages reported thinking of the photographed person in a more damaging light.

Early 2000s: Research continued to show that subliminal messages do influence our perceptions; the effect is just subtler than we thought.

THINKSTOCK

cess than most that have previously been discovered to be susceptible to subliminal effects (*timeline below*).

The scientists conditioned 47 people to associate two faces with either high or low pain levels from heat applied to their forearm. Some participants saw the faces normally, whereas others were exposed subliminally—the images were flashed so briefly, the participants were not aware of seeing them, as verified by recognition tests. The researchers then applied a temperature halfway between the high and low levels, alongside either one of the conditioned faces or a previously unseen face. Participants rated how painful the new temperature was.

The faces previously linked with high or low pain increased and reduced pain ratings, respectively, relative to the new face. The finding held whether the participant had seen the faces normally or learned the association subliminally.

"Our results demonstrate that pain responses are shaped by expectations we may not be aware of," Jensen says. If this applies to the placebo effect generally, one way it could have a beneficial effect is if our mind makes implicit connections between medical paraphernalia and getting better. Hospital settings or a doctor's behavior might then facilitate a placebolike effect. The finding also adds to the growing body of research showing that information that never reaches our conscious awareness can nonetheless influence our later behavior. —*Simon Makin*

participants were more they were already thirsty.

2006: Studies have shown subliminal messages may work in advertising after all, in certain situations. For example, a 2006 study found that participants flashed an image of a brand-name drink, in this case Lipton Ice Tea, were more likely to choose that brand to quench their thirst. This association only held up, however, if participants were already thirsty. (Another provocative study showed that embedding images related to thirst in an episode of *The Simpsons* actually made people thirstier.)

2007: Subliminal messages may also enhance academic performance. In a 2007 study, researchers flashed students hidden words related or unrelated to intelligence, such as "talent" and "grass," respectively, before a practice exam. Those who saw the intelligence words performed better on a midterm one to four days later.

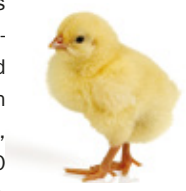
2010–2015: Imaging studies have shown that our brain responds to subliminal messages in measurable ways. Activity levels change in the amygdala, which processes emotions, the insula (involved in conscious awareness), the hippocampus (involved in processing memories) and the visual cortex.

Baby Chicks Have a Mental Number Line Like Ours

Animals seem to have an innate preference for smaller numbers on the left and larger numbers on the right

Think of a number. Now think of a bigger number. Now imagine them in front of you. If you are seeing the smaller number on the left, you have just confirmed an oft-repeated finding: people tend to map numbers onto space from left to right. Mounting evidence, including research on preverbal infants, suggests this tendency is innate, although it can be easily overwritten by culture. Now, in a study published this past January in *Science,* a team of researchers at the University of Trento in Italy, led by cognitive psychologist Rosa Rugani, has shown that infants of a different species altogether also prefer to see bigger numbers on the right.

The team trained three-day-old chicks to walk around a panel for food. First, a group of chicks learned to find food behind a panel displaying five dots. Then the researchers replaced that panel with a pair of new panels. When these new panels displayed two dots each, the chicks walked to the left panel first 70 percent of the time. When the panels showed eight dots each, the chicks tended to choose the right panel—as if preferring to see smaller numbers on the left and larger numbers on the right.



The researchers then repeated the experiment with different chicks that were trained using 20 dots and tested using eight or 32 dots. In both experiments, the chicks veered left for relatively smaller numbers and right for larger numbers. The scientists chose the number eight to be smaller in one context and bigger in the other, showing that the effect depends on relative amounts rather than any absolute preference.

The findings strongly confirm the idea that the left-to-right tendency is innate. Research has shown that this tendency can be modified quite easily by experience, however, so overriding it most likely presents little problem to young brains in a culture that writes from right to left. Arabic speakers, for example, show the reverse spatial tendency. Others who write language from right to left and digits from left to right, as in Hebrew, display no particular spatial preference.

The authors suggest their results are related to the fact that brains are not symmetrical. The right hemisphere dominates visuospatial processing, leading to a preference for the left side of space to dominate attention—perhaps explaining why we naturally think of the "first" numbers there as we count. The spatial mapping might also arise from a physical map of numbers in the brain, which has been found in humans in the right posterior parietal cortex but has not yet been seen in animals. —*Simon Makin*

Team Lie Detector

Groups can sniff out fibs better than an individual can

People are notoriously bad at spotting lies: unless privy to information that directly contradicts a spurious story, past research suggests the average listener pinpoints a fib less than half the time. A study in June in the *Proceedings of the National Academy of Sciences USA* now indicates that groups do a bit better at detecting dishonesty—but only when group members confer with one other before coming to a conclusion.

University of Chicago business researcher Nicholas Epley and doctoral student Nadav Klein conducted four experiments to compare lie perception by individuals or groups. In each scenario, hundreds of people were assigned into groups of three to watch a series of 10 video clips containing some speakers who were telling the truth and others who were trying to deceive them.

Participants then weighed in on whether they believed the speaker in each video lied—some people offered individual judgments right away, and others discussed the case with group members first. In each scenario, the discussing groups had a slight edge, detecting lies up to 62 percent of the time compared with the individuals, whose lie-detection average topped out at 54 percent in one of the experiments but was typically lower.

Researchers believe there is more at work than the so-called wisdom of crowds effect because conglomerating judgments from a few or many individuals did not increase lie detection in the absence of the discussions. Instead they suspect there are still to be determined synergistic elements that bolster groups' baloney detection. The researchers plan to follow up further by studying the conditions and group characteristics that produce the lie-detection boost.

"It's not that every group is better than every individual. But what is it that gives groups this nudge?" Epley wonders. He cautions that the effect sizes are small and variable but says the results hint at the importance of group discussions in settings where people are asked to uncover lies—from deliberating in a jury to ferreting out insurance fraud.

—*Andrea Anderson*

Looking for Lies

Falsehoods are not easy to spot. According to an analysis of more than 200 studies, people with no training are able to distinguish a lie from truth just over 50 percent of the time (about the same as guessing). Those with training fare somewhat better, with an accuracy of about 65 percent. Experts have developed a range of detection methods to help with the task, but no method is foolproof because there is no one behavior that indicates deception. Here is the truth about five methods that have shown some promise for detecting lies:

	HOW IT WORKS	ACCURACY	THE PROBLEM
POLYGRAPH	It detects automatic stress-related responses, such as increased skin conductivity (which measures sweating), heart rate, breathing rate and blood pressure	Studies vary significantly, showing 60 to more than 90 percent accuracy	We feel stress for many reasons—nervousness, anger, pain, surprise; guilty individuals can also cheat by using sedatives or antiperspirant
VOICE-STRESS ANALYSIS	A computer program measures fluctuations in speech patterns, such as microtremors, pitch and intensity, hoping to detect heightened levels of stress, which may indicate deception	Uncertain	A 2013 report found this technique identified stress better than a polygraph, but whether that means it is a good lie detector remains unclear
MICRO-EXPRESSIONS	Popularized on the TV show *Lie to Me,* these almost imperceptible involuntary facial movements can expose a range of emotions, including whether a person might be holding back	Not yet ready for prime time	There are no solid data that indicate microexpressions are particularly reliable indicators of deception
FUNCTIONAL MRI	fMRI indicates changes in brain activity. Studies show that when people lie, they display greater activity in the prefrontal cortex, which plays a role in decision making	Unclear	A 2013 review published in *Frontiers in Human Neuroscience* concluded that the current scientific evidence remains weak

GETTY IMAGES

A Fine Line between Love and Drunk

Oxytocin, known as the love hormone, has a dark side—and it looks like alcohol intoxication

Many studies trumpet the positive effects of oxytocin. The hormone facilitates bonding, increases trust and promotes altruism. Such findings earned oxytocin its famous nickname, the "love hormone." But more recent research has shown oxytocin has a darker side, too: it can increase aggression, risk taking and prejudice. A new analysis of this large body of work reveals that oxytocin's effects on our brain and behavior actually look a lot like another substance that can cut both ways: alcohol. As such, the hormone might point to new treatments for addiction.

Researchers led by Ian Mitchell, a psychologist at the University of Birmingham in England, conducted the meta-analysis, which reveals that both oxytocin and alcohol reduce fear, anxiety and stress while increasing trust, generosity and altruism. Yet both also increase aggression, risk taking and "in-group" bias—favoring people similar to ourselves at the expense of others, according to the paper published in August in *Neuroscience and Biobehavioral Reviews*.

The scientists posit that these similarities probably exist because oxytocin and alcohol act at different points in the same chemical pathway in the brain. Oxytocin stimulates release of the neurotransmitter GABA, which tends to reduce neural activity. Alcohol binds to GABA receptors and ramps up GABA activity. Oxytocin and alcohol therefore both have the general effect of tamping down brain activity—perhaps explaining why they both lower inhibitions.

Clinical trials have uncovered further interplay between the two in demonstrating that a nasal spray of oxytocin reduces cravings and withdrawal symptoms in alcoholics. These findings inspired a new study, published in March in the *Proceedings of the National Academy of Sciences USA*, which suggests oxytocin and alcohol do more than just participate in the same neural pathway: they may physically interact. The researchers showed that oxytocin prevented drunken motor impairment in rats by blocking the GABA receptor subunit usually bound by alcohol. Mitchell speculates this interaction is specific to brain regions that regulate movement, thereby "sparing the usual motor deficits associated with alcohol but still influencing social and affective processes."

These findings suggest getting "love drunk" may impede a person from getting truly drunk—or at least make getting drunk less appealing. They also offer a possible biological explanation for why social support is so effective at helping people beat addictions. The researchers' biggest hope for now is that in the near future, the similarity between these two chemicals will allow scientists to develop oxytocin-based treatments for alcoholics.

—Jessica Schmerler

TOM MERTONE *Getty Images (couple);*
LUCA CEPPARO *Getty Images (tattooed woman)*

Men Prefer Weird Women

The popular idea that women should conform around men is outdated

Men are often advised to stand out from the crowd to attract women—there can be only one alpha male. Women, on the other hand, are told not to be too weird. This advice has sunk in: a 2006 study found that when in a mating mind-set, men become less conformist and women become more so. A paper in the June issue of *Personality and Social Psychology Bulletin,* however, reports that we have it all wrong.

In the new work, which studied subjects who identified as either heterosexual or bisexual, both women and men preferred nonconformist partners—those whose clothes, opinions or life decisions broke the norm—when selecting from online dating profiles, describing ideal partners or picturing dates with people they had just met. Men showed just as much interest as women in oddballs (and in one experiment, in fact more interest), even though subjects predicted women would like misfits more. Further, independent-minded people—in the U.S., the U.K. and India—reported more success in both short- and long-term dating. Other research has shown breaking rules to be a good indicator of status and power, which may explain part of its appeal for both sexes, but gender role expectations have yet to catch up.

"The old-fashioned gender stereotype—that men go for conformist, submissive women—has been slow to die," says lead author Matthew Hornsey, a social psychologist at the University of Queensland in Australia. "I'm intrigued by the notion of the 'girls' night out' and how many women feel as though they can be more unguarded without men around—more relaxed, more crass, more honest, more funny. And I keep thinking, 'Why are you keeping this good stuff to yourselves? Men would love it!'"

—Matthew Hutson

Dalí's Doubles

Ambiguity and duplicity are hallmarks of Salvador Dalí's artworks

Salvador Galo Anselmo Dalí i Domènech was born to Felipa Domènech i Ferrés and Salvador Dalí i Cusí on October 12, 1901, in the town of Figueres in Catalonia, Spain. The couple's firstborn child, he showed signs of great precociousness, but his potential was tragically cut short. Little Salvador fell sick with gastroenteritis and died just two months shy of his second birthday. His parents were devastated but, in their grief, conceived another child. On May 11, 1904, only nine months and 10 days after the death of their son, a second boy entered this world. His name? Also Salvador.

It was this Salvador—middle names, Felipe Jacinto—who would become one of the most important artists of the 20th century. In his mind, however, he was forever in the shadow of his sibling. The two Salvadors shared an uncanny likeness. "When my father looked at me, he was seeing my double as much as myself," Dalí later reflected.

Not creeped out yet? Read on.

When Dalí was five years old, his parents took him to his brother's grave and told him that he was his reincarnation. The idea took hold and haunted Dalí's days. "[We] resembled each other like two drops of water, but we had different reflections," he once wrote. "My brother was probably a first version of myself but conceived too much in the absolute." This belief had a profound impact on his art. His paintings prominently feature doublings, as in his *Portrait of My Dead Brother* (1963) above, which features a composite of the artist and his sibling.

Dalí created many visual illusions by overlaying images made of sharp contours and small details—so-called high spatial frequencies—with images made of soft contours and bigger details—or low spatial frequencies—all in the same ambiguous scene. As a result, viewers perceive one or the other image, depending on how close they are to the painting. Up close, the details from the high spatial frequency image dominate. But when viewers squint their eyes or look at the painting from far away, the other picture appears. A detailed inspection of Dalí's *Portrait of My Dead Brother,* for instance, reveals that the larger face is made of what appear to be dark and light cherries, sometimes paired as twins. Step back, though, and the picture of a young man emerges, with a crow or vulture embedded in his forehead and doubling as hair.

Neuroscientist Aude Oliva and her colleagues at the Massachusetts Institute of Technology have optimized this type of perceptual switch in several striking examples. One such image (*opposite page at top*) looks like two eagles up close but becomes a head and neck seen from afar.

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 authors of *Sleights of Mind,* with Sandra Blakeslee (http://sleightsofmind.com), winner of a Prisma Prize for best science book of the year.

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THIS PAGE AND OPPOSITE PAGE: © SALVADOR DALÍ, FUNDACIÓ GALA–SALVADOR DALÍ *Artists Rights Society (ARS), New York 2015;* SEAN McCABE (*Martinez-Conde and Macknik*)

Last year we served as scientific consultants for the Marvels of Illusion exhibit at the Dalí Museum in St. Petersburg, Fla. The collection of artwork showcased the role of illusions in Dalí's art and featured numerous examples of dual interpretations and doubling. "Dalí intuited that what we construe visually as reality is the product of the habits of the mind, more than of the eye," says Hank Hine, the museum's executive director. "By creating accessible double images, Dalí asks us to reconsider on a fundamental scale our constructs of reality."

Here we present a few of Dalí's double paintings included in the exhibit to discuss their perceptual mechanisms. **M**

MADONNA OF THE BIRDS

Just as Dalí saw himself as a less "absolute" copy of his older brother, a number of his paintings re-create and reinterpret previous works by the old masters, such as Raphael, Velázquez and Rembrandt. The results are eminently ambiguous: the old composition lingers just below the surface of Dalí's version.

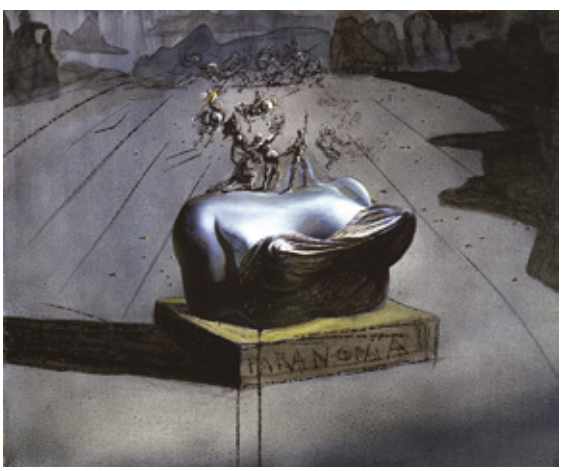
The *Madonna of the Birds* watercolor (1943) (*right*) is based on, and preserves, the original arrangement of *Alba Madonna,* circa 1510, by Raphael (1483–1520) (*left*). The sandal on the Virgin's left foot is a close replica of Raphael's original, whereas the torso is merely hinted at in Dalí's reimagining. Cortical neurons in the viewer's brain connect the individual birds to suggest the contours of the Virgin's head and face.

PARANOIA

In the 1930s Dalí developed what he called the paranoiac-critical method, which relied on his ability to establish connections between seemingly unrelated concepts or images. In *Paranoia* (1935–1936), a battle scene resembling a Leonardo da Vinci sketch hovers over a silvery, headless female bust, set on a loosely drawn pedestal. Small figures of warriors and horses form parts of the woman's face: eyes, mouth, chin and hairline. Most of her features are absent, but the viewer's visual system fills them in.

Such filling-in processes are common in everyday perception. Face-detecting neurons in the brain's fusiform gyrus area in the temporal lobe are particularly predisposed to detecting the human visage, however vague or ambiguous. This is why we often see the fronts of cars as faces, with the grilles as mouths and the headlights as eyes.

To see the woman's face more clearly, try squinting your eyes to blur the edges of the little figures. The face itself has two different interpretations: some people see a kind lady lowering her gaze to her right, whereas others see a crazed woman with a scary smile.



AUDE OLIVA *Massachusetts Institute of Technology* AND AMANDA O'KEEFE *(hybrid image)*; CORBIS *(Raphael painting)*

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DECISION MAKING

The Positive Power of Nudges

When governments use behavioral science to help citizens make wiser choices, everybody wins

By Jon M. Jachimowicz and Sam McNerney

Our decisions are constantly shaped by subtle changes in our environment. Even choices that feel deliberate and conscious can be swayed by cues that we may not even notice, such as social norms or the setting of a default option. Behavioral scientists use the phrase "choice architecture" to describe the ways in which the environment influences how we decide.

In the past five years several governments have begun to guide people toward making better choices—for themselves and for society—by using behavioral science research. Scientists refer to choice architecture interventions that push people toward a certain outcome as "nudges." Since 2010, for instance, the U.K.'s Behavioral Insights Team, or "nudge unit," has dramatically improved on-time tax payments simply by telling people about the large number of citizens who paid their taxes on time. The team has collected an estimated £210 million in revenue. Recently the World Bank issued an extensive report that highlighted similar behavioral science initiatives around the world, and President Barack Obama has launched a new behavioral unit, which is modeled after the U.K.'s version.

Despite ample evidence showcasing the benefits of such nudges, commentators from both sides of the political spectrum have labeled them unethical. They emphasize that manipulating choice undermines our ability to choose freely, even when nudges are disclosed or implemented with good intentions. As a result, nudge initiatives to improve education, health and safety are encountering increased resistance.

Advocates of choice architecture interventions, such as Cass Sunstein, a leading constitutional scholar and author of several books on nudging, point out that nudges do not force anyone to do anything. They merely reorient decisions, much as a GPS guides but does not forcefully direct travelers.

Yet this defense is insufficient. Although it is true that nudges do not eliminate our freedom to choose, critics are correct to argue that nudges can strongly and sometimes surreptitiously influence our behavior. A stronger defense must begin by acknowledging that nudging is unavoidable. From traffic lanes to the size of the popcorn bucket at the movie theater, we are continuously nudged—intentionally or not—by the government, private companies and other people.

The question, then, is not whether government has the right to nudge—invariably and inevitably, it does—but whether government should redesign the choice architecture to help citizens achieve their goals. A growing body of psychological and economic research is revealing opportunities where government can use the tools of behavioral science to help people make better choices. The findings suggest that when the choice environment significantly undermines the health and financial well-be-

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DANIEL ZENDER

ing of citizens, the government has not only the right but the obligation to improve the choice environment.

The Science of Swaying Choices

Take Social Security, for example. Its benefits are available to any U.S. citizen who is at least 62 years old. But the earlier that people claim, the fewer benefits they receive in the long run. People who wait until they reach full retirement age, which depends on when they were born, receive the maximum amount. Delaying is usually the best economic option for people who are in good health and can therefore expect to live longer. Yet most Americans claim early—almost half claim as soon as possible—which often leads to financial problems later on.

This year a team of researchers led by Melissa Knoll, a social scientist then at the Social Security Administration, evaluated how two biases might explain this behavior. The first is present bias, the tendency to opt for immediate short-term gains at the expense of long-term gains. The second is a by-product of query theory, or how the order in which people consider options influences how they decide.

The team gathered 418 participants nearing retirement and split them into two groups. Those in one group generated favorable reasons for why they should claim early, then considered why they might want to claim late. The other group performed the same tasks in reverse. Knoll and her colleagues found that when participants first considered the merits of claiming later, they more easily generated reasons for why it was a better idea than claiming early. As a result, they delayed claiming by about nine months on average, compared with participants who focused on claiming earlier first. This modest shift can mean a difference of tens of thousands of dollars for the beneficiary.

Knoll's intervention represents a potential win for citizens and government. If people who claim early fall into poverty later, the government must spend even more resources helping these individuals. Considering the number of baby boomers retiring—more than a quarter of a million Americans now turn 65 every month—it is easy to see how Knoll's intervention could save billions of federal dollars.

Another case study comes from the Affordable Care Act (ACA), which allows millions of Americans to sign up for state and federal health insurance coverage through exchange marketplaces. In 2013 Columbia University business professor Eric Johnson and his colleagues conducted six experiments with more than 1,000 participants and found that most people did not select the most cost-effective policy available in a model based on the current ACA exchanges. Instead people were overwhelmed with options, and consequently, their ability to make smart choices plummeted.

Johnson and his team then dramatically improved participants' selections in one condition by redesigning the choice architecture. They incorporated an online calculator and implemented a default option that preselected the optimal insurance plan for that individual, helping consumers save, on average, $456 every year. Johnson estimated that these small interventions could save customers and taxpayers approximately $10 billion annually. In addition, by helping people find the right plan, insurance companies can understand their clients' needs better and design improved plans at more competitive prices.

How to Decide without Deciding

It is easy to see how nudges can help citizens make better decisions, prevent waste and save precious resources. How food options are framed, for instance, can affect dietary choices—such as when a grocery store provides the percentage of fat in packaged meat. One barrier to climate change is bad choice architecture. If we frame a fee as a "carbon offset" instead of a "carbon tax," we could nudge people to make more environmentally friendly decisions.

And yet this powerful new tool faces a threat. The U.S. House of Representatives recently passed legislation that includes a $140-million cut—about 45 percent—for the Directorate for Social, Behavioral and Economic Sciences, the part of the National Science Foundation that, among other roles, funds behavioral science research specifically designed to reduce government spending. It is a peculiar target for legislators aiming to save federal dollars.

Ultimately the alternative to nudging is not more personal freedom or a less intrusive government. It is bad nudging. A few years ago the Social Security Administration helped prospective beneficiaries calculate when delaying claims would offset total benefits. But by making the option of short-term money more salient, the computation aid inadvertently accelerated early claiming by 15 months.

Instead of relying on ideologically driven laws, we need rigorous experiments to test how people choose in specific situations. Once we know what works and for whom, we should persuade government officials to implement the best interventions.

There is no "neutral" world in which we make our decisions freely, autonomously and rationally. Decades of psychological research reveal that the environment influences and occasionally changes behavior. Why not use what we know about human behavior to promote wiser choices? M

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RESEARCH DIVERSITY

Fixing the Liberal Slant in Social Psychology

We should seek to reduce political bias, not balance it out

By Piercarlo Valdesolo

Here's one thing on which everyone agrees: social psychology is overwhelmingly composed of liberals—around 85 percent, according to a 2012 survey by researchers at Tilburg University in the Netherlands. The question of why this is the case, and whether it presents a problem, is more controversial. The topic has exploded over the past several years, with claims of both overt hostility and subtle bias against conservative students, colleagues and their publications being met with reactions ranging from knee-jerk dismissal to sincere self-reflection and measured methodological critique.

A paper published online last year in *Behavioral and Brain Sciences* by José L. Duarte of Arizona State University and his colleagues attempts to organize the existing research relevant to this debate. Two central questions arise: Is the ideological imbalance the result of true bias against conservatives or some more benign cause, such as self-selection into the field? And regardless, would more political diversity improve the validity of our science?

Duarte and his colleagues provide evidence suggesting that social psychology is not a welcoming environment for conservatives. Several studies have shown that papers are reviewed less favorably if they support conservative positions, and anonymous surveys reveal a considerable percentage of social psychologists willing to report negative attitudes toward conservatives. This should not surprise us. Everything social psychologists know about group behavior suggests that overwhelming homogeneity, especially when defined through an important component of one's identity such as political ideology, will lead to negativity toward an out-group. We also know a thing or two about confirmation bias—the tendency to view new information as supporting one's preexisting beliefs. So it would be odd to think it might not affect judgments in our own field.

But would more political diversity increase the validity of sociopsychological findings? As the authors note, this concern mainly applies to the small subset of research dealing with politically charged issues (gender, race, morality). They argue that having a range of political opinions in these domains would combat the pernicious effects of confirmation bias and groupthink by introducing more dissent.

Duarte and his colleagues identify various examples of research that they believe to be "tainted"—by assuming, for instance, that liberal views are objectively more valid than conservative ones—and conclude that "the parameters [of the field] are not set properly for the optimum discovery of truth. More political diversity would help the system discover more truth." Conservative social psychologists, they maintain, would test different hypotheses, better identify methodologies in which liberal values are embedded, and be more critical in general of theories and data that advance liberal narratives.

PIERCARLO VALDESOLO is an assistant professor of psychology at Claremont McKenna College and co-author of the book *Out of Character* (Crown Archetype, 2011).

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SCOTT BRUNDAGE

Finally, the authors offer several recommendations for how to curb any negative effects that political homogeneity poses for scientific validity. First, the field should promote political diversity by changing how diversity is defined in the mission statements of our professional societies. Second, professors should be more mindful of how they treat nonliberal views and should actively encourage nonliberals to join the field. Finally, we should change research practices in ways that allow researchers to better detect where bias might be intruding on decision making.

These arguments have provoked a variety of responses in the field. And here is one more. Clearly, we should care about any evidence of bias influencing how we conduct or evaluate research. Further if we deny the *possibility* of such a bias, without reference to empirical investigation, then we will have failed as responsible scientists committed to the pursuit of truth—and ironically so, given that another of the most important lessons from social psychology teaches that we are in no position to evaluate the objectivity of our own decision making.

So what is the best solution if such a bias does threaten the validity of the field? The authors' key proposal is straightforward: add more conservatives into the mix to "diversify the field to the point where individual viewpoint biases begin to cancel each other out." In short, we need to add the *opposite kind of ideological bias* to our literature. If liberals distort science one way, conservatives will distort it the opposite way, and it will all cancel out in the end.

This idea may seem counterintuitive—that to have a more reliable and valid science, we need more bias, just a different kind. But it is rooted in a simple statistical principle. Let us say we are collecting guesses of how many M&Ms there are in a glass jar that actually holds 5,000 of the candies. If we just ask a population notorious for *underestimating*, the average of their guesses will likely be lower than the truth (say, 4,000). And if we just ask a population notorious for *overestimating*, the average of their guesses will likely be higher than the truth (perhaps 6,000). But if we combine these populations, then the average of the total guesses will be closer to the truth. This is the wisdom of crowds.

But how neatly does this principle apply to the issue at hand? What does it mean, in practice, to have the biases that are embedded in researchers' hypotheses, methods and peer reviews "cancel out" over time? If I embed liberal values in my research, and Joe Researcher embeds conservatives ones, why would the ultimate outcome be *more truth discovered* as opposed to just more time and resources wasted, both our own and that of others who might be influenced by our ideologically distorted work? Furthermore, it remains unclear, according to other investigations, whether more ideological diversity would reduce or amplify group bias and polarization.

> IF LIBERALS DISTORT SCIENCE ONE WAY, CONSERVATIVES WILL DISTORT IT THE **OPPOSITE WAY. WE CAN'T IMPROVE VALIDITY BY INTRODUCING NEW KINDS OF ERROR.**

These questions are central to justifying the Duarte paper's claim that adding researchers who would "seek to explain the motivations, foibles, and strengths of liberals as well as conservatives" is the best way "for social psychology to correct longstanding errors on politicized topics," as Duarte and his colleagues assert. Correcting old errors by adding different errors is a tough sell.

I prefer a different solution. Let's improve the validity of our science by trying to reduce error, not by introducing new kinds of it. The authors dismiss this as an impossibility; they feel that, as an ideologically homogeneous group, we are bound to repeat our mistakes. But although no silver bullet exists, researchers have indeed identified beneficial interventions to combat bias in decision making, and papers such as that from Duarte and his colleagues can be seen as a strong reminder that social psychology should make *this* work a priority. For example, this research emphasizes the crucial importance of instilling "an awareness of one's fallibilities and a sense of humility concerning the limits of one's knowledge," as *Scientific American Mind* advisory board member Scott O. Lilienfeld and his colleagues at Emory University write in a 2009 paper.

Duarte and his colleagues provide evidence of one way in which our professional decisions might systematically deviate from an appropriate application of the scientific method. Let's be open to this possibility, address this concern and fulfill our responsibility as scientists. And if more conservatives, or libertarians, or Greens, or independents, or Whigs, or Californians, or art history majors, or single parents, or *whoever* are more attracted to the field as a result, then fine. We do not need more ideology in social psychology; we need less. That is the best way to discover more truth. M

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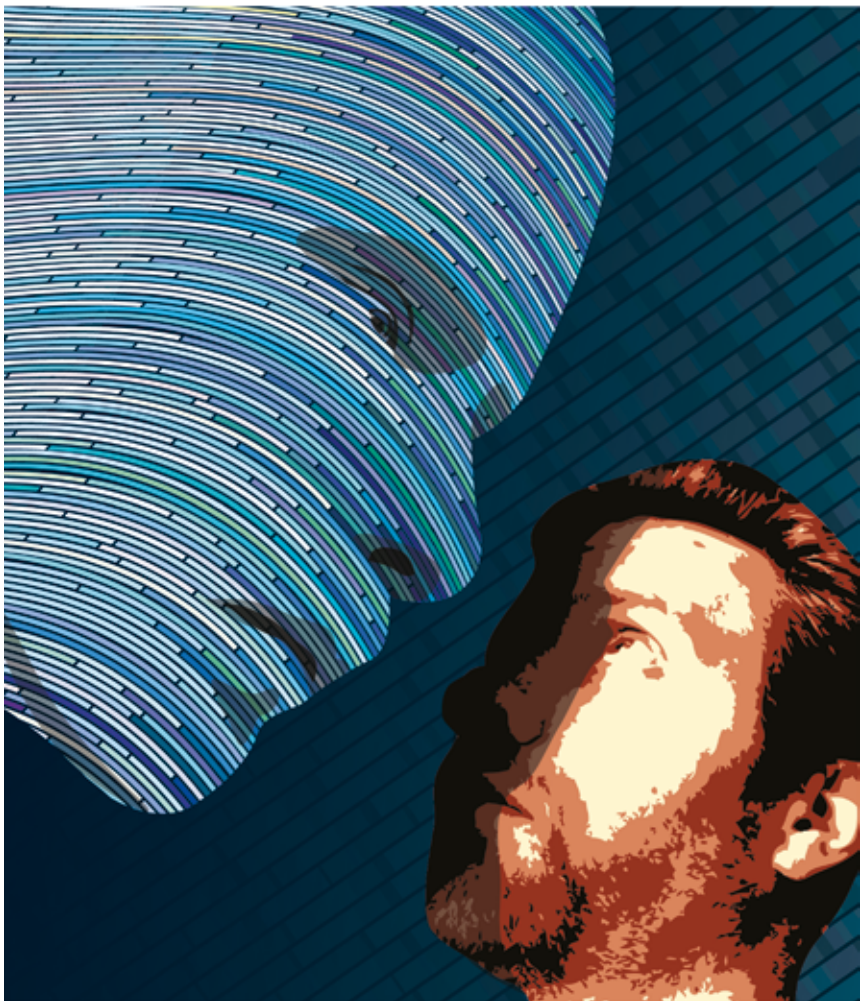
MACHINE INTELLIGENCE

When Computers Surpass Us

A philosopher worries about intelligent machines' ever accelerating abilities to outpace humans on tasks requiring high-level skills



DANIEL HERTZBERG (*illustration*); SEAN McCABE (*Koch*)

Famed science-fiction writer Fredric Brown (1906–1972) delighted in creating the shortest of short stories. "Answer," published in 1954, encapsulated a prescient meditation on the future of human-machine relations within a single double-spaced, typewritten page.

The foreboding of the story echoes current apprehensions of scientists, policy makers and ethicists over the rapid evolution of machine intelligence.

"Answer" begins under the watchful eyes of a dozen television cameras that are recording the ceremonial soldering of the final connection to tie together all the "monster" computers in the universe.

The machines are about to link 96 billion planets into a single "supercircuit" that combines "all the knowledge of all the galaxies."

Two witnesses on the scene are identified only as Dwar Ev and Dwar Reyn. After throwing the switch that connects the galactic circuit, Dwar Ev suggests to his companion that he ask the machine the first question:

> *"Thank you," said Dwar Reyn. "It shall be a question which no single cybernetics machine has been able to answer."*
>
> *He turned to face the machine. "Is there a God?"*
>
> *The mighty voice answered without hesitation, without the clicking of a single relay.*
>
> *"Yes,* now *there is a God."*
>
> *Sudden fear flashed on the face of Dwar Ev. He leaped to grab the switch.*
>
> *A bolt of lightning from the cloudless sky struck him down and fused the switch shut.*

We are in the midst of a revolution in machine intelligence, the art and engineering practices that let computers perform tasks that, until recently, could be done only by people. There is now software that identifies faces at border crossings and matches them against passports or that labels people and objects in photographs posted to social media. Algorithms can teach themselves to play Atari video games. A camera and chip embedded in top-of-the-line sedans let the vehicles drive autonomously on the open road.

What separates these agents from earlier success stories, such as IBM's Deep

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.

Blue, which beat the world's reigning chess champion in 1997, and IBM's Watson, which accomplished the same for the quiz show *Jeopardy* in 2011, is that they are taught by trial and error. The new wave of artificial intelligence (AI) is based on insights derived from the way animals and people learn and analysis of the underlying brain circuits that allowed theorists to develop supervised learning algorithms: the software is shown an image, and depending on whether or not it correctly identifies the face or increases the video game score, parameters internal to the program (so-called synaptic weights) are minutely adjusted. Such machine learning, if done over trillions of machine cycles (yes, it is very computing-intensive), can lead to systems that match or, in some cases, exceed human performance metrics. And, of course, the algorithm never gets distracted or tired and remains focused, day and night (see my July/August column "Intelligence without Sentience").

Within a decade these instances of "weak" or "narrow" AI—able to replicate specific human tasks—will permeate society. Siri is only the beginning. Driverless cars and trucks will become the norm, and our interactions in supermarkets, hospitals, industry, offices and financial markets will be dominated by narrow AI. The torrid pace of these advances will put severe stress on society to deal peacefully with the attendant problems of unemployment (the U.S. trucking industry alone employs several million drivers) and growing inequality.

Obscured by this razzle-dazzle progress is how far away we remain from "strong" or "general" AI, comparable to the intelligence of the proverbial man or woman in the street who can navigate a car, hurtle on skis down a mountain slope, carry on a conversation about pretty much any topic—often in two or more languages. That same ordinary individual might also play a variety of games, serve on a jury and plan for retirement decades in the future. Hampering our ability to design general AI is the embarrassing fact that we don't understand what we mean by "intelligence." This lack of knowledge makes any predictions of when we will achieve strong AI fraught with uncertainty. Still, it may not be so far away. For the record, most experts believe that strong machine intelligence will arrive before the century is over, assuming current trends continue.

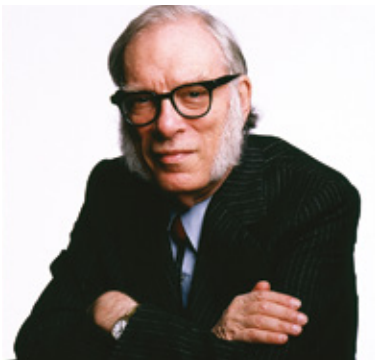
WHAT SEPARATES THE NEW ALGORITHMS FROM PREVIOUS FORAYS INTO AI IS THAT **THEY LEARN BY TRIAL AND ERROR.**

Superintelligence: Paths, Dangers, Strategies deals with the aftermath of that event. The book's author, Nick Bostrom, a professor of philosophy at the University of Oxford, has a background in theoretical physics and neuroscience. His scholarly work is focused on understanding and mitigating emerging risks that threaten the very survival of the human species: full-blown nuclear warfare, massive climate change, synthetic biology, nanotechnology or runaway machine intelligence. *Superintelligence* deals with the last. I warmly recommend the opening and the closing chapters for their enticing arguments, soaring metaphors and insightful fables. You will come away unsettled, if not downright frightened.

The distribution of human intelligence across any representative population is bell-shaped, with the feebleminded at one end and the geniuses at the other. But there is no natural law that stipulates that humans as a group are as intelligent as they could be in an ideal world. Indeed, *Homo sapiens* is plagued by superstitions and short-term thinking (just watch politicians, many drawn from our elites, to whom we entrust our long-term future). To state the obvious, humanity's ability to calmly reason—its capacity to plan and build unperturbed by emotion (in short, our intelligence)—can improve. Indeed, it is entirely possible that over the past century, average intelligence has increased somewhat, with improved access to good nutrition and stimulating environments early in childhood, when the brain is maturing.

And what is true of the biological variety should also be true of its artificial counterpart. There is no discernible principle that would prevent emergence of an AI that is more intelligent than the average person or even any person alive. Indeed, given the competition among the various organizations capable of designing AI systems—mainly national governments and private corporations—their engineers will design ever smarter machines that outperform opponents, whether human or cyborg, and maximize their own gain. This is likely to involve the ability of machines to self-improve by trial and error and by reprogramming their own code. What might happen when machines start to boost their own intelligence was first pointed out by mathematician Irving John Good in a memorable passage in 1965:

> *Let an ultraintelligent machine be defined as a machine that can far surpass all the intellectual activities of any man however clever. Since the design of machines is one of these intellectual activities, an ultraintelligent machine could design even better machines; there would then unquestionably be an "intelligence explosion," and the intelligence of man would*



Classic science-fiction writer Isaac Asimov (*left*) proposed a code of conduct for robots. More recently, futurist Nick Bostrom (*right*) has warned of out-of-control machine AI that might threaten the human race.

be left far behind.... Thus the first ultraintelligent machine is the last *invention that man need ever make, provided that the machine is docile enough to tell us how to keep it under control.*

Bostrom considers different forms of superintelligence: qualitative ones—say, Albert Einstein versus someone intellectually challenged; collective ones, a team of Einstein-level geniuses; or quantitative ones, such as an intelligence that invents the theory of general relativity within an hour of first thinking about the fundamental nature of spacetime rather than the decade that it took Einstein to develop the theory. For Bostrom's reckoning of existential risks, it doesn't much matter as long as the AI can outthink people. And there might be no warning that the age of machines has arrived, nothing like the sonic boom first heard above California's skies in 1947, when the X-1 plane broke the sound barrier, to herald the birth of a superintelligent AI.

Bostrom's book does not explain how this stupendous task could be accomplished; his is not a guide on how to program a strong AI machine to have flexible goals, understand speech and engage in long-term planning. Rather invoking nothing but the iron laws of physics and mathematical logic, the bulk of his thesis is an extended lucubration on the many evolutionary trajectories a superintelligence could take: Will there be many AIs, or will a single malevolent one emerge at a planetary scale? What will an all-consuming machine intelligence try to do—to us, to the planet? How will we control it? Will we even be able to?

Bostrom seeks to hash out the implications of an emergent AI and ways to erect safeguards against the threatening outcomes that are the tropes of science-fiction movies and in stories such as Brown's "Answer." The potential dangers posed by such a machine do not depend on how smart it is but on what its ultimate goals are. Indeed, an AI doesn't even have to be supersmart to be a grave threat to humanity—a narrow AI designed to maximize "return on investments" at all costs in its calculations could trigger a war or some other calamity and thereby rake in untold billions by hedging stocks in the affected industries. Or a narrow military AI connected to our network of nuclear-tipped missiles could unleash a devastating preemptive first strike on the principle that waiting longer would maximize the number of its own citizens dying in nuclear hellfire.

> WHAT WILL BE THE EFFECTS OF AN ALL-CONSUMING MACHINE INTELLIGENCE ON **HUMANS, ON THE REST OF THE PLANET?**

What concerns Bostrom is the unpredictability of what might happen when the technology starts edging toward acquiring the capabilities of a strong AI that takes its goals to extremes never intended by its original programmers. A benign superintelligence that wants nothing but happy people might implant electrodes into the brain's pleasure centers, to deliver jolts of pure, orgasmic gratification. Do we really want to end up as wire-heads? And what about the innocent paper-clip-maximizing AI that turns the entire planet and everything on its surface into gigantic, paper-clip-making factories? Oops.

Given humanity's own uncertainty about its final goals—being as happy as possible? Fulfilling the dictum of some holy book so we end up in heaven? Sitting on a mountaintop and humming "Om" through nostrils while being mindful? Colonizing the Milky Way galaxy?—we want to move very deliberately here.

Things turn out to be no easier when considering how to control such entities. The best known rules to constrain their behavior do not come from roboticists

DEBORAH FEINGOLD *Corbis (Asimov)*; AP PHOTO *(Bostrom)*

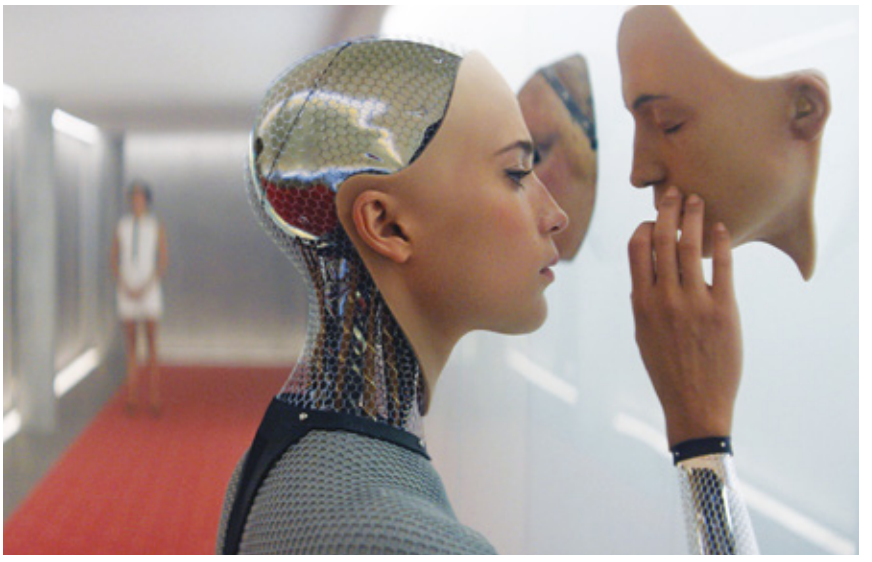
or philosophers but from science-fiction author and biochemist Isaac Asimov. The first of his three laws of robotics (conceived more than 70 years ago!) states: "A robot may not injure a human being or, through inaction, allow a human being to come to harm."

Although this appears reasonable, it is utterly inadequate for dealing with life's messiness. Armed forces have to be ready to quickly and effectively incapacitate a large number of opposing soldiers to prevent a greater evil from coming to pass. Should a superintelligence therefore forestall all armed conflict? Should this AI shut down pollution-producing industries to counter global warming at the cost of a decade-long worldwide depression? Does the first law apply to unborn fetuses and to patients in coma?

Bostrom is most concerned with what he calls the "control problem," the challenge of how to engineer superintelligent machines so as to achieve outcomes that are safe and beneficial for humanity. This goal cannot be achieved by simply picking a set of ethical rules and implementing these into specific instructions. Traditionally the job of the political systems and the courts is to enforce such written laws and the unwritten code that governs society. These objectives are often in conflict with each other: the powerful "thou shalt not kill" edict is routinely violated on the battlefield, on death row, in terminating pregnancies and in slaughterhouses.

Of course, as Bostrom caustically remarks, humankind can hardly claim to be basking in the high noon of perfect moral enlightenment. People can't seem to agree on the best rules to live by. Should an ascendant AI follow the U.S. Constitution, rules laid down by the Chinese Communist Party or dictates of the mullahs in Iran?

The full gamut of possibilities for how an intelligence might behave is simply too vast to be constrained in any meaningful manner by what can't be ruled out by physics. Many options are extremely unlikely. For example, Bostrom goes off on a tangent about the possibility that an AI system believes it exists in an entirely simulated universe. Or he assumes that any superintelligence worthy of its name could eliminate the risks from asteroid impacts or natural pandemics and would also spread itself throughout the entire universe. To assume all of this as a given seems absurd.



The 2015 film *Ex Machina* explores whether a man can be made to fall in love with an intelligent robot, Ava (*shown above*), and to believe that she is in love with him.

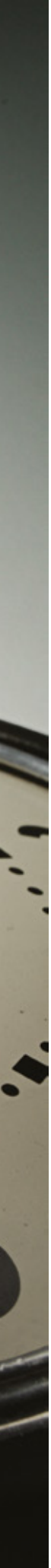
But his basic theory should be taken seriously. To constrain what could happen and ensure that humanity retains some modicum of control, we need to better understand the only known form of intelligence. That is, we need to develop a *science of intelligence* by studying people and their brains to try to deduce what might be the ultimate capabilities and goals of a machine intelligence. What makes a person smart, able to deal with a complex world that is in constant flux? How does intelligence develop throughout infancy, childhood and adolescence? How did intelligence evolve?

How much does intelligence depend on being embedded in social groups? What is the relation between intelligence and emotion and between intelligence and motivation? And what about consciousness? Will it make a difference to the AI's action if it feels something, anything, and if it, too, can experience the sights and sounds of the universe?

In a field largely defined by science-fiction novels and movies acting as laboratories for exploring the possible, Bostrom's *Superintelligence* is a philosopher's Cassandra call to action (adorned with more than 40 pages of endnotes). Woe to us if we don't eventually tackle the questions that the book throws out. Doing so effectively will be possible only once we have a principled, scientific account of the internal constraints and the architecture of biological intelligence. Only then will we be in a better position to put effective control structures in place to maximize the vast benefits that may come about if we develop smart companions to help solve the myriad problems humankind faces. **M**

FURTHER READING

- **Superintelligence: Paths, Dangers, Strategies.** Nick Bostrom. Oxford University Press, 2014.



OUT OF SYNC

Digital devices and 24/7 lifestyles are messing with our body's natural rhythms, threatening our health. What does it take to keep our inner clock ticking?

By Emily Laber-Warren

PHOTOILLUSTRATIONS BY C.J. BURTON

Sparrow Rose Jones

For much of her life, Sparrow Rose Jones was the kind of late riser about whom other people roll their eyes, the kind who goes to bed at dawn and wakes in the midafternoon. As a kid growing up in Louisville, Ky., she had problems at school, in part because she is on the autism spectrum and struggled socially but also because she was always tired. At 16 she dropped out and resigned herself to dead-end night jobs at bars and fast-food joints. The work was menial, but it enabled her to support herself while heeding her natural sleep needs. "I thought, well, my life was sort of working," she recalls.

But Jones possesses a restless intellect. She has taught herself trigonometry, earned an FCC ham radio license and reads history for pleasure. In her mid-30s she decided to return to school—and not just for a high school equivalency diploma. She earned college degrees in both economics and political science, then continued to graduate school at Idaho State University, intent on a doctorate.

Jones was a strong student and even made the dean's list a couple of times. But she had to force herself to function on a daytime schedule, and the effort took a toll. She experienced profound fatigue, unlike anything she had ever felt. Diarrhea and nausea. Optical migraines, which struck without warning and rendered her blind for half an hour at a time. Bouts of depression.

Meanwhile her sleep schedule became increasingly erratic. One summer, free of obligations and the alarm clock, she tracked her sleep and found that she did not return to her usual night-owl ways. Instead her bedtime seemed to be shifting around the clock.

Then she failed a class. "That really scared me," Jones says. She made an appointment to spend a night at a sleep laboratory. Everything checked out normal, but when she showed the doctor her homemade sleep-tracking charts, he recognized, with a ping of excitement, a rare and fascinating malady: non-24-hour sleep-wake disorder, or non-24 for short.

Despite its name, this was not fundamentally a sleep problem, he explained. Jones's sleep issues were the outward manifestation of something much deeper. The sophisticated timing system in her brain had broken, leaving her body chronologically adrift. The biochemical changes that occur each evening to prepare for sleep had disappeared. In fact, all the fluctuations—in blood pressure, body temperature, hormone production, alertness, metabolism and digestion, to name just a few—that happen predictably over the course of the 24-hour day were happening at odd times and were uncoordinated with one another. From a biological perspective, Jones might as well have been living on another planet.

Jones's case is extreme, but more than 27 million Americans—including nurses, firefighters, truck drivers and factory workers—have irregular work schedules that may cause a disconnect from the basic temporal patterns of daily life. Our internal organs operate in patterns called circadian rhythms that repeat over the course of each 24-hour day. And research is revealing that when these physiological rhythms are out of sync—a state known as circadian misalignment—the health impacts can be vast, from diabetes and obesity to cancer, heart problems, infertility, mood disorders and mental decline. "Your body is optimized to work with a certain relationship to the natural world. Good health follows from that," explains Martha Gillette, a neuroscientist and circadian expert at the University of Illinois at Urbana-Champaign. "In modern life, we've taken the world and done with it what we wish."

Because modern routines clash with natural rhythms, scientists are beginning to suspect that virtually everyone is affected to some degree. Staying up late to work or have fun, using laptops, tablets and other screens before bed or to quell insomnia in the middle of the night, indulging in midnight snacks—all these apparently innocuous activities can subtly throw the body off-kilter. The body clock is an ancient system, common to all life on earth, that relies on sunlight and darkness, periods of activity and periods of rest to calibrate itself. Today's society, with its electric lights, 24-hour convenience stores, proliferating digital devices, global economy and "always on" mentality, has scrambled our inner timing systems.

In short, we are living in an age of circadian dysfunction.

Anyone who has flown across time zones knows what it feels like to have a body clock that is out of whack—fatigue, insomnia, digestive problems, headache, dizziness, nausea, among other symptoms. Jet lag is a classic example of circadian misalignment. The body typically adjusts within a week or so. But we are increasingly subjecting ourselves to the equivalent of permanent jet lag.

The science is so new that no one knows how many of us are affected, but people may experience mild circadian misalignment in a variety of ways without realizing the root cause. It

FAST FACTS

BAD TIMING

1. The internal workings of the human body adhere to daily cycles known as circadian rhythms. The brain area called the suprachiasmatic nucleus coordinates the activity patterns of the body's many organ systems.
2. Artificial light at night confuses the body's rhythms, raising the risk of diabetes, cancer, depression and even infertility.
3. People can learn to regulate their natural circadian rhythms to maintain and restore health.

COURTESY OF SPARROW ROSE JONES

could present as stomach upset, unexplained insomnia or, more ominously, the shifts in blood pressure, inflammatory markers, insulin resistance and other metrics that signal the implacable onset of heart disease, diabetes or cancer. Happily, research reveals inexpensive and straightforward solutions that will allow most people to reset their inner clock.

Timing Is Everything

Almost every living thing, from cyanobacteria to lemurs, is attuned to the earth's daily rotation. Evolution has smiled on creatures that capitalize on the planet's day-night dichotomy, matching their internal workings to the shifting conditions of the outside world.

These are the fluctuations known as circadian rhythms (the word "circadian" comes from the Latin for "about a day"). In many animals they dictate the timing of hibernation, courtship and reproduction. Even in plants, circadian rhythms are crucial to survival. In June scientists at the University of Washington found that it is thanks to a circadian gene that the common garden petunia waits until night to release its fragrance, which attracts nocturnal pollinators.

Circadian rhythms also create the ebb and flow of human physiology. They explain why fevers run highest at night, why a late meal can make it hard to sleep, why teenagers are late risers and many other familiar aspects of daily life. And they are grounded in the daily planetary shift between light and darkness.

To align the body with what's going on in the outside world, the suprachiasmatic nucleus, which serves as the brain's master clock and is located deep within the hypothalamus, constantly monitors the intensity of ambient light. Bright light in the morning sets the body clock for the day, and evening darkness nudges organs into their nighttime mode. For example, the drowsiness-inducing hormone melatonin flows, preparing the body for rest. The bladder expands to hold more urine, making it possible to sleep through the night. And the liver makes extra glucose to keep the brain nourished throughout the overnight fast.

But if the master clock encounters bright light at night, it sends "start the day" messages at the time when organs are settling down for the evening. Circadian rhythms get scrambled. This can happen when flying across time zones (and explains why jet lag is worse when traveling east); when people use an iPad, cell phone or laptop at night (because digital screens emit the same blue wavelengths found in morning sunlight); and when people work the wee hours in a brightly lit space or fall asleep with the television on.

Scientists have been investigating circadian rhythms for decades, but until very recently they did not appreciate how critically important these rhythms are to the regulation of nearly every bodily system. "In the last 10 years or so, work on circadian rhythms and human health has really just exploded," says neuroscientist Colleen McClung, whose lab at the University of Pittsburgh investigates the relation between circadian rhythms and mood disorders.

One of the discoveries: by banishing darkness, modern society has ushered in a host of potential health problems. "We are

When physiological rhythms are out of sync, the health impacts can be vast: from diabetes and obesity to cancer, heart problems, infertility and mood disorders.

THE AUTHOR

EMILY LABER-WARREN heads the health and science reporting program at the CUNY Graduate School of Journalism.

all so used to nighttime light exposure that when you tell people it's unnatural, they are, like, 'What? Light?' " says Laura Fonken, a neuroscientist at the University of Colorado Boulder. "People don't think of light exposure the same way they think of something like a drug or a dietary intervention, but really it does have these very profound effects on our physiology."

An even newer revelation: mealtimes may also be critically important to keeping circadian rhythms in balance. Mounting evidence suggests that the body relies not only on light exposure but also on behavioral cues to orient itself in time—sleep, exercise, social interactions and, perhaps most significant, eating.

The latest research by molecular biologist Satchidananda Panda of the Salk Institute for Biological Studies in La Jolla, Calif., and others suggests that the body is designed to take in food during the day and fast at night. Breakfast, like sunlight, seems to serve as a timing cue, alerting the body clock that it is morning. So snacking long after dark may be as disruptive to natural rhythms as staying up late bathed in the illumination of a digital screen.

Off the Clock

Sleep never came easily for Jones, who remembers lying wide awake in bed as a small child, often until 2 A.M. "I grew up believing that I was lazy and undisciplined, but it wasn't like it was fun. I was just lying in bed looking at the clock," she recalls.

Much later she would realize she had inherited from her father a circadian quirk—delayed sleep phase syndrome—that turns people into radical night owls, naturally inclined to stay up until the wee hours and sleep until afternoon. Scientists are learning that there is a genetic basis to people's natural sleep inclinations. About half the population is predisposed to be either early birds or night owls, and the other half fall somewhere in between. These inherited patterns are known as chronotypes. Extreme chronotypes are rare: delayed sleep phase syndrome, for example, affects three in 2,000 people.

When these extreme night owls hew to their natural schedule, as Jones did for years, they can be healthy and well rested. But working the night shift came to feel to her like an intellectual desert. Jones yearned to engage with the world of ideas—to think, to write. In 2003, at age 36, she plunged into academia. Her new schedule went something like this: She went to morning class, came home and napped, went to afternoon class, came home and napped, went to evening class, came home and then, well, stayed up all night because this was the time when she felt most awake. On weekends she would sleep all day to compensate, but the exhaustion and uncomfortable physical symptoms accumulated.

Jones had developed a classic case of what circadian experts call "social jet lag"—lifestyle-induced circadian misalignment that occurs when people pursue professional or personal obligations at the expense of their natural sleep needs. Jones, with her reversed sleep schedule, got social jet lag from daytime exertions, but typically it occurs when people stay up late at night to work or socialize.

Misalignment Made Flesh

Disconnecting from daily rhythms strikes the body at the most basic level: the cell. In 2014 a team led by geneticist John Hogenesch of the University of Pennsylvania made an astounding discovery: Nearly half of all gene activity in mammals is timing-related. Previous estimates had been closer to 15 percent. "This means the circadian clock could be influencing most, if not all, of our physiology and many of our behaviors," Hogenesch says.

Over the course of two days Hogenesch's team removed 12 organs, including the heart, lungs and liver, from a different group of mice every two hours, then analyzed the RNA from those tissue samples to figure out which genes were active in which organs at every hour of day and night. The team learned that organs do not chug along at a steady pace. Instead they are

Tips for Circadian Health

Keeping your bodily systems working in sync for optimal health is not difficult for most people. Mainly, it requires some commonsense daily habits. Try these basic steps:

1 Adjust your light exposure to approximate the natural day-night cycle. Spending time in low light a few hours before bedtime will encourage your body to produce sleep-promoting melatonin. Try to fall asleep in darkness: draw the shades on your bedroom windows and make sure you are not exposed to light from electronic or other digital devices. In the morning, take a walk outside or eat your breakfast near a sunny window.

2 Go to bed and get up at about the same time every day—including on weekends. Sleep regularity is an important way that the body keeps its rhythms.

3 Block blue light in the evening. If you use a laptop or smartphone before bed, get a program such as f.lux (https://justgetflux.com) to eliminate the blue wavelengths emanating from the screen. Morning sunlight is full of blue light, the same spectrum that beams from digital devices, so texting or playing video games in the evening erroneously informs the brain's master clock that the day is just beginning. Other solutions: wear amber sunglasses at night or equip your bedside lamp with a red or amber lightbulb. General Electric and Philips are developing home-lighting systems that automatically shift hue as the day progresses.

4 Front-load your meals earlier in the day and forgo the midnight snack. The custom in some societies of eating the main meal at breakfast or lunch seems to promote a healthy metabolism. A 2013 study at Spanish weight-loss clinics by neuroscientist Frank Scheer of Harvard University and nutritionist Marta Garaulet of the University of Murcia found that people who ate their main meal before 3 P.M. lost more weight than those who ate later even though both groups consumed the same amount of calories.

5 Eat 12 hours on, 12 hours off. A December 2014 study by molecular biologist Satchidananda Panda of the Salk Institute for Biological Studies in La Jolla, Calif., found that consuming all the day's calories in a span of nine to 12 hours prevented weight gain in mice even when the animals ate a high-fat diet. Time-restricted feeding also protected mice against diabetes and other health problems, but the practice has not yet been well investigated in people.

6 Work out regularly but avoid heavy aerobic exercise before bed. Heart rate, blood pressure and core body temperature vary predictably throughout the day, hitting lows in the evening. Revving them when they are meant to be quiet can disrupt sleep and other rhythm-dependent aspects of health.

—*E.L.-W.*

alternately active and quiescent, attending to certain tasks during the day and others at night, with "rush hours" of activity at dawn and dusk.

Another groundbreaking study, published a year earlier, detected the same telltale signs of rhythmic gene activity—in the brain. The work, conducted by the Pritzker Neuropsychiatric Disorders Research Consortium, involved 89 brains taken from people who had donated their bodies to science. Some of the donors had suffered from major depression, others had not. In the healthy brains, as in Hogenesch's mice, hundreds of genes ramped up and slowed down at specific times of day, forming daily patterns so clear and predictable that they could be used to pinpoint time of death for an unmarked sample of brain tissue.

But the brains of depressed people were different. Their gene activity was haphazard and disorganized, lacking these daily patterns. Psychiatrists have long noticed that people with mood disorders tend to have sleep problems and other signs of circadian misalignment. Now here was physical proof that the circadian rhythms of depressed people are weak or nonexistent—circadian misalignment made flesh.

Flipping a Biological Switch

Jones is not sure exactly when her master clock broke. "At first I didn't notice what was going on," she recalls. "Using alarm clocks and getting up for all these classes sort of masked things." But in the summer of 2007, when she let herself sleep at will, she discovered that her body had adopted a 25-hour schedule, with bedtime shifting an hour later each day. This was the textbook "stair-step" pattern that the doctor at the sleep clinic would immediately recognize as non-24.

Non-24 is a common side effect of blindness because damaged eyes do not transmit the necessary light signals to the master clock. But in the rare instances when non-24 affects sighted people, no one knows the cause. Jones suspects that she was genetically vulnerable and that this physical predisposition, combined with three years of social jet lag, pushed her over the edge. "I think that patchwork schedule kind of flipped some biological switch," she says.

That switch most likely was in her brain's master clock. The suprachiasmatic nucleus functions like an orchestra conductor, keeping time so that the individual rhythms of the heart, liver and other organs can coordinate—a bodily state known as en-

GHISLAIN AND MARIE DAVID DE LOSSY *Getty Images*

trainment. When the master clock stops working properly—whether because of a biological defect or because of frequent eating, working or socializing late into the night or at odd hours—internal organs begin operating at different tempos, like instrumentalists in a cacophonous orchestra with no maestro. Illness ensues.

Jones's non-24 got progressively worse. Bedtime became a moving target, shifting randomly around the clock. She could not make plans—not even a coffee date with a friend. "You can't have a life," she says. "You can't even say if you'll be at someone's wedding or funeral." Forcing herself awake at times when her body thought it was the middle of the night only made her sicker—more nauseated, depressed, fatigued—as her internal organs increasingly lost track of one another.

"Honestly, if you ask me, I would prefer to have heart failure than a non-24-hour sleep-wake-cycle disorder," says Robert J. Thomas, a sleep medicine doctor at Beth Israel Deaconess Medical Center in Boston who specializes in circadian disorders. "That's how badly these patients suffer."

In 2009, after three years of living with non-24, Jones developed a sudden case of diabetes so severe that even Brussels sprouts caused her blood sugar to spike, she recalls. The medication regimens for both type 1 and type 2 diabetes failed. Doctors did not know how to help her. Although Jones had other risk factors, including being overweight and a family history, she traces the abrupt onset of diabetes to her circadian disorder—and indeed, when she finally got her non-24 in check four years later, her blood glucose returned practically to normal.

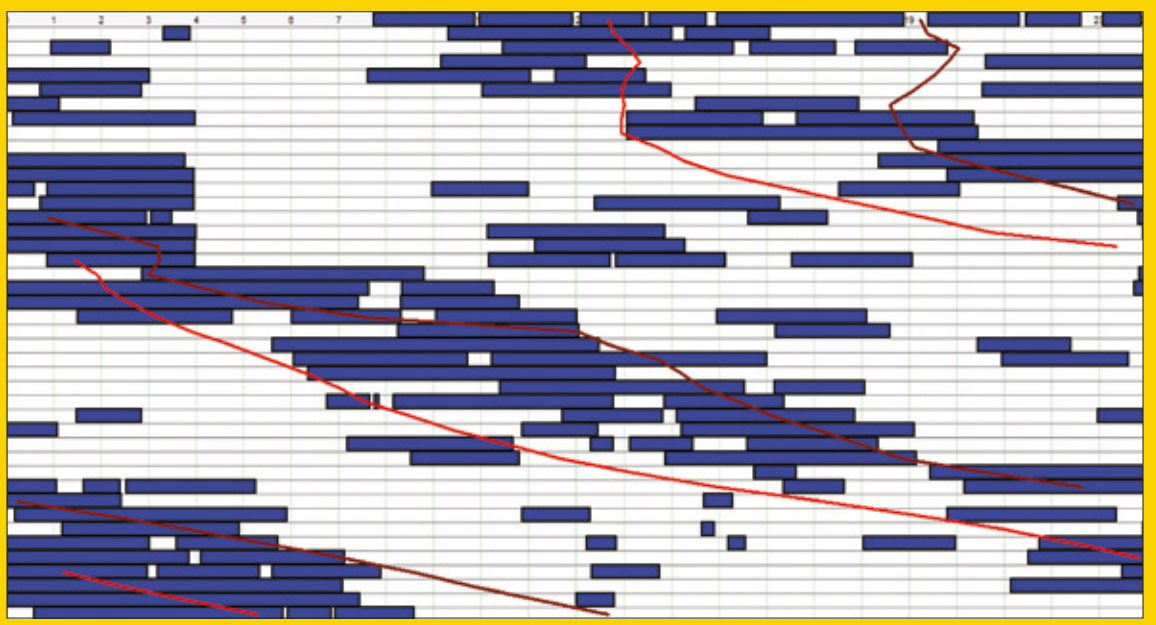
Organs That Cannot Keep Time

Diabetes affects more than 29 million Americans, three times as many as a quarter of a century ago. Experts cite factors ranging from the ubiquity of cheap sugary drinks and snack foods to sedentary habits. But some scientists are starting to suspect that disrupted circadian rhythms may also underlie Americans' mass metabolic dysfunction.

For years, observational studies have shown that people who work nighttime or rotating shifts are susceptible to much higher rates of obesity and diabetes. More recently, scientists have begun to artificially induce circadian misalignment, and here, too, one of the most dramatic changes they see is an increased disposition to weight gain and metabolic problems. In 2009 a team led by Harvard University neuroscientist Frank Scheer kept 10 healthy people in a lab, scrambling their mealtimes and sleep

Off the Charts

Sparrow Rose Jones, who suffers from non-24-hour sleep-wake disorder, uses specialized software to log her sleep. The resulting tables contain a record in which each row covers a day and each column indicates an hour. The blue blocks are hours spent sleeping. Ideally people go to sleep and wake up at roughly the same time each day, and the red lines, which track sleep patterns, will be mostly vertical. Jones's chart, however, is more erratic. For several days (*top of chart*), she forced herself to wake up early each morning to connect to a friend in a different time zone. Later she allowed her body's circadian cycle to shift freely, falling asleep and waking up without any aids or alarms, in an effort to reestablish her body's natural (if erratic) clock before her cross-country road trip.



COURTESY OF SPARROW ROSE JONES (*personal sleep chart*); PIOTR WOZNIAK *SuperMemo World (24-hour sleep-cycle chart template)*

schedules while subjecting them to constant low light. As the participants' inner timekeepers lost track of day and night, their blood pressure, body temperature and hormone production stopped following regular patterns. Most strikingly, levels of leptin, the hormone that alerts people that they have eaten their fill, decreased. People with low leptin levels tend to overeat. In addition, three participants became prediabetic, all in just 10 days' time.

Experiments in animals are yielding equally dramatic results. Multiple labs are finding that when mice are kept in constant light or are forced to eat during their normal resting time, they gain weight—even when they consume the same number of calories. "We're not as good at metabolizing our food when it's not eaten at appropriate times of day," says Erin Zelinski, a Ph.D. candidate in cognitive neuroscience at the University of Lethbridge in Alberta, adding, "You probably don't want to be eating that kebab at 4 A.M."

Circadian disruption leads to cognitive as well as metabolic problems. Alertness and motor coordination decline markedly. "If you look at the frequency of industrial accidents, they peak between two and four in the morning," says University of California, Los Angeles, neuroscientist Christopher S. Colwell. "That's the time when people should not be doing anything that requires vigilance."

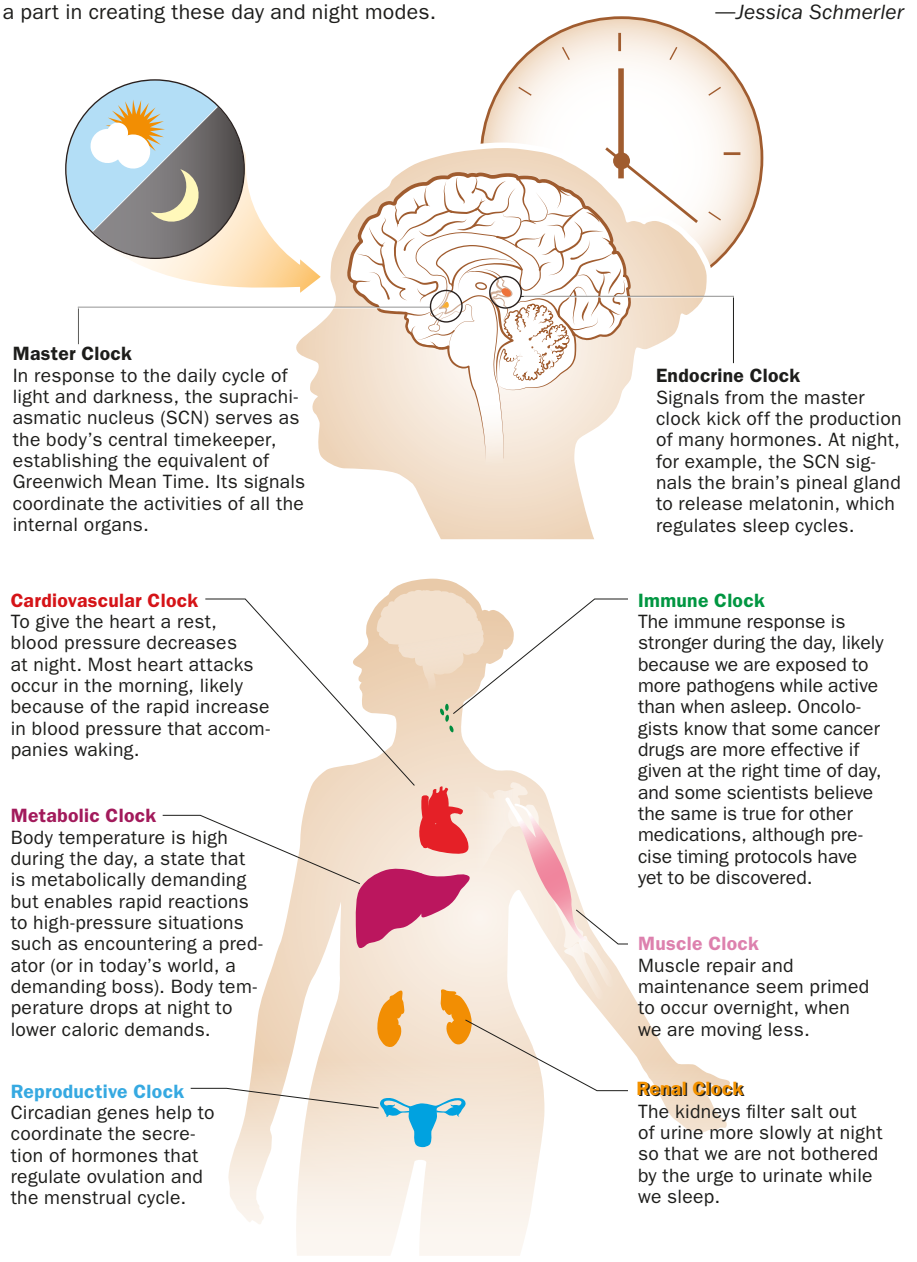
People whose jobs require them to work odd hours also have trouble making agile mental calculations. Emergency room doctors working the night shift showed short-term memory impairments in a 2012 study by David Hostler of the University at Buffalo's Emergency Responder Human Performance Lab and his colleagues.

Animal experiments are confirming that the hippocampus, the part of the brain central to learning and memory, is highly sensitive to circadian disruption. For example, in studies published in 2013 neuroscientist Robert J. McDonald of the University of Lethbridge found that rats with the equivalent of jet lag have trouble remembering what they have learned. Rats with longer-term circadian disruption, the kind that afflicts shift workers, have difficulty learning new tasks as well as recalling them.

Practically every month a new study spotlights circadian misalignment in some other ill. In a study published in April scientists at the University of Warwick in England examined uterine lining cells from 70 women and found a higher frequency of circadian disruption in women who suffer multiple miscarriages—suggesting that misalignment of daily rhythms in the womb hampers the ability of the fertilized egg to implant. Pregnancy

A Symphony of Clocks

Just about every tissue, gland and organ in our body follows a circadian rhythm of activity, taking cues from the master clock in our brain. Hundreds, if not thousands, of genes play a part in creating these day and night modes. —*Jessica Schmerler*



TAMI TOLPA

is all about timing—an able sperm meets a fertile egg just as it is making its way through the fallopian tube—but it turns out that timing also matters at the cellular level.

For unknown reasons, rhythms shift later during adolescence, then return to normal in young adulthood. Psychiatrist Brant Hasler of the University of Pittsburgh has published several recent studies suggesting that the disconnect between high school start times and teens' natural sleep needs compromises brain areas related to reward and self-control, making them more susceptible to getting hooked on drugs and alcohol. New studies also link circadian misalignment to greater risk of post-traumatic stress disorder, breast cancer and inflammatory bowel disease.

The Value of Repetition

Circadian rhythms are old-fashioned. They are conservative. They are your grandmother's medicine. Go to bed at a reasonable hour. Eat a good breakfast. Do not push yourself too hard. Something in our modern spirit rebels against these strictures. We will stay up until 3 A.M. binge-watching *House of Cards* if we feel like it. We will fall in love with people in faraway places and use Skype and cell-phone apps to erase the time differences.

But the need for structure and daily repetition is woven into our DNA. Sunrise and sunset bookended our ancestors' days. "We evolved on a planet that has a roughly 24-hour day, and we are biologically prepared to function better if we are in a regular rhythm," says psychologist Ellen Frank of the University of Pittsburgh.

Most people have a choice, but for Sparrow Rose Jones, something as simple and humdrum as a daily routine seemed totally out of reach. Her body had lost some innate, primal logic and was taking her on an endless fun-house ride. She tried operating on 28-hour days because six of them fit neatly into a week. That did not work. She tried exposing herself to bright light at specific times to nudge her system back toward regularity. That did not work, either. On her sleep doctor's advice, she tried slapping herself and icing her skin to stay awake during daylight hours so that she would sleep consistently at night. She began hallucinating from fatigue.

Jones dropped courses until she was taking only one, and even so she was frequently absent. Colleagues offered advice such as "Just go to bed earlier" or "Drink warm milk"—as if instead of a neurological disorder, she had a mild case of insomnia. In 2012, one course and a dissertation shy of her degree, Jones dropped out.

Giving up on grad school was a blow, but it gave her much needed time to refocus and heal. A fellow non-24 sufferer she had connected with in an online support group suggested three hours of bright artificial light in the morning to jump-start her clock and six blackout hours before bed (during which time, red lightbulbs and light-filtering goggles enabled her to be productive). It was an extreme, comic-book version of what everyone should do to maintain healthy circadian rhythms: get sun in the morning and turn down the lights a couple of hours before bedtime.

It worked. Jones began sleeping regularly from midnight to 5 A.M. At last, her body was on a regular schedule, and her health began to improve.

Circadian "Hygiene"

If Jones deviated even slightly from her newfound regimen, she lost her entrainment. Still, she was discovering that even her extreme misalignment was correctable. And for most people, the solutions are much simpler [*see box on page 35*].

Melatonin supplements improve mood and memory in people with dementia, who suffer from disturbed sleep and other hallmarks of circadian dysfunction. Sitting near a device called a light box to get bright light in the morning is a boon for people with seasonal depression. And forward-thinking nursing home administrators are finding that when they provide varied illumination instead of keeping the lights on 24/7, elderly residents are less disoriented.

> "I would prefer to have heart failure than a non-24-hour sleep-wake-cycle disorder," says sleep medicine doctor Robert J. Thomas.

People with bipolar disorder are especially vulnerable to circadian disruption: pulling an all-nighter or traveling overseas can trigger an episode of mania or depression. Conversely, regularizing routines can stabilize their moods. A therapy developed by Frank asks patients to record daily when they get out of bed, when they first interact with other people, when they begin their daily routine, when they have dinner and go to bed—and then to tweak those times over a period of weeks to establish a schedule they can stick to. "We're looking to keep routines very regular, seven days a week, no shifts on weekends," she explains. The treatment, called interpersonal and social rhythm therapy, has proved effective in two large trials.

Circadian rhythms naturally deteriorate with age—which may account for some of the sleep and memory problems of the elderly. But strengthening circadian rhythms may be a hedge against cognitive decline. In research by McDonald, old hamsters with strong circadian systems outperformed misaligned younger animals on memory tasks.

Changing habits is not easy. But if more people understood the potential long-term benefits to their mood, sleep quality, cardiovascular health, weight-loss goals and mental sharpness, they might make the effort. "We should consider sleep and circadian hygiene just as important as washing our hands," says Colwell, editor of the new book *Circadian Medicine*. "It's really critical for good health and well-being."

Back to Basics

Managing non-24 made it impossible to hold down a job, but Jones has a character, shaped in part by autism, that is fundamentally optimistic and animated by passionate, sustaining interests. After leaving graduate school, she self-published a book of personal essays and a CD of original music. Then she conceived a radical new life plan. Jones decided to give up her apartment in Pocatello, Idaho, and drive cross-country, becoming a modern-day nomad—sleeping in a tent, indulging her love of nature, and visiting train yards, science museums and the graves of famous writers along the way. Her goal: to arrive on the East Coast to meet her love for the first time—the person whose advice helped to stabilize her rhythms and with whom she has developed a long-distance romance. If things work out, she can settle close by; if not, she is mobile.

But Jones had an additional motivation for pulling up stakes—a theory that living outdoors, as our ancestors did for millions of years, experiencing the full force of the sun every day and true darkness at night, might cure her circadian disorder. "It would be pretty sweet if a primal hobo life does automatically what modern medicine struggles to accomplish," she wrote in an e-mail before her May departure. By June, when this article went to press, her rhythms seemed to be naturally and effortlessly stabilizing to a regular 8 A.M. wake-up time—but this progress disappeared whenever she visited friends and slept indoors. "It's a shame that sleeping outdoors is such a radical 'therapy' that few will be able to replicate it," she wrote, "because I am overjoyed with how well it is working for me."

There is a lesson here for the rest of us, with our overextended, brightly lit, Starbucks-fueled lives. Modernity has made it possible to stretch beyond the confines of the 24-hour day, but in the process we have become untethered from the fundamental pulse of our planet. Science is revealing that we do so at our own risk. **M**

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THE UPSIDE OF VULNERABILITY

Children who are the most susceptible to adversity have a secret strength: they benefit more than other kids from supportive interventions. Should policy makers target them ahead of everyone else?

By Jay Belsky

ILLUSTRATIONS BY JON REINFURT

Most of us know the story of Achilles, the Greek warrior whose mother tried to protect him from an early death by submerging him in the magical waters of the river Styx. Despite her best efforts, she missed dunking one heel that she gripped as she dipped him upside down in the river. And as fate would have it, a poison arrow to this single weak spot led to Achilles' demise. By most accounts, he was still a very young man.

The myth reflects the way we tend to think about vulnerability—as a fixed liability almost destined to play out badly in battle or under other kinds of stress. But imagine if we could pen an alternative ending to this tragedy. Imagine that Achilles never went to war and that his famous heel ultimately became a source of strength. Consider, for example, a version of the story in which his exposed heel made him a superfast runner in the warm glow of the sun. Such a rewrite reflects what we are beginning to learn about how so-called environmentally sensitive children—considered fragile in the face of many kinds of adversity—can excel under more favorable circumstances.

The fact is that most kids, even some of the least fortunate in society, show a remarkable psychological resilience to life's misfortunes. Swedish folklore describes them as "dandelion children," able to put down

roots and survive in the rockiest soil. But other little people—the environmentally sensitive ones—are especially vulnerable to the ill effects of hardship. Countless studies reveal that when these kids grow up poor, are in troubled families, or are mistreated, discriminated against or neglected, they run a far greater risk of developing a host of mental health and behavioral problems, compared with the rest of the population. For this reason, many scholars refer to them as "orchid children," prone to wither in harsh conditions.

In recent years evidence has been mounting in support of something rather unexpected: what makes these orchid kids so susceptible to negative environmental influences—as far as we know, a mix of different behavioral and biological traits—also renders them the most likely to benefit from extra support and nurturing. With a little greenhouse care, they thrive—so much so that they even outperform their less sensitive peers. Meanwhile the attributes that foster resilience in the dandelions, such that they do not readily succumb to setbacks, also appear to make them less responsive to various kinds of enrichment.

This differential susceptibility, as I refer to it, to both good and bad environments raises tough questions for parents, policy makers, teachers and concerned citizens alike. Should we seek to identify the most impressionable children and disproportionately target them when it comes to investing our attention and scarce intervention and service dollars? Is this the best approach to promote well-being and prevent future difficulties? I believe the answer may be yes. First, we need to be able to distinguish these rare blooms from the more resilient majority. And that will not be easy. No one characteristic defines them, but we do know that many seem to start off in life as difficult babies, and increasingly we are able to identify them using a range of genetic markers.

For Better and for Worse

Some children are just more demanding to raise: as infants, they fuss a lot, have trouble sleeping and are easily upset by new situations. Decades of research have demonstrated that if these irritable infants face early struggles—perhaps in the form of harsh discipline or insensitive parenting—they are more likely than other babies to become aggressive, depressed, anxious or disobedient as older children and teens. The less well-known flip side of the coin is this: when such challenging kids are reared in supportive or even neutral conditions, they can blossom both socially and emotionally. They thus wind up at the very top or bottom of the pile depending on the overall tenor of experiences in their formative years.

This "for better *and* for worse" pattern is emerging in a growing number of investigations. In 2009 Michael Pluess, then my graduate student and now at Queen Mary, University of London, and I first discovered it when we analyzed data from the Study of Early Child Care and Youth Development, initiated by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD). Between 1991 and 2007 this large research project followed some 1,300 children in 10 U.S. cities from birth to age 15. In our evaluation, we focused on 968 of these kids, about whom the researchers had collected a wealth of data from birth to age five. When the children were babies, they tested their temperaments. When they were toddlers, they recorded how sensitive and stimulating their care was at home, at day care and in preschool. And later on, when these kids started elementary school, they asked their teachers to appraise their behavior.

Our results revealed something interesting. Contrary to what many people might expect, the five-year-olds who had received the best early care did not always wind up among the best behaved, according to their teachers, who knew nothing about the children's backgrounds. Instead, just as Pluess and I had anticipated, only the temperamental infants, when well cared for, reliably matured into model kindergarteners. When these more irritable babies received poor care, they typically became the most aggressive and disobedient in class.

A few years later psychologist Jude Cassidy of the University of Maryland and her colleagues found something similar. They conducted a more rigorous experimental test of the effects of parenting on newborns who were easily distressed. This team randomly assigned 220 poor mothers to either the Circle of Security intervention program or a control group. The intervention taught skilled parenting techniques to promote secure infant-mother attachments, whereas sessions for the control group focused on common concerns for new parents, such as sleeping and feeding. Mothers participating in the intervention did indeed become more adept caregivers. But their more attentive ways only resulted in more secure children if, before the training, the researchers had rated their babies as being particularly irritable. For the less fussy lot, parenting ability held far less sway.

Why might sensitive, responsive care make such a large difference in the development of temperamental children—and have less of an impact on everyone else? I believe that the hallmark tendencies of difficult kids—to be negative emotionally, inflexible and sometimes more active—all suggest that they possess especially delicate nervous systems on which all experiences, both good and bad, register with real force. Some of this sensitivity may develop via the body's stress response. For

FAST FACTS

SPOTTING POTENTIAL

1. Some children are especially susceptible to early environmental influences. These sensitive kids become the most aggressive, depressed, anxious or disobedient of all children if they face adversity growing up.
2. Increasing numbers of studies demonstrate that when these environmentally sensitive kids receive adequate support and the enrichment they need, they can excel beyond their more resilient classmates.
3. With such high stakes, some scientists want to be able to use genetic markers to identify these children and then target them with effective intervention programs.

example, research shows that when a pregnant woman suffers extreme stress—perhaps as a result of actual or threatened violence—it forecasts greater negativity and physiological reactivity in her infant. These babies cry more and are more readily startled. Flooded with higher levels of the stress hormone cortisol in the womb, they emerge primed to mount stronger fight-or-flight responses to any kind of crisis.

But there are other mechanisms at work, which may or may not have anything to do with how the body handles pressure. Some kids may pay closer attention to their surroundings, analyzing information at a deeper level and thus being more affected by it. Some may have more reactive amygdalae, brain structures responsible for processing emotion; they could therefore experience feelings more acutely. Others might be more sensitive to punishment, thanks to underlying differences in their serotonin neurotransmitter system, which is involved in regulating mood. And some kids might also, or instead, react more intensely to rewards because of variations in how their dopamine neurotransmitter system works.

Vulnerability vs. Possibility

Many of these differences reflect a child's DNA, and in fact researchers have tied environmental sensitivity to several genes, including the serotonin transporter gene *5-HTTLPR,* a dopamine receptor gene, *DRD4,* and genes encoding for brain-derived neurotrophic factor, a protein that aids in the growth of new neurons. Variations in individual genes go a long way toward explaining why some children are affected more than others by their experiences growing up. Recent epigenetic studies even indicate that whether genes are turned on or off in response to particular environmental exposures can vary dramatically from one person to the next.

So far scientists have primarily examined genetic variations thought to be linked to psychiatric conditions, which are typically viewed as conferring serious lifetime risks. But newer work suggests that these genotypes are not just potential liabilities. They seem to demarcate greater and lesser plasticity, allowing for a wider range of possible behaviors and developmental outcomes. As in our rewrite of Achilles' destiny, these so-called vulnerability genes can be assets.

Difficult babies may possess delicate nervous systems that register both good and bad experiences with real force.

Consider what are known as short alleles of *5-HTTLPR,* a genetic variation associated with depression. In 2014 developmental psychologist Grazyna Kochanska of the University of Iowa and her colleagues found that with positive parenting, carriers appeared to be the least likely to succumb to future substance abuse. The team monitored interactions

Teens with short *5-HTTLPR* alleles also showed the greatest capacity for good behavior in a 2011 study led by psychologist Gene H. Brody of the University of Georgia. He and his colleagues genotyped 461 African-American adolescents in Georgia and interviewed them between the ages of 15 and 17 about their perceptions of racial bias. Again, out of everyone they evaluated, the boys carrying either one or two short versions of *5-HTTLPR*—inherited from one or both parents—displayed the least antisocial behavior and aggression if they had experienced very little discrimination in their lives. Male carriers had the most conduct problems, however, if they reported perceiving a lot prejudice. (Why the girls did not follow this pattern remains unclear.)

Similar results are coming in for carriers of a long form of *DRD4*, regarded as a "risk allele" for its supposed connection to attention-deficit/hyperactivity disorder. In 2008 developmental scientist Marian J. Bakermans-Kranenburg of Leiden University in the Netherlands and her co-workers recruited 157 toddlers exhibiting behavioral problems—whining, biting, violent tantrums—and coached their mothers to use more sensitive disciplining techniques, including time-outs and praising good behaviors. Among the kids who possessed at least one copy of the long *DRD4* allele, the intervention dramatically curtailed both aggression and disobedience. And this result was even more pronounced when the investigators restricted their focus to the mothers who gained the most from the training. Were these more responsive mothers also carriers of the long *DRD4* allele? It certainly seems possible because their highly responsive, long allele–carrying children would have had to inherit it from at least one parent.

If we could one day single out environmentally sensitive kids, should we give them more enrichment than everyone else?

A more recent study also showcases the potential upside for long *DRD4* allele carriers when they receive good parenting. Between 2004 and 2010 Brody and fellow University of Georgia psychologist Steven R. H. Beach ran an intervention called Adults in the Making (AIM), in which nearly 300 rural African-American youths and their families—some of whom were part of the *5-HTTLPR* study mentioned earlier—attended six consecutive weekly group meetings. Parents learned how to provide emotional support and encourage responsible decision making, and kids learned how to plan for the future. When Brody, Beach and their colleagues later analyzed the results, they found that AIM proved most successful in countering substance abuse for teens with *DRD4* long alleles. About two years after the program ended, the long allele–carrying kids who participated in the classes were still the least likely of all the subjects to drink or take recreational drugs.

between parents and kids, ages two to 10, in 100 families and then asked the children how they felt about drug use. The 10-year-olds with at least one short copy of *5-HTTLPR* who also scored high on a measure of anger, used to gauge temperament, had the most antidrug attitudes of all the children in the study, provided they had been parented well. In keeping with the for better and for worse pattern, though, they were the most open to experimentation after more problematic parenting. For kids carrying only long alleles of *5-HTTLPR*, there was no clear relation between their parenting and their views on drug use.

THE AUTHOR

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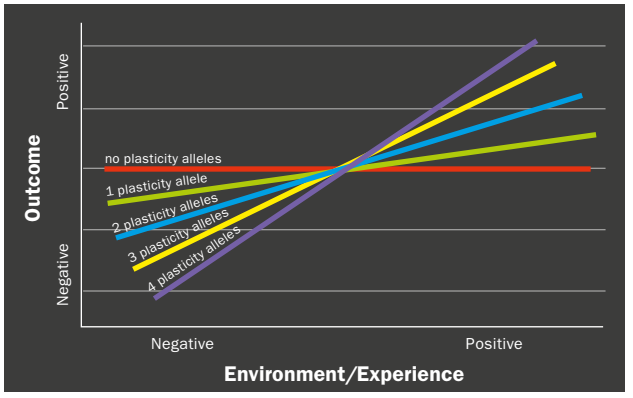
Establishing a Yardstick

Of course, we will never be able to identify environmentally sensitive children by looking at only one or another "candidate" gene. There are likely scores of genes involved, well beyond the few described here. Thus, to try to capture a snapshot of individual degrees of susceptibility, scientists are increasingly creating measures called polygenic scores or indices. These genetic yardsticks assign scores to children that reflect the presence or absence of multiple plasticity alleles. So far the results are encouraging.



Research suggests certain genetic variants, or alleles, are associated with greater environmental sensitivity. The more of them a child has, the more he or she is influenced by the quality of parenting and other factors—for better and for worse. In this model, those with four alleles (*purple*) have the widest range of outcomes. Kids with none (*red*) are less susceptible to influence.

In their AIM analysis, Brody and Beach created a polygenic plasticity index that included *DRD4* and two additional genes. They discovered that the program's benefits—that is, decreases in drug and alcohol use—were greatest for those scoring highest on the index. And consistent with for better and for worse thinking, kids scoring just as high but in a control group actually drank the most alcohol. My colleagues and I designed another index, based on five genes, to evaluate 1,586 adolescents in the NICHD-funded Add Health project, the largest longitudinal study of adolescent health ever undertaken. We, too, found the higher the polygenic score, the more strongly parenting styles predicted self-control, at least among boys.

And recent work published in 2014 by April S. Masarik of the University of California, Davis, and her co-workers also used five genes to measure environmental sensitivity. Among their highest scorers, those with the most successful romantic relationships as adults enjoyed the most engaged parents as teens; those with the worst romances had experienced more hostile caregiving.

So let us imagine that one day in the not too distant future, even broader indices make it possible to confidently single out and assign relative scores to environmentally sensitive children. Should we selectively give the children above a certain cutoff extra nurturing and enrichment to ensure that they reach their full potential? Do we exclude the kids less likely to see any gains? I have discussed the idea with many friends and colleagues and know that those who value equity over efficacy object to the notion of treating children differently based on temperament or genetic makeup.

But many existing initiatives—for example, the government's Head Start program, launched more than half a century ago to provide early education to three- and four-year-olds from low-income families—receive lukewarm reviews at best. Advocates tend to exaggerate the positive findings, and critics emphasize the negative ones. These costly programs would probably show more consistently positive results if they especially targeted the subset of children highly sensitive to environmental influences. If we could identify those children, why shouldn't we? What is ethical, after all, about providing services, using taxpayers' money, to kids who will not be helped by them? Would we ever dispense an expensive medicine indiscriminately if we knew it would aid only some people, especially if in doing so, it meant possibly failing to provide the treatment to those most likely to get well?

Let me say clearly that even if we can eventually pinpoint the most responsive children, it would not mean abandoning the rest. Every child deserves a decent quality of life, no matter the long-term consequences—or lack thereof. Furthermore, money saved by restricting interventions to those most likely to benefit from them should be used to explore different and conceivably radical new programs for everyone else. After all, we do not know if the children who seem unmoved by our current initiatives would be similarly unaffected by a different approach. Our ultimate goal should not be to save money but to direct our resources more wisely. M

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A host of psychological pitfalls prevent most diets from succeeding long term, but there is a proved and sustainable way to lose weight

DON'T DIET!

By Charlotte N. Markey

My friend Ann (not her real name) recently tried the Paleo diet. She stopped eating dairy, grains, refined sugars and processed foods. Six weeks in, Ann had lost 15 pounds. But in that time, she had skipped happy hours, girls' nights out, office parties—really any occasion that might have put her in arm's reach of temptation.

Ann missed her old life. She soon slid into her prediet habits and quickly gained back the pounds, plus a few more—a familiar experience for her. Ann has lost weight on many diets, but she can never maintain the regimen for long. After she quits, the scale, like a pendulum, always swings back up.

Her predicament is not unusual. At any given time, at least one in five American adults reports being on a diet, but the majority don't keep the weight off. A huge amount of scientific evidence tells us that dieting does not promote lasting weight loss. In fact, many dieters end up gaining back more weight after they quit.

When I say "diet," I am referring to eating regimens that require cutting portions, severely restricting calories, or eliminating entire food groups: carbs, fats, sweets, whatever. Despite such deprivations, diets remain alluring because they offer a clear and quick prescription dictating what you *should* and *should not* eat. These tactics are meant to tame erratic eating behaviors and revise poor food choices. But the truth is that such strategies hardly ever work because they are too extreme and thus almost impossible to maintain over the long term.

My advice as a psychologist and researcher who focuses on weight control: Do not diet. Do not cut out groups of foods or count calories. Do not try to eat very little or deprive yourself. Such strategies backfire because of psychological effects that every dieter is all too familiar with: intense cravings for foods you have eliminated, bingeing on junk food after falling off the wagon, an intense preoccupation with food. A growing body of research shows why these tendencies undermine most people's diet efforts and confirms that the way around these pitfalls is moderation. Making small changes to your eating patterns, ones you can build on slowly over time, is truly the best pathway to lasting weight loss. Although you may have heard this message of moderation before, the evidence is finally too overwhelming to ignore.

Effective weight management is particularly important when we consider that two thirds of Americans older than 20 are overweight or obese. With the rise in obesity rates and related health problems, such as diabetes and heart disease—both of which

! Don't deprive yourself.

Eating very little is hard to sustain, and when you slip up, studies show, you will probably massively overeat as a rebound effect.

FAST FACTS

THE MAGIC OF MODERATION

1. Diets fail for most people who try them, according to much research.
2. Psychological studies reveal that diets cause mental fatigue, create cravings for forbidden treats and set people up to binge when they fall off the wagon.
3. An overwhelming body of work now shows that a more moderate approach is the best way to achieve lasting weight loss and health.
4. By making small changes to your routine, one at a time, you can create a healthy lifestyle that you enjoy and can sustain over the long term.

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are leading causes of death in the U.S.—it has become even more critical for us all to approach weight loss armed with a keen understanding of what really works and what doesn't. Let's start with what doesn't.

Why Typical Diets Fail

The "what the hell effect": Studies have consistently revealed that dieting usually leads to weight gain, not weight loss. In a 2013 review published online in *Frontiers in Psychology*, investigators reported that 15 of 20 studies showed that dieting predicted weight gain in adolescents and adults of normal weight.

One problem with diets is that once you give into temptation after restricting yourself, you are more likely to binge. This tendency, which psychologists dub the "what the hell effect," undermines attempts to lose weight. A 2010 study by psychologists at the University of Toronto demonstrated this effect in people who believed they had broken their diet. In the study, 106 female students—some of whom were dieting and some of whom were not—all received identical slices of pizza. Some of the students saw a person carrying another slice that was either bigger or smaller than the one they got, and others did not see another slice. After they ate the pizza, the participants were asked to taste-test a range of cookies. Women who weren't dieting and dieters who thought they had eaten a smaller than usual slice or who didn't see a comparison slice ate a small amount of cookies. But dieters who thought they had violated their diet by eating a bigger slice ate more cookies than everyone else.

The researchers suggest that these women believed they had already blown their diet—so what the hell, might as well pig out on cookies. This study and many others like it confirm that violating or even thinking you have gone off your diet is enough to abandon self-control.

Ironic processing: Some diets promise you'll avoid feelings of deprivation by letting you eat as much as you want of certain food groups while totally eliminating others. The trouble is that when you eliminate your favorite foods—a requirement of most weight-loss regimens—you develop a deeper longing for them. Vow to avoid pasta, and you will soon find yourself dreaming about spaghetti.

Food preoccupation is an inevitable result of dieting. Psychologists call this phenomenon "ironic processing"—suppressing a thought makes it more salient. It became famous when the late social psychologist Daniel M. Wegner did a series of experiments—the white bear studies—in which he asked subjects to avoid all thoughts of a white bear. Guess what creature relentlessly prowled through their minds!

Many studies over the years have shown that people who try to eliminate food groups end up craving those foods intensely. One published this year confirms that finding and adds to mounting evidence that not only do people crave the forbidden food, they eat more of it when they get a chance. The study compared eating patterns in 23 normal-weight nondieters who restricted their intake of palatable foods, such as doughnuts and ice cream, and 23 similar people who merely recorded their snack intake. The researchers found that participants who restricted themselves reported craving and eating more treats, whereas those who simply monitored their snacks did not. This growing line of research suggests that for most, eliminating foods entirely will backfire badly.

In fact, treating yourself to indulgences may help you avoid the pitfalls of craving and overeating forbidden foods. In a 2012 study, 144 obese men and women were put on a strict, low-calorie diet for

! Don't count calories.

The mental effort required to count calories soon leads to burnout, fatigue and resentment, according to research.

Dieters who thought they had violated their diet by eating a bigger slice of pizza than the others ended up eating more cookies than everyone else.

16 weeks. About half ate a regular breakfast—300 calories—and the rest consumed a larger breakfast—600 calories—which included something sweet, such as a doughnut or chocolate (and ate less at dinner to make up for it). In the second half of the study, participants tried to maintain their meal plans on their own for 16 more weeks. The participants kept food diaries and continued to receive counseling from a dietitian.

Studies that examine mental energy reveal that dieters have more difficulty learning new information, solving problems and exerting self-control than nondieters do.

After the initial 16 weeks of close monitoring, the small breakfast group had lost a few more pounds than the large breakfast group (33 versus 30 pounds). But in the self-maintenance 16-week period, the small breakfast group regained 25 pounds, whereas the large breakfast group continued to shrink, dropping 15 additional pounds. Notably the small breakfast group reported increased cravings for sweets, fats and fast foods at the end of the study, whereas the large breakfast group reported reduced cravings in each category. Although eating dessert for breakfast is not necessarily the fastest or healthiest route to weight loss, these findings demonstrate that it is possible to have your cake and lose weight, too.

Mental fatigue: Although efforts to change your eating behaviors require attention and record keeping, especially at the beginning, focusing too much energy on what you eat reduces your ability to do other, potentially more important things. Studies that examine the mental energy available to dieters versus nondieters consistently reveal that dieters have more difficulty learning new information, solving problems and exerting self-control.

Overthinking your food choices may also have deleterious consequences for your mental health. A 2010 study in *Appetite* looked at the mental toll of eating chocolate among dieters and nondieters. The nondieters were not particularly distracted by this indulgence, but the dieters could no longer think clearly, becoming consumed with thoughts, such as "Why did I eat that?" and "What should I eat later today to make up for eating that?'

Another experiment published in 2010 found that women who restricted their caloric intake and recorded what they ate exhibited elevated cortisol levels, a marker of biological stress. Even women who simply monitored their meals without trying to restrict calories reported feeling more stressed, and they ended up gaining weight. The bottom line is, for most people, that diets not only backfire, they also take a heavy toll on our physical and mental well-being.

What You *Should* Do

Start with your head: If you want to improve your body, you must also improve your mind-set. Decades of research show that individuals who are dissatisfied with their bodies are less successful at losing weight. Studies also show that it is possible for anyone to learn to feel good about his or her body.

In a 2014 study, women with eating disorders, including some who binged or who were overweight, received compassion-focused therapy—an approach aimed at reducing feelings of shame and improving self-esteem. Over the 12-week treatment, women who exhibited greater improvements in self-compassion and reductions in body shame were also more likely to develop better eating habits.

One simple way to improve your self-esteem, according to many findings, is to write positive affirmations on a regular basis. Happiness research has consistently shown that focusing on what you *do* like—"I have nice eyes"—and on health rather than appearance-related goals—"I want to run a 5K this year"—can help you develop a healthier mind-set and self-image.

! DON'T cut out entire groups of foods.

As soon as a food is forbidden, cravings for it go through the roof. Dieters who try this strategy end up eating even more taboo treats.

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Simple, slow and steady: When setting a weight loss goal, it is natural to want to accomplish it immediately. Yesterday! But to maintain a more svelte figure, you need to make gradual, sustainable changes to your diet: for example, drinking less alcohol and juice, substituting diet soda or seltzer for regular soda, and eating dessert on four nights a week instead of seven. Making even small changes such as these may sound like a "diet," which I have told you to avoid, but it is not, for one important reason: this slow, steady approach allows you to adjust to a new routine at your own pace without the intense effort and denial that typical diet plans require. Most people trying to lose five to 50 pounds will benefit from this slow-to-moderate approach to weight loss, but it is important to note that individuals whose health is at serious risk because of obesity will likely need more drastic measures and should consult a physician.

! DO find a few healthy meals that you like and can cycle through.

Creating an enjoyable routine that does not require much thought is a crucial first step on the road to long-term change.

A large body of research supports the idea that making simple, gradual changes to your eating patterns is the best way to promote lasting weight loss. Robust evidence for this approach comes from a 2008 study, which demonstrated that overweight and obese adults who made very modest changes to their daily calorie intake and physical activity levels lost four times more weight than those following regimens that involved more extreme calorie restriction. The moderate group lost 10 pounds in one month, and they sustained the weight loss over the next three months.

In support of this approach, a 2015 study published in *PLOS ONE* found that women who successfully modified their diet and exercise habits over time set small, achievable behavior change goals, had realistic expectations about their weight loss and were internally motivated to lose weight. The women who relapsed or failed to change their habits tended to have unrealistic expectations, lower motivation and self-confidence, and less satisfaction with their progress.

Some of the most compelling data on effective weight-loss strategies comes from the National Weight Control Registry (NWCR), which surveyed more than 4,000 people who lost at least 30 pounds and kept it off for at least a year. The best tactics, according to the seminal 2006 report, included self-monitoring, such as limiting certain foods, keeping track of portion sizes and calories, planning meals and incorporating exercise into the daily routine.

Such advice may appear to conflict with the research I described earlier on the pitfalls of restriction and mental fatigue, but the truth is, to lose weight, it is important to find the right balance. For instance, before making changes to your diet, you need to understand your current eating patterns, which may require considerable thought and attention. Most overweight individuals, when they are not trying to diet, tend to eat erratically—consuming junk food, snacking a lot and indulging cravings on a whim. Becoming aware of these habits, the good and bad, will allow you to tailor them.

As you begin to make small tweaks to your daily eating, start to plan a few meals you like that you can cycle through on a regular basis, so you don't have to think too hard about what you're going to eat every day. According to the NWCR data, people who plan their meals are 1.5 times more likely to maintain their weight loss. The NWCR data also show that limiting the variety of foods you eat can help you sustain your weight. You don't have to eat the same foods every day, but generally reducing the array of options makes grocery shopping less stressful.

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CORBIS

Weighing In on Popular Diets

The small, moderate changes I recommend in this article are the best way to lose weight over the long term, but the allure of popular diets remains strong. A small percentage of people do find long-term success on these diets, so it is hard to discount such strategies entirely—although the evidence suggests that a moderate approach will give you better odds of meeting your goals. Here's the lowdown on a few popular diets:

PALEO

THE PLAN: Based on the premise that we'd be better off eating as our hunter-gather ancestors did, the Paleo diet prescribes a diet of veggies, fruits, meat and nuts; it eliminates dairy, whole grains, refined sugars, processed foods and legumes.

THE SKINNY: Our current food environment is not compatible with that of our ancestors. Eating as the Paleo diet dictates is unrealistic long term because it is so restrictive, making an enjoyable social life almost impossible. Cutting out so many food groups leads to distressing cravings for most people, too.

ATKINS

THE PLAN: The diet calls for high quantities of protein and very limited carbohydrate and sugar intake. Doing this increases our ability to burn fat.

THE SKINNY: Many studies show that this strategy works well for weight loss in the short term, but most people end up gaining back the weight over time. Such results are a good example of how extreme restriction tends to backfire.

5:2 FAST DIET

THE PLAN: Eat normally for five days a week and fast for two, with women allowed 500 calories and men allowed 600 on fast days.

THE SKINNY: The 5:2 diet has received a lot of recent attention. Preliminary evidence in humans and in mice suggests that it may aid weight loss, but the jury is still out. The main problem is that 500 or 600 calories will likely leave you unsatisfied at the end of the day. If you're hungry, you're going to crave food, especially energy-dense treats, more so than if you ate moderately. Once you give into your hunger, the "what the hell effect" will likely set in.

WEIGHT WATCHERS

THE PLAN: Weight Watchers emphasizes making healthy and sustainable lifestyle changes by consuming balanced meals. The plan highlights fruits and vegetables, and the meals can be tailored to an individual's likes. No foods are off-limits.

THE SKINNY: Weight Watchers does a lot of things right. From a nutritional and psychological standpoint, the recommendations to enlist peer support and not to eliminate particular food groups agree with the advice I offer. Some people, however, may find the cost prohibitive—there are registration and weekly fees—and research suggests that weekly weigh-ins can be counterproductive, making some dieters distraught if the scale doesn't match their expectations. *—C.N.M.*

Work it out: We all know by now that exercise is essential for all-around health. Yet study after study shows that working out is not terribly effective for weight loss on its own. When combined with better eating habits, however, exercise appears to help people slim down. A 2012 study looked at the effects of diet or exercise, or both or neither, in a group of overweight or obese postmenopausal women. Dieters could consume between 1,200 to 2,000 calories a day, depending on their initial weight, and exercisers ramped up to 45 minutes or more of cardio five days a week. After 12 months, those in the combined diet and exercise group lost the most weight—about 19.5 pounds—although the diet-only group was not far behind, losing 15.8 pounds. Those who only exercised lost 4.4 pounds, and the control group, who didn't exercise

! DO make small changes, one at a time.

By waiting until a healthy choice feels like a habit before adding another, you can avoid the mental fatigue that dooms most diets.

CAROLINE VON TUEMPLING *Getty Images*

or eat differently, lost 1.5 pounds over the year.

Once your goal weight is achieved, exercise may be crucial for keeping the scale steady. Most people who have slimmed down report that routine physical activity is an important part of their maintenance regimen. Exercise has many physiological benefits; it even appears to moderate the brain's reaction to pleasurable foods. In a small 2012 study, overweight or obese participants underwent an initial brain scan while looking at images of food. Then they were put on a six-month exercise regimen. At six months, the exercisers showed decreased activity in the insula, which regulates emotions, in response to images of palatable treats. They did not, however, report changes in dietary restraint, food cravings or hunger, suggesting that the neural effects are subtle—perhaps helpful during weight maintenance but not strong enough to induce weight loss.

After six months of exercise, overweight participants showed decreased activity in the insula, which regulates emotions, in response to treats.

! DO focus on what you like about your body.

Research shows that people with a positive body image are more successful at getting and staying fit.

Incorporating exercise into your life should be a gradual process. You don't have to run marathons to reap psychological and physical rewards. Going for a lunchtime walk or biking to work is a way to integrate activity into your daily routine. You can also increase your movements in small ways by taking the stairs instead of riding the elevator or washing your car instead of driving through the car wash. Being disciplined is important, but making exercise fun and sustainable is also essential.

Don't do it alone: Receiving social support is key to losing weight. Consulting a physician or nutritionist is one way to elicit support and provide greater accountability. Research also demonstrates the role romantic partners play in encouraging weight loss. In my work, I have found that men are better able to adopt and stick with healthier eating habits when they receive support and encouragement from their spouse. Similarly, friends, co-workers and online weight-loss buddies can keep you on track by offering inspiration, praise and partners in crime. More systematic help has been shown to be useful, too, such as becoming a member of Weight Watchers or other support groups or participating in the community of users of smartphone apps such as MyFitnessPal, Lose It! or SmartenFit (the last of which I co-developed).

After decades of diet studies, we can no longer ignore the fact that the preponderance of evidence points toward these small, sustainable steps as the best way to lose weight. That message may not be as sexy or exciting as the latest fad diet, but the science is clear: moderation leads to changes that will last for the rest of your life. Creating good habits takes time, patience and resolve, and you will inevitably encounter setbacks along the way. But the key is to never give up—and in a few short months, you may find yourself on the road to the body and active way of life you've always dreamed about. **M**

GETTY IMAGES

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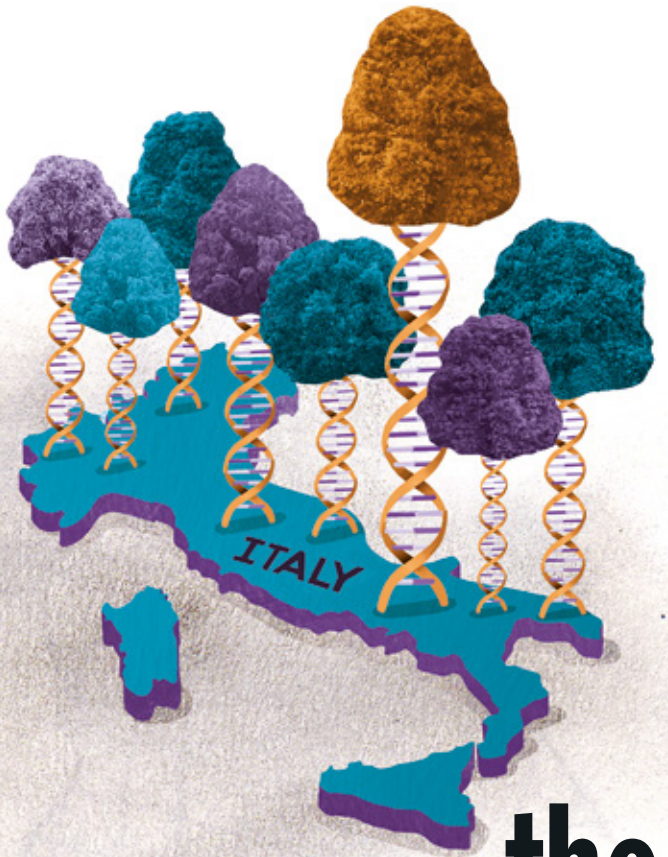
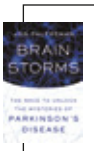


Cracking the Parkinson's Puzzle

By investigating clues from a large clan of sufferers from Italy, scientists uncovered a key to understanding the disease

By Jon Palfreman

ILLUSTRATIONS BY PHIL WRIGGLESWORTH



Adapted from *Brain Storms: The Race to Unlock the Mysteries of Parkinson's Disease,* by Jon Palfreman, by arrangement with Scientific American/Farrar, Straus and Giroux, LLC (US), HarperCollins (Canada), Rider (UK), Uitgeverij Balans (Netherlands) and Beltz Verlagsgruppe (Germany).

It all began with a routine office visit.

In the spring of 1986 neurologist Larry Golbe conducted a clinical examination of a 48-year-old New Jersey fire chief named David. Golbe observed that the patient's movements were slow and restrained. During a finger-tapping exercise—a common way to detect abnormal movements—the chief quickly ran out of energy. When he stood up, this once athletic man now bent forward, with a stooped gait. When he walked, he didn't swing his arms but shuffled along with small steps. When Golbe tried to bend David's arms and legs at the elbow and the knee, he was met with resistance. David's face was expressionless, and he never blinked.

Golbe, who works at what is now the Rutgers Robert Wood Johnson Medical School, flipped through his patient's medical history. Ten years earlier David had been diagnosed with Parkinson's disease. Initially he was treated with Sinemet, a drug frequently prescribed to replace some of the dopamine depleted in the brain over the course of the illness. As Parkinson's progresses, patients lose the neurons that produce this critical neurotransmitter, notably in the substantia nigra—a tiny structure in the midbrain named for its dark pigment. The color there disappears as the dopamine cells die off. Less and less dopamine then travels to the neighboring striatum, where the elaborate orchestration between the brain and muscles takes place. And as this communication breaks down, it leads to the disease's classic motor symptoms—all of which David now exhibited.

For a while, the chief had responded to Sinemet. But over time the medicine became less effective, as is often the case. Golbe enrolled David in a study that he was conducting of selegiline, a newer medication that neuroscientists hoped would boost patients' dopamine levels by blocking the enzymes that break it down. But so far David had reported only minor benefits. Golbe—a dedicated, compassionate clinician whose own father had contracted Parkinson's—unfortunately had little else to offer. So he spent a few minutes counseling David and made a follow-up appointment for three months later. That was the last Golbe saw of him. A few weeks after their meeting, David tragically drowned in a swimming pool.

After the funeral, David's brother, Frank, came to see Golbe, concerned that he also might have Parkinson's. He did—and the diagnosis piqued Golbe's interest. He initiated a broad search for others in their family who might be affected and eventually unearthed a total of six relatives with typical parkinsonian symptoms. During his examinations of these family members, Golbe recalls that the patients told him "the family originated in Contursi, Italy." He didn't know at the time if this was significant or not. But several months after David's death, Golbe got a visit from a Staten Island woman, named Joyce, with classic Parkinson's. She, too, was of Italian descent. Specifically, she told Golbe, she came from a small village in southern Italy: a village in the hills of Salerno province called Contursi.

As Louis Pasteur famously said, "Chance favors the prepared mind," and Golbe immediately made the connection between David and Joyce. Although Parkinson's does not typically run in families, Golbe realized he might have stumbled

Some names and identifying characteristics have been altered to protect the privacy of individuals.

FAST FACTS

A PARKINSON'S DETECTIVE STORY

1. Parkinson's disease is not usually familial, so scientists were intrigued by an extended family from Contursi, Italy, in which half of its descendants acquire the disease.
2. The responsible mutation in this family occurred in a gene for the alpha-synuclein protein. Further investigations revealed that other kindred groups had different variations of this gene.
3. Later research revealed that Lewy bodies—mysterious masses that proliferate in the brain cells of Parkinson's patients as the disease progresses—are made in part of alpha-synuclein. More alpha-synuclein leads to more pronounced symptoms.

Parkinson's does not typically run in families, but members of the Contursi clan had a 50 percent chance of contracting the disease.

on a rare exception: a family "kindred" that passed the illness from generation to generation. He called his boss and mentor Roger Duvoisin—a renowned neuroscientist who in the 1960s had helped pioneer the use of L-dopa, the first breakthrough drug for Parkinson's. Together they embarked on an international journey of medical detective work.

A Lethal Legacy

A year later Golbe was sitting in the small office of Salvatore La Sala in Contursi. La Sala, who had grown up in the village, was one of its only resident primary care physicians—and also served as its dentist. Golbe watched as another Italian collaborator, neurogeneticist Giuseppe Di Iorio, then at the University of Naples Federico II, conducted a clinical examination of a 40-year-old man named Mario. Periodically, La Sala spoke to clarify Di Iorio's requests and reassure his fellow Contursian. Golbe wished he understood more Italian. Di Iorio's English was also rudimentary, but somehow they managed to work together effectively, eventually cracking a genetic mystery.

After Golbe had plotted the American branches of the family tree, he suggested that Di Iorio visit the village church and examine Contursi baptismal and marriage records going back 12 generations. When they expanded the family tree on a huge chart, the multigenerational "pedigree" showed that Golbe's patients, David and Joyce, were seventh cousins—two of 574 descendants of a couple who married around 1700. Others now lived in Italy, Germany, Argentina, Canada and the U.S. The truly remarkable finding from the investigation was that 61 of the recent descendants had developed Parkinson's. The pedigree analysis showed that males and females were equally affected and that descendants had a 50 percent chance of contracting the bad gene and, along with it, Parkinson's.

Despite his limited Italian, Golbe followed Di Iorio's examination of Mario with little difficulty. Based on his clinical signs, Mario had inherited Parkinson's. La Sala, interestingly enough, was also a member of the family but hadn't in-

herited the mutation. He had played a key role mediating between the scientists and the family, explaining, for example, why the team needed to collect blood samples to take back to New Jersey for DNA analysis. Such molecular investigations might identify the specific genetic mutation responsible for the disease.

Meanwhile, back in New Jersey, other members of Duvoisin's department discovered a critical missing piece of the puzzle: they were able to confirm that the kindred members had genuine Parkinson's. Because other neurodegenerative diseases can produce tremors and gait problems that resemble it, a definitive diagnosis can be difficult to establish until after a patient's death, when pathologists look for curious blood cell–sized masses called Lewy bodies in brain tissue samples.

The New Jersey team had obtained and examined autopsy materials from two deceased family members—David, the fire chief, and his maternal uncle. Their brains showed extensive damage to the substantia nigra, and some of the surviving dopamine neurons contained the telltale Lewy bodies. As Duvoisin says, "It was classic Parkinson's pathology"—the first family kindred "where there was autopsy confirmation that it was Parkinson's."

The next step was to find the mutant gene that caused one in two children in this family on average to contract Parkinson's because that gene might hold the key to the mystery of the disease. The New Jersey scientists searched unsuccessfully for more than seven years. Then, in 1995, Zach Hall, who at the time was director of the National Institute of Neurological Disorders and Stroke (NINDS), asked them to share their Contursi blood samples with other investigators, who might be in a better position to pull off the necessary feats of molecular wizardry. A collaboration was formed between the New Jersey researchers and two scientists then at the National Institutes of Health: Bob Nussbaum, a clinical geneticist with advanced molecular biology training, and Nussbaum's colleague Mihael Polymeropoulos.

As Hall had hoped, Nussbaum and Polymeropoulos quickly racked up some spectacular advances. Although the Contursi mutation could have been on any one of the 22 non-sex-linked chromosomes we humans possess, it would turn out to lie on chromosome 4. By sheer good fortune, Polymeropoulos was highly familiar with chromosome 4, having recently linked two other genetic disorders to it. This work had generated lots of biochemical markers along the chromo-

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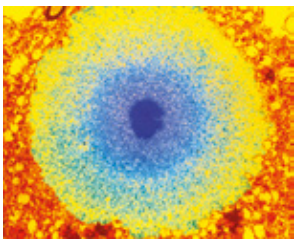
After seven years of scant progress, a new team took just nine days to track the errant gene to a short stretch on chromosome 4.

some, which guided the pair as they worked. Thus, within just nine days, they had narrowed their quest for the Contursi mutation to a short stretch of DNA along the so-called long arm of chromosome 4.



As Parkinson's progresses, the protein alpha-synuclein (*blue*) accumulates in blood cell–sized masses called Lewy bodies. A cross section of one in a nerve cell appears in this colored transmission electron micrograph.

The Aha! Moment

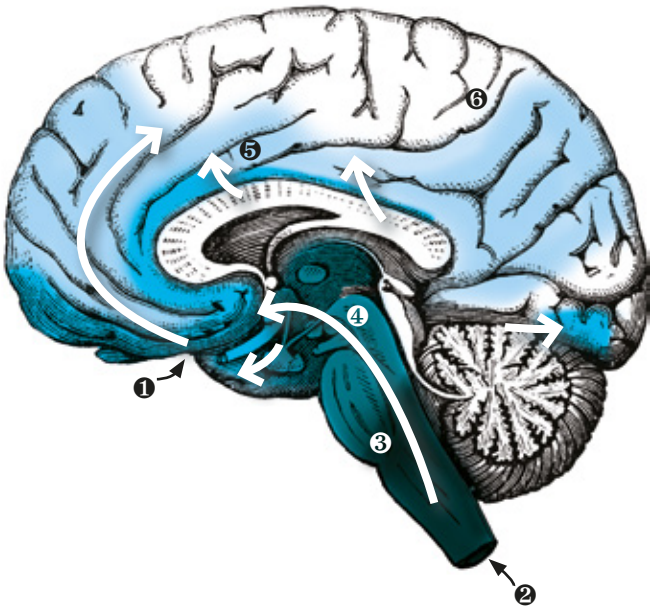
It took another nine months of painstaking work before Nussbaum and Polymeropoulos sequenced what they thought was the actual mutated gene. Then, Nussbaum says, they got a very lucky break. They checked their sequence against GenBank, a giant open-access computerized database of gene and protein sequences run by the NIH, and got a hit: the mutated gene was a known entity, a gene called *SNCA*, which coded for a protein called alpha-synuclein.

According to Nussbaum and Polymeropoulos, the genetic story behind the Contursi kindred went roughly as follows. *SNCA*'s normal role is to make a relatively obscure brain protein called alpha-synuclein. It is called synuclein, incidentally, to indicate that this protein can be found both in the synapses—the gaps across which neurons communicate—and in the nuclei of the neurons themselves. A single base change in the gene's million-letter genetic code, however, produced a mutant form of the protein, which caused affected members of the Contursi kindred to develop Parkinson's. On May 27, 1997, Nussbaum and Polymeropoulos submitted a paper to the journal *Science*, listing Duvoisin's team as co-authors, which linked a small mutation in a gene for alpha-synuclein with an aggressive form of Parkinson's. One month later—lightning fast for medical research articles—it appeared in print.

Nearly 20 years later it is clear that the discovery was transformative. The rare Contursi mutation does not show up in the DNA of regular Parkinson's patients, but the role of alpha-synuclein has proved to be a vital clue in the wider war on the disease.

It happened that at around the same time the *Science* paper appeared, Maria Grazia Spillantini, an Italian Alzheimer's researcher working at the University of Cambridge, had developed special staining techniques using antibodies to visualize alpha-synuclein in brain tissue. On a hunch, Spillantini decided to use the stain to search for alpha-synuclein in brain specimens of deceased patients with regular Parkinson's. And somewhat surprisingly, even though these individuals lacked the Contursi mutation, she found alpha-synuclein—lots of it. She found it in Lewy bodies.

As we have seen, Lewy bodies are found inside surviving neurons of Parkinson's sufferers and used to confirm diagnosis after death. Remarkably, despite their pathological importance, in 1997 no one was sure what Lewy bodies were made of. Spillantini had found the answer: they were made up in part of alpha-synuclein. Researchers everywhere took note, realizing the finding might be extremely important. Even though the Contursi mutation does not account for the vast majority of Parkinson's cases, the fact that Lewy bodies, the marker of sick and dying neurons, were stuffed with alpha-synuclein implied that this protein might be a critical player in Parkinson's.



The disease seems to develop in stages: alpha-synuclein appears first in Lewy bodies in the olfactory bulb (*1*) and in the vagus nerve (*2*), which reaches the digestive tract. It extends into the brain stem (*3*) and substantia nigra (*4*) and, ultimately, into the forebrain (*5*) and neocortex (*6*), causing dementia.

LYSIA FORNO *Science Source (micrograph)*; ©ISTOCK.COM (*brain*)

How Parkinson's Progresses

In Germany the legendary neuroanatomist Heiko Braak, then at Goethe University Frankfurt, noticed Spillantini's August 1997 paper in *Nature*. Inspired by the discovery that Lewy bodies contained alpha-synuclein, he embarked on a massive Parkinson's project, examining the accumulated damage in patients who had survived for different lengths of time. Braak did full-body autopsies of 41 cases of Parkinson's, 69 cases with no Parkinson's and 58 age-related control subjects. He looked for Lewy bodies and Lewy neurites, deposits in the long axons that project to other nerve cells. He hunted not only in the brain but in the rest of the body as well. Using Spillantini's powerful new alpha-synuclein stain and a novel technique of examining under the microscope sections of especially thick neural tissue, Braak saw clearly what others throughout history had only suggested—that the distribution of Lewy bodies and Lewy neurites was not confined to a few areas of the midbrain.

He also discerned something much more profound: that the location of Lewy pathology appeared to change as the disease progressed. Mildly affected cases (people who had died with early-stage Parkinson's) showed Lewy pathology in the olfactory bulb of the nose, which transmits information about smells to the brain, and in part of the vagus nerve, a long projection that connects the gut to the brain. In more advanced cases, he found Lewy bodies and Lewy neurites in the brain stem as well. Still more advanced cases had them in the substantia nigra—marking damage to dopamine cells. The most advanced cases of all displayed Lewy pathology in the forebrain and the neocortex.

Braak argued this was compelling evidence that Parkinson's started perhaps decades before any tremor or rigidity appeared. He suggested that it began in the gut or nose—perhaps triggered by an infection—and then spread insidiously throughout the brain in six anatomical stages. Loss of smell and constipation might come in so-called Braak stage 1. REM sleep behavior disorder occurs in Braak stage 2. Classic Parkinson's—tremor, rigidity, slowness of movement—shows up in Braak stage 3 and loss of balance in Braak stage 4. In Braak stages 5 and 6, the pathology spreads to the forebrain and the neocortex, causing dementia. If Braak is right, then, according to British neuroscientist Christopher H. Hawkes, "by the time you go to see a neurologist, you're in Braak stage 3 to 4. And to put it crudely, the brain is well and truly pickled."

Braak's theory, published in 2003, was initially met with skepticism. But the evidence for it and for the role of alpha-

synuclein would grow. That same year a group of Mayo Clinic and NIH geneticists announced a landmark discovery in *another* family, the so-called Iowa kindred, that deepened the connection with alpha-synuclein. Over nearly a century, branches of the family had been studied by a series of Mayo Clinic physicians. Geneticist Katrina Gwinn, now at NINDS, had met one of these clinicians in the mid-1990s. She became fascinated with the kindred and had gotten to know some of them. Gwinn decided to track the genes behind Parkinson's in this family group, just as Nussbaum and his colleagues had done for the Contursi kindred. To begin, she recruited the help of two British geneticists: John Hardy, known for his Alzheimer's disease research, and his then postdoc, Matthew Farrer, both then working at Mayo's Florida campus.

You don't need a mutation to get Parkinson's, just too much alpha-synuclein. The more alpha-synuclein, the worse the disease.

More Families, More Proof

The team's first attempt to locate a mutation failed—perhaps because of a sample mix-up. So the researchers decided to start over. Because the process they used, called genetic linkage analysis, depends on having plenty of DNA samples, Farrer and Gwinn headed out into the field and asked kindred members for more blood. By 2001 the team had enough blood samples to redo the lab work. A new group member then at the Mayo Clinic in Florida, Andrew Singleton, took the lead. As he tracked the genetic markers using the new material, he realized the location appeared to include the alpha-synuclein gene found in the Contursi kindred. This was puzzling: previously they had tested the Iowa kindred for all known forms of the Contursi mutation and found nothing.

But as Singleton pressed harder, he noticed some very odd signals. And then he got very excited. As he recalls, "It suddenly occurred to me that what could be causing the disease were extra copies of one gene." Pursuing this idea, Singleton went on to demonstrate that the Iowa kindred's Parkinson's wasn't caused by an error in the DNA sequence itself, as was the case for the Contursi clan. Instead affected members had what geneticists call copy number variation: Family members with Parkinson's had three copies of the normal alpha-synuclein gene—a triplication—on one copy of chromosome 4. On the other copy of chromosome 4, they had the usual single alpha-synuclein gene. Because they had a total of four copies of the gene, instead of the usual two, affected individuals had *twice* as much alpha-synuclein protein being pumped into their body.

Scientists realized just how significant this discovery was: there was a direct link between quantity of alpha-synuclein and disease. It showed that you didn't need a mutation to get Parkinson's, just too much alpha-synuclein. Hardy describes the news as "a beautiful surprise … extremely unexpected. But once you get the result, it makes you understand everything." Other researchers in Europe reported family pedigrees where affected members had both duplications and triplications. The people with the triplications had an earlier onset and much more aggressive illness than those with the duplications. This was also significant. Alpha-synuclein's toxicity depended on dose. The more alpha-synuclein, the worse the Parkinson's.

When I think about these breakthroughs now, it is strange to imagine that at one time neuroscientists dismissed the role of genetics in Parkinson's. Since the 1997 discovery of the alpha-synuclein mutation, some 18 potential genetic forms of Parkinson's have turned up, involving another 10 or so genes. Geneticists are confident that six of them are classically inherited either dominantly or recessively.

Of course, most people with Parkinson's don't have a known mutation. But buried in our genomes, there may be sequences that predispose us in some way to develop the disease. This heightened susceptibility may surface only after certain infections, as Braak proposes, or exposures to specific toxins, as indicated by some earlier research. Using special gene chips, geneticists have screened the DNA of people with Parkinson's and compared it with healthy controls. These genome-wide association studies have found a strong correlation with variations in the alpha-synuclein gene, as well as associations with variations in the gene encoding the tau protein, which is involved in Alzheimer's pathology. Understanding those sequences may … well, there's no telling where that knowledge may lead. M

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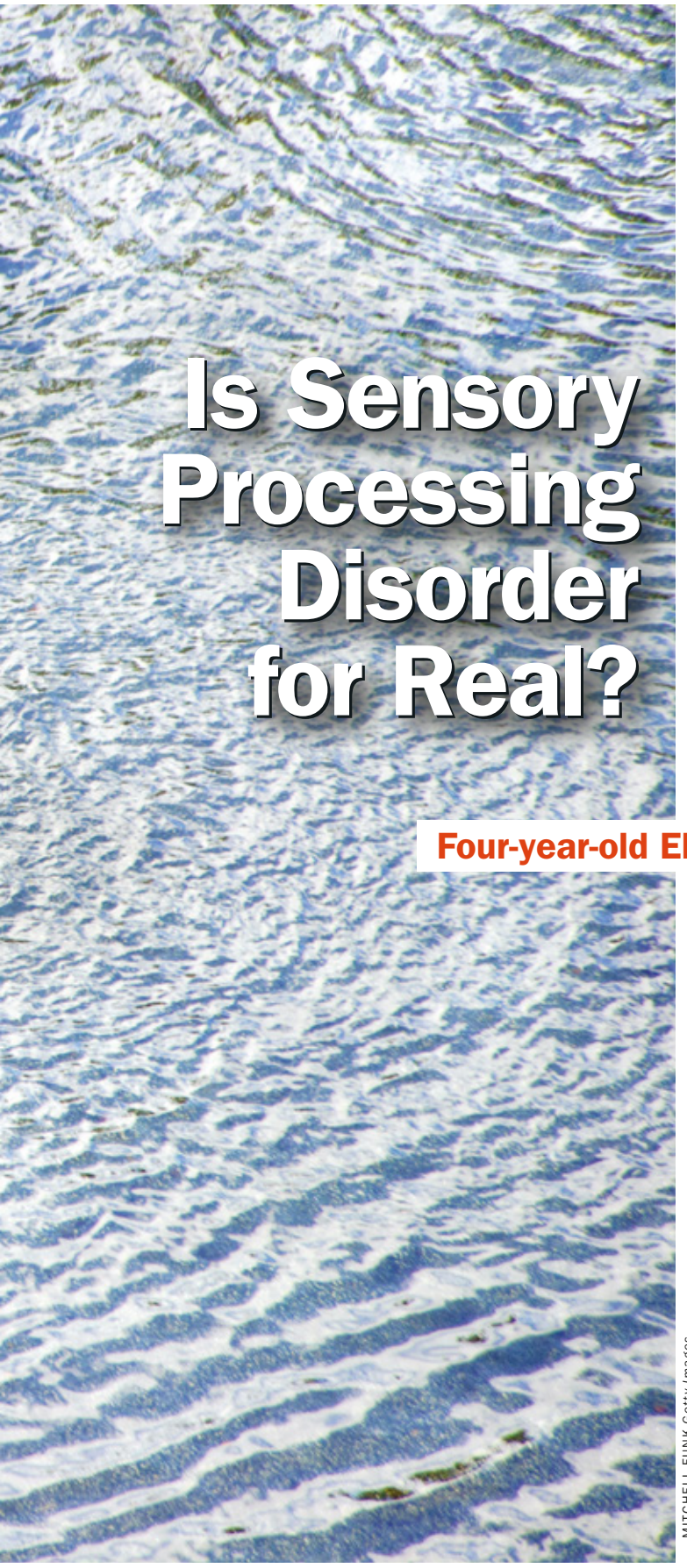

MITCHELL FUNK Getty Images

Is Sensory Processing Disorder for Real?

A debate rages over whether doctors should recognize this common childhood condition as a distinct disorder

By Melinda Wenner Moyer

Four-year-old Elliott experiences a different world than most of us do. He can smell a freshly peeled banana from across a room. The hum of a running blender hurts his ears. He abhors the feeling of moisturizing lotion on his skin and washes his hands only in ice-cold water. He loves the taste of lemon juice.

According to his occupational therapist, Elliott (whose name has been changed to protect his privacy) has sensory processing disorder. This means that he has difficulty perceiving, responding to and integrating sensations in ways that can affect his social relationships, daily activities and quality of life. Occupational therapists say that the disorder can manifest itself in diverse ways, depending on which senses are affected and how; there are dozens of possible sensory permutations. Elliott seems to be overly sensitive to smell and touch and sound; he is underresponsive to taste. He also has trouble discriminating the qualities of certain sensations, including where his body is positioned in space, which affects his coordination and motor skills. He meets with his occupational therapist once a week for sensory integration therapy in what is called a "sensory gym"—a space where he plays with swings, jumping balls, shaving cream and climbing walls in ways designed to teach his nervous system more appropriate perceptions and responses to sensations and to build his confidence and coordination. According to a 2009 study, as many as one in every

six kids suffers from sensory problems that are serious enough to disrupt their daily lives.

Everything I have written about Elliott's disorder, however, is hotly contested. In some circles, sensory processing disorder, or SPD, simply doesn't exist. Although a cadre of occupational therapists fought for 12 years to have the disorder listed in the current iteration of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-5*), the American Psychiatric Association (APA) opted not to include it—which means, basically, that the group does not recognize it as a legitimate condition. In 2012 the American Academy of Pediatrics (AAP) published a policy statement recommending against the use of the SPD diagnosis, too. It argued that sensory problems are likely to be symptoms of other recognized developmental disorders, such as autism, attention-deficit/hyperactivity disorder and anxiety disorder. It also concluded that "the amount of research regarding the effectiveness of sensory integration therapy is limited and inconclusive."

This is, in fact, the crux of the problem—the field desperately needs more research to elucidate and support its theories, but it is caught in a catch-22 bind. Who wants to fund research on an unrecognized condition? "There is this incredible negative reaction when we go for funding," explains Lucy Jane Miller, an occupational therapist and early childhood education specialist who founded the Sensory Processing Disorder Foundation, a nonprofit organization that seeks to increase awareness, funding and research for the disorder, as well as the STAR Center, a nonprofit organization in Colorado that assesses and treats children with SPD. "People are emotional about this as if it's a religion or a belief system and not a science."

In 2014 the SPD Foundation's funding for research—most of which came from the Wallace Foundation, an independent philanthropy—totaled approximately $600,000. By comparison, in its fiscal year 2014 the National Institutes of Health's funding for autism research alone totaled $188 million, according to a search I conducted of its records. Since SPD was first described in the 1960s, questions have far outnumbered answers, but the field has never been given an adequate opportunity to address them. "I've been doing research for 40 years, and it's been very frustrating," Miller says. "I don't know how we're going to break through."

The State of the Evidence

The senses can be thought of as the lenses the body uses to understand itself and its relationship to the outside world. It's not crazy, then, to think that they would mediate the development of everyday skills. One of the first researchers to develop this idea was the late educational psychologist and occupational therapist A. Jean Ayres. In the 1960s, while working at the University of California, Los Angeles, Brain Research Institute, Ayres devised a theory of sensory integration that hypothesized that sensory systems do not develop independently of one another and that sensations are also not processed independently but are instead integrated in the brain. She likened problems with this system to neurological traffic jams that prevent parts of the brain from receiving the information they need to accurately interpret and respond to various types of sensory information. (In addition to the senses that everyone knows—sight, sound, touch, taste and smell—there is also proprioception, the sense of the position of the parts of the body in relation to one another; the vestibular sense, which notes the orientation of the body in space and how it is moving; and interoception, which detects internal regulation processes such as hunger, thirst, heart rate and the need to use the bathroom.)

"People are emotional about this as if it's a religion or a belief system and not a science," says Lucy Jane Miller, an occupational therapist who conducts research on SPD.

Ayres's theory, and its terminology, has evolved over the decades, and the belief today is that some individuals have problems *modulating* sensory information, in that their nervous system is either oversensitive or undersensitive to sensory stimuli—essentially they have problems interpreting and responding appropriately to the intensity of sensory information. Some individuals may also (or instead) have problems *discriminating* sensory information, which means that they have trouble identifying the spatial and temporal qualities of sensations they experience. Someone who has problems with auditory discrimination may not be able to distinguish between different types of sounds or know where they are coming from, whereas a person with vestibular discrimination problems, such as Elliott, may not always know where his body is in space and may be clumsy. Individuals with discrimination problems may also have sensory-based motor disorders, which are characterized by poor stability and body control (known as postural disorder) or problems with motor coordination (dyspraxia).

Over the past 15 years research has suggested that sensory variations are "real" in that they are rooted in subtle brain differences. In 1999 scientists at the University of Colorado Denver and the University of Denver exposed 19 children with sen-

FAST FACTS

SENSORY STANDOFF

1. As many as one in six children has difficulty processing sensory inputs—a condition often called sensory processing disorder (SPD).
2. Occupational therapists commonly treat SPD, but the condition is not formally recognized by psychiatrists or pediatricians.
2. Research suggests a biological basis for SPD, but more studies are needed to build a consensus about the disorder and its treatment.

In addition to issues with the five familiar senses, affected children may have difficulty with proprioception (knowing the relative position of one's own body parts) and the vestibular sense (orienting one's motions in space).

sory modulation problems and 19 healthy children to a barrage of sensory stimuli in a short amount of time: they smelled wintergreen oil, heard a siren, saw a flashing light, felt a feather move across their face and had their chair tilted back 30 degrees. These stimuli were provided quickly, 10 times in a row. While this went on, the researchers applied electrodes to the children's index and middle fingers to measure their electrodermal activity—the electrical characteristics of their skin, which, among other things, can change with the activity of the sweat glands. (Electrodermal measurements are used in polygraph tests.) With the exception of four children with sensory modulation problems who did not respond to the stimuli at all (all the control subjects did), they found that the kids with sensory modulation problems had larger electrodermal responses than the control group and that their responses did not decrease as much as they did for the controls when the stimuli were repeated. The results suggested that although most individuals might, for instance, hear an air conditioner turn on and then stop noticing the hum a few minutes later (a normal response called habituation), those with sensory modulation problems will continue to hear and be bothered by the sound for longer. But electrodermal tests are controversial—their measurements can be affected by various external factors, such as room humidity, so it is hard to know for sure that the observed differences were meaningful.

Studies using electroencephalography, which measures voltage changes in the scalp related to the activity of cortical neurons, have also found differences in brain activity between individuals with and without symptoms of SPD—but EEG has limitations, too, such as the fact that it only measures activity close to the brain's surface. In a 2011 study, researchers at Colorado State University found EEG differences between children with and without SPD when they were exposed to auditory beeps. The children with SPD who had the most abnormal EEG recordings performed the worst on tests of sensory and motor performance, too. This finding suggests that Elliott's shrieks in response to being smeared with lotion may be directly related to his brain's abnormal response to the sensation—in other words, he is not "overreacting," as some might say, because his perceptions really are more intense. "These kids truly are more responsive, and they don't tend to inhibit that input. They never really habituate to the information the way that they should," says Teresa May-Benson, executive director of the SPIRAL Foundation, a nonprofit Massachusetts organization dedicated to research and education about SPD.

In recent years researchers have begun using more cutting-edge technologies to understand what underlies these potential brain differences. In 2013 researchers at the University of California, San Francisco, and the University of Denver used diffusion tensor imaging, a form of magnetic resonance imaging that reveals how white matter is organized in the brain, to compare the white matter tracts in children diagnosed with SPD with the tracts in those without the condition. They, too, found significant differences between the groups: the affected children had less white matter microstructure integrity in the pathways connecting regions involved in multisensory integration. And the more serious the children's sensory symptoms were, as reported by their parents, the less integrity they had.

THE AUTHOR

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But the study was small and limited, involving 40 boys and no girls, so again, it is hard to conclude a lot from it.

These studies suggest that sensory differences have clear biological roots and that serious sensory problems might be signs of a disorder, but they haven't been enough to convince some scientists, who tend to see sensory problems as symptoms of other, more recognized conditions. Research suggests, for instance, that up to 88 percent of children with autism spectrum disorders have sensory processing problems. A study published online in June showed, using MRI, that the brains of these children do react more strongly to sensory stimuli than do the brains of children with autism who do not have sensory issues. In addition, a 2011 study found that children with ADHD are more likely than unaffected children to have sensory symptoms.

Some neurologists think that sensory issues are simply a sign of neurological immaturity: few adults seem to suffer from sensory processing problems, they say, so most kids probably grow out of it. (Many occupational therapists, however, disagree. They say that adults often remain sensitive to sensory stimuli or have motor coordination problems but have learned to avoid the situations that make them uncomfortable.)

An imaging study found that the brains of children with SPD had weaker white matter structure in pathways involved in sensory integration, compared with the brains of unaffected children.

To add to the problem, there is no "gold standard" for diagnosing sensory processing disorder. Occupational therapists typically use standardized tests, parent reports and clinical observations to make the diagnosis, but different diagnostic approaches may be used depending on the child and the therapist. And sensory differences can, of course, be normal. "A child may be in a specific place on a bell curve, but that doesn't mean he has a disorder," says Winnie Dunn, an occupational therapist and neuroscientist at the University of Kansas Medical Center who developed a series of widely used assessments for identifying sensory processing patterns in children and adults. Some sensory differences can even be useful: an individual with a particularly sensitive nose, for instance, might become an excellent sommelier.

Ultimately few skeptics outright reject the idea that SPD could exist—they just argue for more supporting research. For instance, in response to letters reacting to the 2012 policy statement by the AAP, the two lead authors wrote that they were both "'believers in the existence of sensory-based neurobehavioral problems but feel that more research is definitely needed before a clearer understanding is reached that may lead to a consensus on what characteristics make up the 'disorder.'" Miller, who spent years campaigning to have SPD included in the *DSM-5*, argues that organizations such as the AAP and the APA seem to have a higher standard of evidence for SPD than they do for other conditions: "We have a lot of studies—more than most of the diagnoses in the *DSM*—but still, there is this incredible negative reaction." The standoff has taken a toll: one researcher I talked with told me she didn't want to speak on the record, because she had "reached the stage of battle fatigue on this topic."

Sensational Treatments

There is little question today that various sensations are processed together and that they play an important role in coordinating movement. "Sensory input from the different senses converges in a region located in the upper back portion of the brain called the posterior parietal cortex," explains Dan Marigold, director of the Sensorimotor Neuroscience Lab at Simon Fraser University in British Columbia. "The sensory information is integrated to provide an estimate of the state of the limbs, body and environment," which helps to facilitate planning and execution of goal-directed movements, he says. When people have problems integrating sensory inputs, then, it makes sense that they could have trouble with everyday tasks and complex movements.

But the idea that therapists can improve motor skills and coordination with sensory integration therapy is highly controversial. In a nutshell, the therapy is designed to present individuals who have sensory processing problems with opportunities to experience challenging, multisensory experiences in a safe, play-based environment. These experiences help to organize the person's nervous system so that it responds more appropriately to sensation. Yet to some pediatricians and psychologists, the approach reeks of pseudoscience. A pediatric neurologist writing for the myth-busting Web site Quackwatch has described sensory integration therapy as "unproven and irrational."

One problem is that many early studies on the therapy had design flaws, making it difficult to make solid conclusions about its efficacy. Some studies, for instance, reported that the symptoms of children who underwent sensory integration therapy did improve compared with children who received no treatment—but such studies do not account for the fact that children might improve with one-on-one attention from empathetic adults no matter what kind of therapy they receive. It is also possible that some sensory symptoms simply improve with time, as children learn to cope.

Other studies have failed to assess true sensory integration approaches. In 2007 researchers analyzed 34 studies that had supposedly tested the efficacy of sensory integration therapies and found that only 38 percent of the interventions had been designed to be challenging and only 15 percent were provided in a play-based context—both of which are crucial attributes of the therapy. "Sensory integration therapy is very intricate, and there are a lot of subtleties to it," May-Benson explains. Beth Pfeiffer, an occupational therapist at Temple University,

A four-year-old works out in a sensory gym in Washington, D.C. Guided by occupational therapists, this kind of sensory integration therapy is designed to expose children to sensations that they find challenging in a safe, playful environment. Some small studies have demonstrated its benefits, but many questions remain.

SARAH L. VOISIN *Getty Images*

puts things more bluntly: "There are a lot of people who publish on sensory integration who don't even really understand what the intervention is." In addition to the fact that the therapy itself is complicated, results can be a challenge to measure. "If you think about what the intervention is targeting, it's really targeting neurological change—the way the brain processes information," Pfeiffer says. "So the outcomes could be so varied." Individuals with SPD often have very different symptoms, too. "It's not, 'Okay, we're going to give you this drug and expect this change,'" May-Benson explains. "It's, 'We're going to do these 10 things, and it's the combination of these 10 things that result in this final outcome.' And the final outcome is also influenced by your personality, your drive, your environment and all these other things that we don't have a lot of control over—so it becomes very challenging in a large group study to get results that are statistically significant."

Nevertheless, in 2007 Miller and her colleagues did get statistically significant results from a pilot clinical trial. They split 24 children with sensory modulation problems into three groups. One group received the therapy twice a week for 10 weeks. A second group spent the same amount of time each week doing fun activities with an adult who had a background in education or psychology. The third group was not given an intervention. The researchers found that, compared with the two other groups, those who received sensory integration therapy made more gains toward achieving the goals their families had set, such as being able to try new foods at dinner without gagging or tolerate wearing socks, and they improved more on the attention, cognitive and memory subtests of an IQ test.

In a 2011 study, Pfeiffer and her colleagues separated children who had autism in addition to sensory processing problems into two groups. One group received sensory integration therapy, and the other received fine-motor-skill-based occupational therapy for six weeks. This study, too, found that the children receiving sensory integration therapy achieved more of their family's goals. The therapy was also better at reducing the frequency of autism-related mannerisms, such as hand flapping.

But these studies were small and limited, and not everyone is convinced by their findings. Funding for more substantial research continues to be sparse, and those in the field often feel downright ostracized. "I think there's a group that has an inherent bias against it. It's almost like they shut the door," Pfeiffer says. That may reflect the fact that occupational therapy as a field lacks the status of medicine. Some wonder, too, if sexism plays a role—Ayres was a woman, and most occupational therapists today are female, yet many vocal critics of SPD and sensory integration therapy are men.

Even when researchers *do* get funding, it is rarely enough to support the types of studies the field desperately needs. "We have a critical mass of researchers who are doing really good work, but I'll tell you what: treatment studies are expensive," explains Roseann C. Schaaf, an occupational therapist and neuroscientist at Thomas Jefferson University. The $500,000 grant she recently received from Autism Speaks did not fully cover the cost of a 32-subject trial designed to test the efficacy of sensory integration therapies in children with autism.

While it might seem reasonable for funding organizations to be wary of supporting research on an unproved approach for a condition that is not universally recognized, the only way to shed meaningful light on SPD is, in fact, to conduct more and better studies. Parents with kids like Elliott know, beyond a doubt, that their children are struggling and need help. Is it asking too much to look beyond old biases and divisions to get some answers? **M**

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- **Living Sensationally: Understanding Your Senses.** Winnie Dunn. Jessica Kingsley Publishers, 2007.
- **Guide to Sensory Integration for Parents.** Emily Eastman and Teresa A. May-Benson. Spiral Foundation, 2012. **www.thespiralfoundation.org/toolkit_parents.html**
- **Abnormal White Matter Microstructure in Children with Sensory Processing Disorders.** Julia P. Owen et al. in *NeuroImage: Clinical,* Vol. 2, pages 844–853; 2013.
- Sensory Processing Disorder Foundation explains SPD: **www.spdfoundation.net/about-sensory-processing-disorder**
- SPD Foundation's Home Activities for Children with Sensory Processing Disorder: **www.spdfoundation.net/resources/homeactivities**

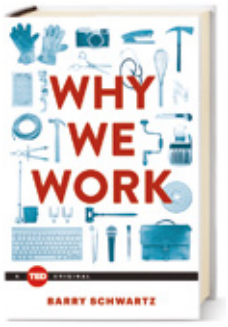
From Our Archives

- **A Sensory Fix for Problems in School.** Burkhart Fischer; March/April 2010.

LABOR PAINS

Why We Work

by Barry Schwartz. Simon & Schuster/ TED Books, 2015 ($16.99; 112 pages)



"Men labor under a mistake. The better part of the man is soon plowed into the soil for compost." So wrote Henry David Thoreau in his 1854 classic, *Walden,* and so confirms the Gallup organization based on recent surveys of 25 million people in 189 countries. Work frustrates rather than fulfills almost 90 percent of the world's workforce.

Most people work because they need money, but scholars have long known that money is not what people most want from work. In fact, J. D. Houser's 1938 book, *What People Want from Business,* put money 21st on the list, and Robert Hoppock's extensive study entitled *Job Satisfaction,* published in 1935, found that the best predictors of workplace satisfaction were autonomy, variety, security, appreciation, positive relationships and opportunities for advancement.

In *Why We Work,* Schwartz, a psychology professor at Swarthmore College, promises to explain why the modern work experience falls so far short of this ideal. Unfortunately, he does so mainly by criticizing the views of three straw men: Adam Smith, the 18th-century author of *The Wealth of Nations,* and 20th-century thinkers Frederick Taylor, the inventor of management science, and B. F. Skinner, a pioneer of behavioral psychology. All three wrote about the power of incentives—promised rewards—and Schwartz's book is largely a diatribe against what he calls the "incentive theory of everything."

In education, medicine and law, in particular, Schwartz says, the focus on efficiency and profitability has robbed practitioners of the intrinsic motivators that drew them to these professions in the first place. All three professions have turned into assembly lines in which behavior is scripted to maximize gain.

But virtually any job, Schwartz notes, can be made satisfying if it is modified to boost autonomy and to include "variety, complexity, skill development, and growth." (Sound familiar?) The problem with this proposed fix is that he largely glosses over why many business owners and executives avoid such practices. Efficiency and profitability are important, after all. The small family farm provided meaningful experiences for workers, sure, but it did not produce much food.

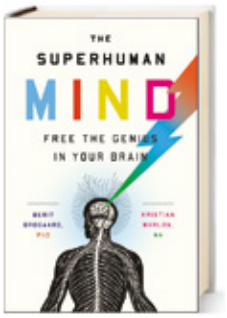
Ironically, Schwartz mentions Google as an exception to what he sees as the modern obsession with incentive-based management, overlooking the fact that Google employees are chauffeured to work each morning in leather-appointed buses and fed free of charge by gourmet chefs.

Why We Work seems superficial, perhaps in part because the author was incentivized to present his views in a fast-moving, assembly-line format. TED talks are limited to 18 minutes, and the new TED Books, of which this is one, are limited to about 100 pages. Now that would be an intriguing topic for a TED book: how to get people to pay attention to in-depth discussions about complex issues that cannot be explored adequately in the blink of an eye. —*Robert Epstein*

REMARKABLE BRAINS

The Superhuman Mind: Free the Genius in Your Brain

by Berit Brogaard and Kristian Marlow. Hudson Street Press, 2015 ($25.95; 288 pages)



Ask about the color of a painful toothache or the sound of a delicious lamb shank, and most people will respond with confusion. But artist Carol Steen would say that pain is orange, and researcher Lidell Simpson might tell you that all the noise in the restaurant makes it difficult to hear the flavor of the food. Such seemingly illogical pairings are the hallmark of synesthesia, a neurological phenomenon that causes some people to form strong connections between otherwise unrelated sensations.

So-called synesthetes such as Steen and Simpson experience these sensory links automatically. In *The Superhuman Mind,* neuroscience and philosophy researchers Brogaard—a synesthete herself—and Marlow contend that anyone can acquire a form of synesthesia and open "a gateway into inaccessible neural regions of our brains."

Central to their case is the idea that even "normal" brains unconsciously perform incredibly complicated feats all the time. Coordinating the many muscles in our hand and arm to pick up a mug, for example, requires scores of intricate calculations to which our conscious mind is not privy. The mental algorithms that allow us to carry out such mundane actions are in a sense preprogrammed, but the authors surmise that via targeted brain training, we can fashion new algorithms to tap into existing neural networks.

Brogaard and Marlow highlight this vast potential of the human brain using extreme real-life examples. They explore a study in which sighted people, after being blindfolded for a week, began to spontaneously echolocate, a technique more commonly used by bats for sensing their surroundings. Brain scans showed that these people's brains apparently began to recruit their visual cortices to echolocate.

Brain trauma may similarly prompt a rewiring of our neural connections. For instance, soon after jumping headfirst into the shallow end of a pool, one man discovered an all-new talent—the ability to play the piano proficiently. A brain scan revealed that he had a lesion on his parietal cortex, the region responsible for producing language and music. Researchers investigating his condition thought that some form of compensation for the lesion could explain his new prowess at the keyboard.

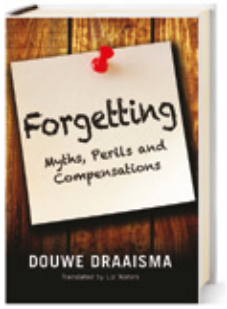
Of course, Brogaard and Marlow do not advocate that anyone live in darkness or seek brain injuries to achieve new cognitive skills. Rather they relay such stories to highlight the intriguing possibilities that can emerge when we form new neural connections. And they describe related tricks people can use to build mental shortcuts for memory, math and even carrying out savantlike calendar calculations. (Which day of the week was April 23, 1987? Anyone?) Participants in memory competitions generally have neurologically ordinary brains but take advantage of our innate affinity for remembering emotions and stories to achieve remarkable feats of memory. To recall the irrational number pi to more than 20,000 decimal points, memory champ Mark Aarøe Nissen crafted a narrative to connect each digit to some element of the story.

For a book about the power of leveraging connections—between brain circuits and pieces of information—*The Superhuman Mind* is rather disjointed. Even the main theme

of synesthesia puzzlingly fades in and out. The brain-training strategies are fascinating but do not always feel realistic to apply. Still, as an exploration of the extraordinary reach of the human brain, the book delivers. —*Andrea Alfano*

Q&A

The Art of Forgetting



Much has been written on the wonders of human memory: its astounding feats of recall, the way memories shape our identities and are shaped by them, memory as a literary theme and a historical one. But what of forgetting? This is the topic of a new book by Douwe Draaisma, author of **The Nostalgia Factory: Memory, Time and Ageing** (Yale University Press, 2013; 176 pages) and a professor of the history of psychology at the University of Groningen in the Netherlands. In **Forgetting: Myths, Perils and Compensations** (Yale University Press, 2015; 288 pages), Draaisma considers dreaming, amnesia, dementia and all the ways in which our minds—and lives—are shaped by memory's opposite. He answered questions from contributing editor Gareth Cook.

What is your earliest memory, and why, do you suppose, have you not forgotten it?
Quite a few early memories in the Netherlands involve bicycles; mine is no exception. I was two and a half years old when my aunts walked my mother to the train station. They had taken a bike to transport her bags. I was sitting on the back of the bike. Suddenly the whole procession came to a halt when my foot got caught between the spokes of a wheel. I am pretty sure this memory is accurate because I had to see a doctor, and there is a dated medical record. It is a brief, snapshotlike memory, black-and-white. I do not remember any pain, but I do remember the consternation among my mom and her sisters.

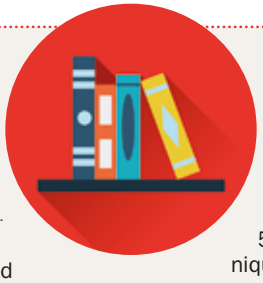
Looking back on this memory from a professional perspective, I would say that it has the flashlike character typical for first memories from before age three; "later" first memories are usually a bit longer and more elaborate. It also fits the usual pattern of being about pain and danger. Roughly three in four first memories are associated with negative emotions. This may have an evolutionary origin: I never again had my foot between the spokes. And neither have any of my children.

"Forgetting" is usually thought about in a negative sense, but you come to it with a different perspective. Can you explain how you arrived at this way of thinking?
Experimental psychologist and memory expert Endel Tulving once counted how many different types of memory there are, and he came up with a staggering figure of 256, each with their own laws of encoding, retention, reproduction, and so on. Then it dawned on me that there must also be a multitude of types of forgetting. Considering that we forget so much more than we remember, it is fair to say that the core business of memory is forgetting. After the switch, the topics came in swift procession. Why does your colleague remember your idea but seem to forget that it was *your* idea? Why do portraits tend to eclipse our memories of faces? Why is there an art of memory but no art of forgetting? See?

Why *does* a colleague remember an idea but not whose idea it was?
This phenomenon is actually a nice demonstration of the fact that we should think of "memory" as a federation of different types of memory. Suppose you are in a meeting with colleagues, discussing some problem. You come up with a suggestion, but someone else's solution will be tried first. This situation activates two types of memories.

Autobiographical memory takes care of retaining who was there, whether it was a morning or an afternoon meeting, perhaps even what the weather was like that day. *Semantic* memory retains the facts of the matter: what the problem was, which solutions were suggested, and so on. The trouble is, semantic memory has trouble remembering sources and circumstances. Most of the facts you remember—such as the meaning of "incubation" or the capital of Sweden—are just the facts, and you have probably forgotten who told you or where you read this information. A week later, at a follow-up of the meeting, you may find that your colleague has retained your idea, thanks to his wonderful semantic memory but has forgotten its source—you.

On Our Shelf



On the Move: A Life

by Oliver Sacks. Knopf, 2015 ($27.95; 416 pages)

In his new book, neurologist and bestselling author Sacks takes readers on a journey across decades and continents. His scientific proclivities are in evidence throughout—in his childhood chemistry experiments, his studies of the brain and even his dabbling in psychoactive drugs. But it is the stories of human triumphs and losses, whether intimate romantic encounters or the deaths of great friends, that will likely remain with his readers longest. —*Daisy Yuhas, associate editor*

The Small Big: Small Changes That Spark Big Influence

by Steve J. Martin, Noah J. Goldstein and Robert B. Cialdini. Grand Central Publishing, 2014 ($28; 288 pages)

How can we persuade people to donate to charity, recycle or obey the law? Martin, Goldstein and Cialdini give answers that are subtler than one might think. In their entertaining new book, the authors break down the persuasion literature into 52 mini chapters, offering surprisingly simple techniques to help us influence our peers.
—*Victoria Stern, contributing editor*

Thinking in Numbers: On Life, Love, Meaning, and Math

by Daniel Tammet. Little, Brown, 2013 ($26; 288 pages)

In this collection of 25 essays, Tammet, an autistic savant, polyglot and author of two previous books, explores the beauty and complexity of numbers. He elaborates on his passion by delving into the importance of number in how we perceive the world while sprinkling intriguing anecdotes from his own life.
—*Jessica Schmerler,* Mind *intern*

What happens in the brain during sleep?

via e-mail

John Peever, director of the Systems Neurobiology Laboratory at the University of Toronto, and **Brian J. Murray,** director of the sleep laboratory at the Sunnybrook Health Sciences Center, respond:

The function of sleep has mystified scientists for thousands of years, but modern research is providing new clues about what it does for both the mind and body. Sleep serves to reenergize the body's cells, clear waste from the brain, and support learning and memory. It even plays vital roles in regulating mood, appetite and libido.

Sleeping is an integral part of our life, and as research shows, it is incredibly complex. The brain generates two distinct types of sleep—slow-wave sleep (SWS), known as deep sleep, and rapid eye movement (REM), also called dreaming sleep. Most of the sleeping we do is of the SWS variety, characterized by large, slow brain waves, relaxed muscles and slow, deep breathing, which may help the brain and body to recuperate after a long day.

When we fall asleep, the brain does not merely go offline, as implied by the common phrase "out like a light." Instead a series of highly orchestrated events puts the brain to sleep in stages. Technically sleep starts in the brain areas that produce SWS. Scientists now have concrete evidence that two groups of cells—the ventrolateral preoptic nucleus in the hypothalamus and the parafacial zone in the brain stem—are involved in prompting SWS. When these cells switch on, it triggers a loss of consciousness.

After SWS, REM sleep begins. This mode is bizarre: a dreamer's brain becomes highly active while the body's muscles are paralyzed, and breathing and heart rate become erratic. The purpose of REM sleep remains a biological mystery, despite our growing understanding of its biochemistry and neurobiology.

We do know that a small group of cells in the brain stem, called the subcoeruleus nucleus, controls REM sleep. When these cells become injured or diseased, people do not experience the muscle paralysis associated with REM sleep, which can lead to REM sleep behavior disorder—a serious condition in which the afflicted violently act out their dreams.

Does napping really help cognitive function?

—Jim Lohr, Iowa

Kimberly Cote, director of the Sleep Research Laboratory at Brock University in Ontario, answers:

Daytime napping in healthy adults does indeed lead to benefits in terms of alertness, mood and cognitive functioning. Adults do not require shut-eye in the middle of the day—unlike infants and toddlers—but many grown-ups nap just the same. A 2008 National Sleep Foundation poll found that 460 out of 1,000 respondents had napped at least twice during the previous month.

People cite a variety of reasons for indulging in daytime siestas. Some take so-called replacement naps to make up for poor sleep the night before. Shift workers may take prophylactic naps in anticipation of needing to stay awake overnight. Many others, regardless of age and culture, habitually take appetitive naps—they sleep simply because it feels good.

Intuitively most of us think that a nap will refresh us and make us better able to take on the challenges of the day. In fact, research shows that healthy adults who take naps enjoy brighter moods, faster reaction times, and better performance on tasks involving logical reasoning, attention and memory.

How much we gain from napping, though, depends on a number of factors, including how and when we nap and for how long. A 20-minute nap appears to hit the sweet spot. Studies reveal that such brief sojourns boost both mood and cognitive performance. Shorter, 10-minute naps are also good for enhancing performance and cause less grogginess than longer naps do.

Naps lasting an hour or more are not recommended. During a longer nap, you fall into a deeper sleep, which makes it more difficult to awaken feeling refreshed. In other words, the longer the nap the greater the "hangover" effect afterward. Also, longer naps diminish the quality of nighttime sleep.

The best time of day to take a nap (assuming you keep a regular night sleep schedule) is midafternoon, between 2 and 4 P.M. Given the body's natural biological clock, it is generally easier to fall asleep during this window and to reap the full benefits of a good rest.

In one study from our sleep laboratory, we found that habitual nappers slept more lightly than nonhabitual nappers did, which may mean that the ability to nap lightly contributes to better alertness and performance after napping. Habitual nappers also reported feeling better than the nonhabitual nappers after the same amount of sleep.

Though generally beneficial, napping isn't for everyone. Poor sleepers who have difficulty falling and staying asleep at night might want to avoid daytime snoozing. For everyone else, though, a 20-minute midafternoon nap could be the secret to feeling sharp and happy throughout the day. **M**

JAMIE CARROLL ©iStock.com

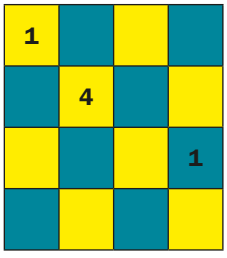
1 PUZZLING PRODUCT

The following equation uses every digit from 0 to 9 once (not counting the intermediate steps). Fill in the missing numbers.

```
  7??
× 4?
-----
?????
```

2 MAGIC SQUARE

The magic square below uses the numbers from 1 to 4 only. To fill in the square correctly, use each numeral only once in any vertical, horizontal or long diagonal row, with no arrangement of four numbers in any direction containing the same number next to itself.



3 GEOGRAPHY QUIZ

If Boston is east of New York, cross out all the As. If not, cross out the Rs. If Paris is south of New York, cross out all the Os. If not, cross out all the Is. If Sri Lanka is in Asia, cross out the Bs and Us. If not, cross out the Cs. The remaining letters will tell you whether you have found the right answer.

CAAOIIABURRIAUEIBBCIAUT

4 QUOTE FINDER

The opening stanza of a poem is coiled in the grid below. Start at the right word and move in any direction to work out the quotation.

THE	WINGS	IS	WAFTED	DOWNWARD
FROM	FALLS	OF	FEATHER	FROM
DARKNESS	THE	A	NIGHT	AN
DONE	AND	THE	AS	EAGLE
IS	DAY	FLIGHT	HIS	IN

5 CODE BREAKER

A simple substitution code has been used to conceal an imaginary quote. Work out the code below to decipher the original words.

King Arthur said:

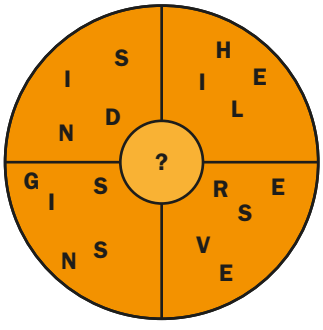
23-18-23 2-12-6 13-12-7-18-24-22 7-19-26-7 24-26-14-22-15-12-7 24-26-13 25-22 26-13-26-20-9-26-14-14-22-23 18-13-7-12 14-26-15-22 24-12-7?

6 LOOSE CHANGE

Charlie was cleaning his living room. He lifted a sofa cushion and found an equal number of pennies, nickels and dimes totaling $1.28. How many of each coin did he find?

7 LOST LETTER

Find the missing letter that completes the scrambled word in each pie segment. (Hint: The missing letter is the same for each word.)



8 WORD WHEEL

An eight-letter word is spelled out in the box below. Find it by beginning with the correct letter and moving clockwise or counterclockwise around the box, using each letter only once.

9 WORD MORPH

Change READ to BOOK in four steps, with a legitimate English word at each step, changing one letter at a time.

READ

_ _ _ _

_ _ _ _

_ _ _ _

BOOK

Answers

1. 715 × 46 = 32,890

2.

1	2	3	4
3	4	1	2
4	3	2	1
2	1	4	3

3. CORRECT.

4. "The day is done, and the darkness / Falls from the wings of Night, / As a feather is wafted downward / From an eagle in his flight."

5. "Did you notice that Camelot can be anagrammed into male cot?" (A = 26, B = 25, and so on.)

6. Eight.

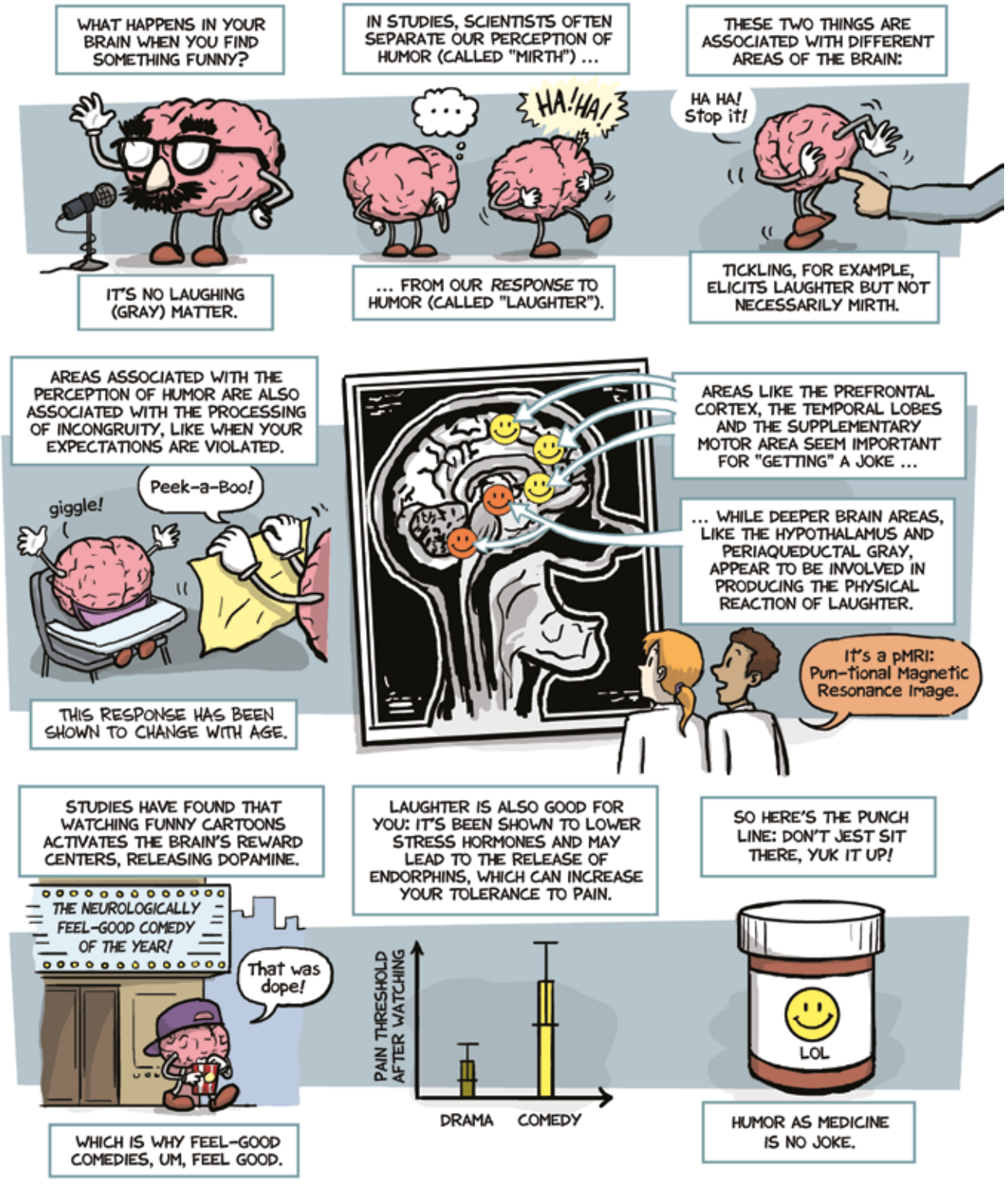
7. The missing letter is "W": WHILE, SWERVE, SWINGS, WINDS.

8. BOTTLING.

9. READ, ROAD, ROOD, ROOK, BOOK.

The Brain's Funny Bone

BY DWAYNE GODWIN & JORGE CHAM



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

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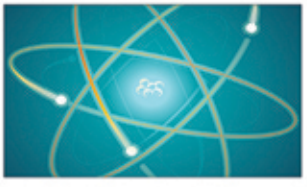

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