

# SCIENTIFIC AMERICAN **MIND**

BEHAVIOR • BRAIN SCIENCE • INSIGHTS

March/April 2016

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

## AUTISM: It's Different in Girls

*page 48*

# THE BEST DIET FOR YOUR BRAIN

**Optimal Eating  
to Stay Happy  
and Sharp**



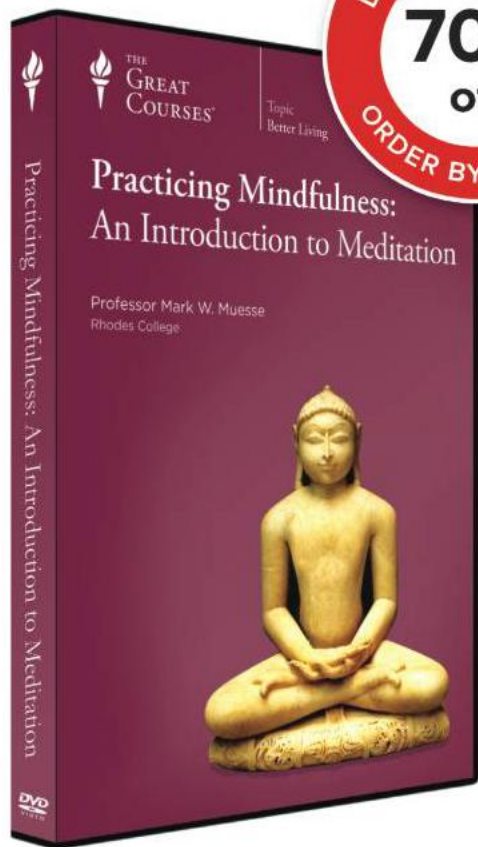
**Reading between  
the "Likes"**  
What Social Media  
Reveals about Us

**How Imaginative  
Play Boosts  
Learning**





THE  
GREAT  
COURSES®



## Discover the Essence of Mindful Meditation

In recent decades, science has confirmed that meditation, when correctly practiced, offers lasting benefits for your physical, mental, and emotional health. Now, in **Practicing Mindfulness: An Introduction to Meditation**, experienced meditator and professor Mark W. Muesse gives you a clear understanding of the essence of meditation—and how best to practice it.

In 24 detailed lectures filled with guided exercises, he teaches you the principles and techniques of sitting meditation, the related practice of walking meditation, the use of meditative awareness in activities such as eating and driving, and more. Emphasizing clarity and practical understanding, his course will leave you with a solid basis for your own practice and for bringing meditation's empowering benefits into every area of your life.

**Offer expires 03/16/16**

**THEGREATCOURSES.COM/5MIND**  
**1-800-832-2412**

## Practicing Mindfulness: An Introduction to Meditation

Taught by Professor Mark W. Muesse  
RHODES COLLEGE

### LECTURE TITLES

1. Mindlessness—The Default Setting
2. Mindfulness—The Power of Awareness
3. Expectations—Relinquishing Preconceptions
4. Preparation—Taking Moral Inventory
5. Position—Where to Be for Meditation
6. Breathing—Finding a Focus for Attention
7. Problems—Stepping-Stones to Mindfulness
8. Body—Attending to Our Physical Natures
9. Mind—Working with Thoughts
10. Walking—Mindfulness While Moving
11. Consuming—Watching What You Eat
12. Driving—Staying Awake at the Wheel
13. Insight—Clearing the Mind
14. Wisdom—Seeing the World as It Is
15. Compassion—Expressing Fundamental Kindness
16. Imperfection—Embracing Our Flaws
17. Wishing—May All Beings Be Well and Happy
18. Generosity—The Joy of Giving
19. Speech—Training the Tongue
20. Anger—Cooling the Fires of Irritation
21. Pain—Embracing Physical Discomfort
22. Grief—Learning to Accept Loss
23. Finitude—Living in the Face of Death
24. Life—Putting It All in Perspective

**Practicing Mindfulness:**  
An Introduction to Meditation  
Course no. 1933 | 24 lectures (30 minutes/lecture)

**SAVE UP TO \$185**

DVD ~~\$254.95~~ **NOW \$69.95**  
CD ~~\$179.95~~ **NOW \$49.95**

+\$10 Shipping, Processing, and Lifetime Satisfaction Guarantee  
Priority Code: 122441

For over 25 years, The Great Courses has brought the world's foremost educators to millions who want to go deeper into the subjects that matter most. No exams. No homework. Just a world of knowledge available anytime, anywhere. Download or stream to your laptop or PC, or use our free mobile apps for iPad, iPhone, or Android. Over 550 courses available at [www.TheGreatCourses.com](http://www.TheGreatCourses.com).

**EDITOR IN CHIEF AND SENIOR VICE PRESIDENT:**  
 Mariette DiChristina

**EXECUTIVE EDITOR:** Fred Guterl  
**MANAGING EDITOR:** Claudia Wallis  
**SENIOR EDITOR:** Kristin Ozelli  
**ASSOCIATE EDITOR:** Daisy Yuhas  
**EDITOR AT LARGE:** Gary Stix

**ART DIRECTOR:** Patricia Nemoto  
**ASSISTANT ART DIRECTOR, IPAD:** Bernard Lee  
**PHOTO RESEARCHER:** Liz Tormes

**CONTRIBUTING EDITORS:**  
 Gareth Cook, Robert Epstein, Ferris Jabr,  
 Emily Laber-Warren, Karen Schrock Simring,  
 Victoria Stern, Sandra Upson

**COPY DIRECTOR:** Maria-Christina Keller  
**SENIOR COPY EDITOR:** Daniel C. Schlenoff  
**COPY EDITOR:** Aaron Shattuck  
**PREPRESS AND QUALITY MANAGER:**  
 Silvia De Santis

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

**SENIOR PRODUCT MANAGER:** Angela Cesaro  
**PRODUCT MANAGER:** Cianna Kulik  
**DIGITAL PRODUCTION MANAGER:** Kerrissa Lynch  
**WEB PRODUCTION ASSOCIATES:**  
 Nick Bisceglia, Ian Kelly

**EDITORIAL ADMINISTRATOR:** Ericka Skirpan  
**SENIOR SECRETARY:** Maya Hartly

**SENIOR PRODUCTION MANAGER:** Christina Hippeli  
**ADVERTISING PRODUCTION CONTROLLER:**  
 Carl Cherebin  
**PRODUCTION CONTROLLER:** Brittany DeSalvo

**BOARD OF ADVISERS:**

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

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

**R. DOUGLAS FIELDS:** Neuroscientist, Bethesda, Md.

**SANDRO GALEA:** Dean and Professor,  
 Boston University School of Public Health

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

**CHRISTOF KOCH:** President and Chief Scientific  
 Officer, Allen Institute for Brain Science

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

**STEPHEN L. MACKNIK:** Professor of Ophthalmology,  
 SUNY Downstate Medical Center

**SUSANA MARTINEZ-CONDE:** Professor of  
 Ophthalmology, SUNY Downstate Medical Center

**JOHN H. MORRISON:** Director, California National  
 Primate Research Center, and Professor,  
 Department of Neurology, School of Medicine,  
 University of California, Davis

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

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

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



## Telltale Patterns

Have you heard about the brain benefits of blueberries? How about caffeine? Or red wine? And let's not forget kale, which seems to be good for all that ails you.

There's no end to the assertions about how one food or another will sharpen your concentration, even out your moods or protect your brain from the ravages of time. Alas, such magic exists only in our hopeful hearts (and popular media). As medical journalist Bret Stetka writes in our cover story: "There is probably no single ingredient, no happy seed from the jungles of beyond, that is sure to secure a better mood or mental acuity into old age." But the good news, he reports, is that evidence indicates there are "specific dietary patterns—calibrated by millions of years of human evolution—that boost our cognitive and psychological fitness."

Starting on page 26, Stetka serves up the evidence for dietary patterns—such as the fish-and-vegetable-rich Mediterranean diet—that are associated with better brain health. He explores why a growing number of mental health experts are incorporating diet into treatment for major depression and other disorders as part of a burgeoning new field called nutritional psychiatry.

Other kinds of behavioral patterns are at the heart of several features in this issue. For decades the criteria for diagnosing autism have been largely defined by how the disorder appears in boys, who are roughly four times as likely as girls to be diagnosed with the disorder. But what if symptoms follow a different pattern in females? Writer Maia Szalavitz presents new evidence that this is the case and that, as a result, many girls and women with autism have been overlooked or misdiagnosed. Turn to page 48 to read about "The Invisible Girls."

Fragile X syndrome is well established as the leading genetic cause of autism. In the late 1990s, however, researchers began to notice some odd patterns of behavior and health affecting the mothers and grandfathers of kids with this condition. In "The Carriers," on page 34, Columbia University psychiatrist Anne Skomorowsky unwinds the mystery of how variants of the fragile X gene can cause a stunning array of symptoms, including infertility in women.

Over the past 20 years an entirely new human activity has exploded globally: social media. In "Status Update," on page 62, data scientist Johannes C. Eichstaedt of the University of Pennsylvania shows how researchers are using telltale patterns in tweets and Facebook posts to predict the mental and physical health of communities and individuals. Think about *that* the next time you update your status!

Claudia Wallis  
 Managing Editor  
 MindEditors@sciam.com



**FEATURES**



**26 In Search of the Optimal Brain Diet**

The field of nutritional psychiatry is taking off as scientists home in on the main ingredients for good mental health and cognitive staying power.

BY BRET STETKA



**34 The Carriers**

A genetic anomaly—the fragile X premutation—puts millions of people at risk for infertility and a neurodegenerative disorder they have probably never heard of.

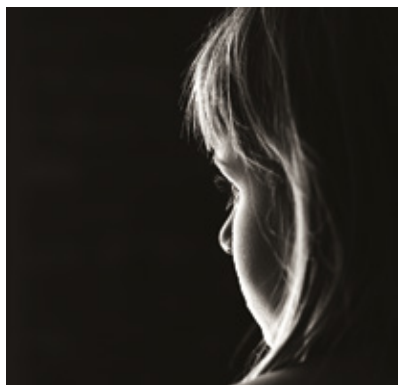
BY ANNE SKOMOROWSKY



**42 The Fantasy Advantage**

Children may absorb some lessons better when they are wrapped in magic and imagination.

BY DEENA WEISBERG



**48 The Invisible Girls**

New research suggests that autism often looks different in females, many of whom are being misdiagnosed and missing out on the support they need.

BY MAIA SZALAVITZ



**56 Can Kids Really Learn to Cooperate?**

Yes—especially if frazzled parents steal a few lessons from game theory. (Book excerpt)

BY PAUL RAEURN AND KEVIN ZOLLMAN



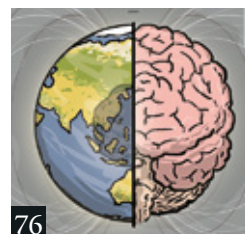
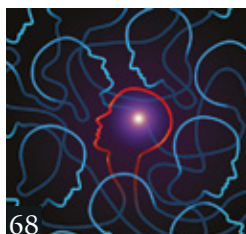
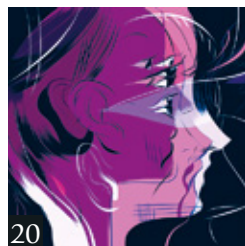
**62 Status Update**

Using powerful new tools, psychologists and data scientists are mining social media to assess mental and physical health from afar.

BY JOHANNES C. EICHSTAEDT



## DEPARTMENTS



### 1 From the Editor

### 4 Letters

### 7 Head Lines

Mind and media: Facebook envy, e-mail angst, teens and texting.

Psychiatric drugs can affect moral decision making.

Teething toys and language learning.

Is sex once a week best for couples?

How to ace a job interview.

Clean teens at risk of opioid abuse.

The world's first safe "smart drug."

Benefits of childhood adversity.

### 18 Illusions

How the magicians of the animal kingdom use visual trickery.

BY SUSANA MARTINEZ-CONDE AND STEPHEN L. MACKNIK

### 20 Perspectives

Is There a Better Way to Diagnose Psychosis?

A new study points the way toward more biologically based diagnosis.

BY THOMAS R. INSEL

### 22 Consciousness Redux

Lessons from a long-forgotten epidemic about the science of sleep.

BY CHRISTOF KOCH

### 68 Reviews and Recommendations

The brain's rage circuit. Powerful insights from social psychology. Upside of uncertainty: Q&A with tech policy expert Jamie Holmes.

### 70 Ask the Brains

Does creativity decline with age? Does it help to confess our secrets?

### 73 Head Games

Test your skills with Mensa puzzles.

### 76 Mind in Pictures

Mental Compass.

BY DWAYNE GODWIN AND JORGE CHAM

Scientific American is a division of Nature America, Inc., an entity of Springer Nature, which owns or has commercial relations with thousands of scientific publications (many of them can be found at [www.springernature.com/us](http://www.springernature.com/us)). *Scientific American Mind* maintains a strict policy of editorial independence in reporting developments in science to our readers.

Scientific American Mind (ISSN 1555-2284), Volume 27, Number 2, March/April 2016, published bimonthly by Scientific American, a trading name of Nature America, Inc., 75 Varick Street, 9th Floor, New York, N.Y. 10013-1917. Periodicals postage paid at New York, N.Y., and additional mailing offices. Canada Post International Publications Mail (Canadian Distribution) Sales Agreement No. 40012504. Canadian BN No. 127387652RT; TVQ1218059275 TQ0001. Publication Mail Agreement #40012504. Canada Post: Return undeliverables to 2835 Kew Dr., Windsor, ON N8T 3B7. Subscription rates: one year (six issues), U.S. \$29.99; Canada, \$34.99 USD; elsewhere, \$39.99 USD. Postmaster: Send address changes to Scientific American Mind, P.O. Box 3187, Harlan, Iowa 51537. To purchase additional quantities: U.S., \$10.95 each; elsewhere, \$13.95 each. Send payment to SA Mind, P.O. Box 4002812, Des Moines, Iowa 50340.

For subscription inquiries, call (888) 262-5144. To purchase back issues, call (800) 925-0788. Printed in U.S.A. Copyright © 2016 by Scientific American, a division of Nature America, Inc. All rights reserved.



PRESIDENT: Steven Inchcoombe  
 EXECUTIVE VICE PRESIDENT: Michael Florek  
 EXECUTIVE VICE PRESIDENT GLOBAL ADVERTISING  
 AND SPONSORSHIP: Jack Laschever  
 PUBLISHER AND VICE PRESIDENT: Jeremy A. Abbate  
 ASSOCIATE VICE PRESIDENT, BUSINESS DEVELOPMENT:  
 Diane McGarvey  
 VICE PRESIDENT, CONSUMER MARKETING:  
 Christian Dorbandt  
 DIRECTOR, INTERNATIONAL DIGITAL DEVELOPMENT:  
 Richard Zinken  
 ASSOCIATE CONSUMER MARKETING DIRECTOR:  
 Catherine Bussey  
 SENIOR CONSUMER MARKETING MANAGER: Lou Simone  
 CONSUMER MARKETING OPERATIONS MANAGER:  
 Kay Floersch  
 E-COMMERCE MARKETING MANAGER: Evelyn Veras  
 MARKETING DIRECTOR: Diane Schube  
 SALES DEVELOPMENT MANAGER: David Tirpack  
 PROMOTION ART DIRECTOR: Maria Cruz-Lord  
 MARKETING RESEARCH DIRECTOR: Rick Simone  
 ONLINE MARKETING PRODUCT MANAGER: Zoya Lysak  
 MARKETING AND CUSTOMER SERVICE COORDINATOR:  
 Christine Kaelin  
 SENIOR COMMUNICATIONS MANAGER: Rachel Scheer  
 SENIOR INTEGRATED SALES MANAGERS: Jay Berfas,  
 Matt Bondlow, Janet Yano (West Coast)  
 SALES REPRESENTATIVE: Chantel Arroyo  
 CUSTOM PUBLISHING EDITOR: Lisa Pallatroni  
 RIGHTS AND PERMISSIONS MANAGER: Felicia Ruocco  
 SENIOR ADMINISTRATOR, EXECUTIVE SERVICES:  
 May Jung

**HOW TO CONTACT US**

**FOR ADVERTISING INQUIRIES:**

Scientific American Mind  
 1 New York Plaza, Suite 4500  
 New York, NY 10004-1562  
 212-451-8893  
 fax: 212-754-1138

**FOR SUBSCRIPTION INQUIRIES:**

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

www.ScientificAmerican.com/Mind

**TO ORDER REPRINTS:**

Reprint Department  
 Scientific American Mind  
 1 New York Plaza, Suite 4500  
 New York, NY 10004-1562  
 212-451-8877  
 fax: 212-451-8252  
 reprints@sciam.com

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

Permissions Department  
 Scientific American Mind  
 1 New York Plaza, Suite 4500  
 New York, NY 10004-1562  
 212-451-8546  
 www.ScientificAmerican.com/permissions  
 Please allow three to six weeks  
 for processing.



**IMAGINE THAT**

**Two words: What if?** Like every family, mine has legends and folklore that may or may not be true. For the longest time one legend was that my father was recruited coming out of World War II by none other than the FBI. My brothers, sisters and I usually laughed it off. But a few years ago that legend became fact when my older brother uncovered a letter addressed to our father from one J. Edgar Hoover. In it, Hoover told my father that since he did not hear back from him, he was going on the assumption that my father was not interested in joining the FBI. My siblings and I were floored.

What if our father *had* accepted the offer? It would have meant a move to a smaller town. In the spirit of your story, “Why We Imagine,” by Felipe de Brigard, I got to thinking how different all of our lives would be—if we would even be here in the first place.

Steve Olenski  
via e-mail

**THE MIND OF A COP**

**I am chilled** by but greatly appreciative of your in-depth article “When Cops Lose Control,” by Rachel Nuwer. I hear many arguments from people around me who try to downplay the idea that race could be a significant factor in these killings. I now understand that people may say they are not racist, but unconsciously

their behavior may still be governed by stereotypes that associate black people with threats. There may be a disconnect between what is understood by the conscious and unconscious mind.

One question that remains with me is whether the officers who have been involved in these shootings can ever participate in future research. They are the ones who have actually been to the emotional place that we all discuss ad nauseam. I wonder if these officers could give us any insight for future training programs and the prevention of these heart-breaking stories.

Thank you for the stimulating articles; I look forward to next month.

Kayla R. Dadgar  
via e-mail

**As a law-enforcement officer** for 41 years, I agree that officers must police fairly and equitably to all, not lose control and only use the necessary and appropriate force to bring a situation under control. As unfortunate as it is, deadly force is at times unavoidable to save the lives of citizens or the officer’s own life. Policing is a dangerous profession, and officers want to return home to their families at the end of their shift, so they use their training, experience and instincts to do so.

The fact is, nationwide, police come in contact with citizens thousands of times every day and only a minute percentage of those contacts result in any force being used, and of those only a small fraction result in the use of deadly force. When deadly force is used and justifiable, unlike on television and in the movies, it takes a mental and physical toll on the officer. Some quit the profession. I have never known an officer who wants to take the life of another.

Jeffrey Chudnow  
via e-mail

**EDITORS’ NOTE:** We received several letters about our error in listing Trayvon Martin as one of the recent casualties of police conflict. Martin was shot by a neighborhood watchman, not by a police officer. We caught the mistake in time for online publication of





## What Really Causes Autism

The mystery is largely solved: autism is primarily a genetic disorder but a complex one that is slowly yielding its secrets

Several actors stand around a circle of swirling colors—black, gold and white painted in the middle of the stage. Interspersed among them are twice as many children. Most of the younger players look with blank, empty expressions, intellectually or physically. One girl, about 12 years old, sits quietly in an electric wheelchair. The professional cast take turns, enacting their young charges into the center of the colorful “island,” where they play simple games—practicing facial expressions and charting words—all based on emotional scenes from Shakespeare’s play *The Tempest*.

By Simon Makin

Every child engages, even those who initially seem uncommunicative. Many react with unquestionable joy. It is possibly one of the most moving things I’ve ever witnessed. But this experience isn’t really for the audience. My ticket reads “*The Tempest*, suitable for 8-14-year-olds with autism,” and the production showcases a novel therapy for autism spectrum disorder (ASD). The approach—pioneered by Kelly Hammer of the Royal Shakespeare Company and developed in conjunction with psychologists at Ohio State University—is unproven. But the idea behind it is compelling: core abilities included in diagnoses such as working with what is often described as the main trial of impairment in ASD: problems with social interaction, communication and imagination. In short, the actors are gifted in the very things that are deficient in the young participants and able to teach progressively across the divide of disability.

The discovery of the children onstage is a willing reflection of just how complicated autism is behind the scenes. An official diagnosis calls for the presence of difficulties described above, along with repetitive behaviors—typically hand flapping, rocking or head banging—before the age of three. That said, ASD unfolds within a wide range of both physical and neurological symptoms. High-functioning people with autism, including those with Asperger’s syndrome (a diagnosis that was removed from the American Psychiatric Association’s manual of disorders), have normal and sometimes high IQs and often show only mild to moderate social deficits. At the other end of the spectrum, children with profound autism are often intellectually disabled and so severely disabled that they seem locked in a world of their own.

Illustration by ALEX WILLIAMSON

MIND.ScientificAmerican.com SCIENTIFIC AMERICAN MIND 47

the article but not in time to fix the print article. We ran a correction in the January/February 2016 issue. We deeply regret the error.

### DON'T CURE MY AUTISM

“What Really Causes Autism,” by Simon Makin, was an excellent read. The author summed up research on the cause of autism well. But the article approached the issue not from the standpoint of an intellectual endeavor but of working toward a cure for a disease. Research such as that featured in the article is funded by organizations run by people without autism, generally with the aim of supporting and listening to the nonautistic parents of autistic children rather than to autistic people themselves.

Autistic people, including me, generally do not want a cure. Autism affects every part of a person and gives us a unique life experience that is sometimes better than that of a nonautistic person, as well as giving us a disability. Autism advocacy groups run by autistic people do not want a cure and instead advocate for better accommodations and acceptance. Finding the cause of autism is a fascinating endeavor, but the knowledge gained should be used to have a better understanding of autism, improve diagnosis and find better ways to make life easier for autistic people, in ways that we ask for.

One more note: Autistic people such as myself do not prefer person-first language (such as “people with autism”), because autism is central to our identity, like race and gender. The attitude behind person-first language, that it stresses the fact that it is in fact a person, implies that it is natural to think of autistic people as something other than people, which autistic people find dehumanizing and undesirable.

“Autistic Reader” via e-mail

### HIDDEN DELUSIONS

The statement in “The Schizophrenia Spectrum,” by Simon Makin [Head Lines], that “most people do not know what it feels like ... to have delusions,” though true, is quite misleading. As opposed to anxiety, which is indeed a feeling, and one that most people feel from time to time, delusions are beliefs, and no particular feeling is attached to them. There is nothing that it feels like to have a belief that does not match reality, even though most people have many such beliefs.

We only say that people have delusions when their beliefs are out of line with the dominant beliefs of their society. A very large number of Republicans believe that climate change is not real, which means that their beliefs do not

match reality, but those of us who believe that they are deluded don’t diagnose them as having schizophrenia, because so many people share this wrong belief.

I don’t see the point of a survey where the researchers do not understand the use of the words in their questions.

Naomi Goldblum via e-mail

### GET OLD, GET HAPPY

“The Positivity Effect,” by Marta Zaraska, discounted some very important economic reasons that make old people happy. As a child of the Great Depression and now pushing 80, I clearly remember the poverty and deprivation of childhood and my struggle as a single mother working for minimum wage and living in substandard rentals. Life was like trying to run through the La Brea Tar Pits in snowshoes.

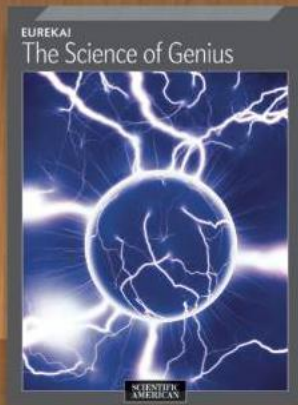
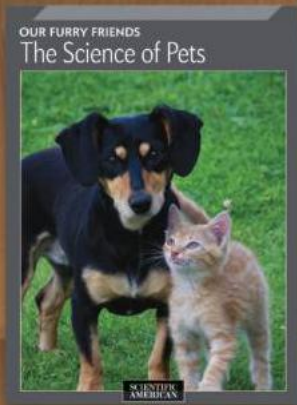
There were millions of women like me. But in old age, I have my small pension and Medicare, and my children are grown, so no financial burden. I’m happily remarried, and we built a home, mortgage-free. Of course, we have health issues but so do the young. I had cancer, and he had a heart attack. Considering that most of our relatives and friends are dead, we are delighted to wake up alive each morning. What is there to be unhappy about? Old age is the best time of life in the U.S. I heartily recommend it.

S. Clark Soap Lake, Wash.

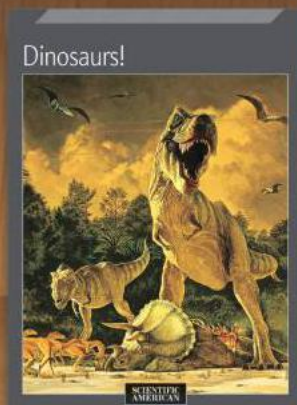
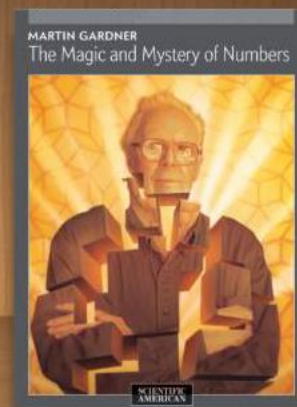
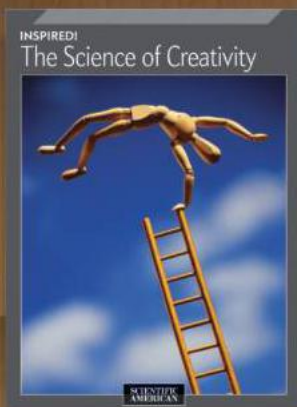
### ERRATUM

In “Synchronized Pupils,” by Diana Kwon [Head Lines, January/February 2016], we misstated Mariska Kret’s affiliation. She is now at Leiden University in the Netherlands.

**HOW TO CONTACT US** FOR GENERAL INQUIRIES OR TO SEND A LETTER TO THE EDITOR:  
 Scientific American Mind  
 1 New York Plaza, Suite 4500  
 New York, NY 10004-1562  
 212-451-8200  
 MindLetters@sciam.com



eBooks  
From the Editors of  
**SCIENTIFIC  
AMERICAN™**



™ Scientific American, Inc.

Start your SCIENTIFIC AMERICAN eLibrary today:  
[books.scientificamerican.com/sa-ebooks](http://books.scientificamerican.com/sa-ebooks)



# Head Lines

A USER'S GUIDE TO THE BRAIN



Your Brain  
on Social Media



## SOCIAL MEDIA AND THE MIND

How do hours of Facebook and constant streams of tweets and Snapchats affect our cognition and mental health? Scientists are beginning to find out, as shown by the research highlighted here. Other researchers use social media as a tool to investigate human behavior: turn to page 62 to see what they are learning.

ILLUSTRATIONS BY HANNAH BARCZYK



## Green with Facebook Envy

Changing how you interact with social media may alleviate its negative effects

Spending a lot of time on Facebook is linked to diminished well-being, according to many studies. Yet questions linger about cause and effect—perhaps people who are already lonely simply spend more time on social media. New studies reveal that Facebook can indeed affect mood and mental state, and whether the effect is positive or negative depends heavily on how a person interacts with his or her contacts. Several of the new findings reveal that when Facebook hurts, the underlying culprit is—you guessed it—envy.

A study published in February 2015 in *Computers in Human Behavior* surveyed 736 college students and found that when Facebook evoked envy, it increased symptoms of depression. But a March 2015 study from the same journal found that Facebook use can actually decrease depression if users sign on seeking social connection and support and then feel they have received it.

Those studies did not attempt to figure

out why some people experienced envy and others did not, but other studies have found that the way a user interacts with Facebook may be crucial. For example, researchers at the University of Michigan and KU Leuven in Belgium tracked 173 students' habits over time and found that passive use—browsing news feeds, for example—led to reduced well-being by increasing feelings of envy. Active use, such as posting and commenting, had no such effect, according to the two studies, published in April 2015 in the *Journal of Experimental Psychology: General*.

Another important factor seems to be how close you are to the people with whom you interact. Two related experiments published in November 2015 in *Computers in Human Behavior* were the first to explore the role of relationship strength in users' emotional responses to posts on the site. Among a sample of 207 American adults and 194 German college students, the researchers found that people more often felt positive emotions than negative ones when browsing the site, and their emotions were amplified when reading posts from someone they knew well.

“Empathy is more pronounced when the relationship is closer, so one is more likely to ‘catch’ the happiness of a close friend than a casual acquaintance,” says study co-author Ruoyun Lin, a doctoral student at the Leibniz Institute’s Knowledge Media Research Center in Tübingen, Germany. Close friends can inspire envy, too, but the researchers found that this type of envy tended to be benign—the overall reaction to a friend’s good news was usually positive.

The takeaway, the experts say, is that you can control how Facebook makes you feel. If you tend to compare yourself with others or get envious easily, you might consider limiting your time spent on social-networking sites or make a conscious effort to use them in active rather than passive ways. “Our findings show the importance of human agency,” says Edson C. Tandoc, Jr., co-author of the February 2015 study and assistant professor in the division of journalism and publishing at Singapore’s Nanyang Technological University. “It is not technology such as Facebook that affects our feelings per se but rather how we use it.” —*Tori Rodriguez*

Older adults who have face-to-face interactions with family and friends have a lower risk of depression compared with those who keep in touch via phone or e-mail.



## Waiting for That E-Mail

A study of 16 billion e-mails reveals how response patterns vary by age

There's nothing like firing off a carefully crafted e-mail and then waiting for what seems like an eternity for a reply. When you finally do get an answer, you might still be frustrated. What do you make of the fact that it is only 10 words long?

We now have some clues about typical e-mail response patterns, thanks to a recent study drawing on 16 billion e-mails sent by more than two million people. The participants were Yahoo Mail users who allowed their anonymized data to be used in what appears to be the largest-ever analysis of e-mail behavior. The researchers, based at the University of Southern California and Yahoo Labs, used algorithms to mine data about the times messages were sent and the number of words they contained, among other factors. Here are some of the surprising revelations:

- The most likely length of a reply is just five words.
- More than 90 percent of replies are sent within a day.
- The younger you are, the faster and more terse your reply (*box at right*).
- Messages sent on weekday mornings got the fastest responses.
- E-mails with attachments took twice as long to get a reply as those without.

The researchers included only users who wrote to one another at least five times in the months covered by the study period. After mining the data, the researchers found they could use their algorithm to predict when an e-mail conversation was nearing its end. For the first half of a dialogue, correspondents usually developed similar reply times and e-mail lengths, lobbing messages back and forth at a regular clip. Yet that similarity decreased as the conversation trailed off.



Many conversations ended with a long lag before one correspondent sent a final brief reply.

Of note to the anxious e-mailer: the more words in a reply, the longer it tended to take for the writer to send it—but only up to 100 words. Beyond that, the time for a reply actually dropped slightly, except for in the oldest age group. So if you're expecting a hefty reply to your mission-critical missive, it won't necessarily take any longer than a 100-word message. That may be some comfort while you wait on the edge of your seat.

—Veronique Greenwood

AGE GROUP	MEDIAN REPLY TIME	MEDIAN REPLY LENGTH
Teenagers	13 minutes	17 words
20-35	16 minutes	21 words
36-50	24 minutes	31 words
51 and up	47 minutes	40 words

## How Boys and Girls Text

Texting has become the most popular form of communication among people under 30. One recent study found that students spend less than six minutes, on average, on schoolwork before being distracted by social media and texting. For a small percentage of teens, texting becomes compulsive—they may try to text less and fail or feel anxiety and frustration if they are kept away from texting. A new study from the American Psychological Association evaluated how 211 girls and 192 boys communicated via text and found notable gender differences in overall behavior and compulsive use:

- Teenage girls use texting for social connection, whereas boys mostly use it to convey information.
- Boys and girls send about the same number of texts every day, but girls are more likely to become compulsive texters.
- Teenage girls who compulsively text see a steeper decline in their grades than their compulsive male counterparts. The researchers suggest the social content of girls' messages may be more likely to distract them from their academic tasks.
- Compulsive texting also appears to affect girls' mental health more than boys', perhaps because girls are more prone to text about negative feelings and to ruminate on those feelings.

—Victoria Stern

46 percent of Twitter users say they often tweet as a way of dealing with or venting anger.

37 percent of them hope the person or group they are angry at will read their rants.





(PHARMA WATCH)

## Psychiatric Drugs May Affect Moral Decisions

By tweaking brain chemistry, they can alter how healthy individuals react to social dilemmas



Morality is malleable, according to much research. Our judgment calls change depending on a host of factors—our mind-set, how hungry we are, whether we feel clean or dirty, the ambient air temperature, and the list goes on. Drugs that affect brain chemistry can alter moral decision making, too, a growing body of work outlined below has found. For now scientists are using these common psychiatric drugs as tools to understand the brain mechanisms underlying morality. Some hope one

day to develop a pharmaceutical remedy for dangerous or harmful behavior.

Researchers conduct the studies on healthy individuals; the results do not necessarily mean that patients who have prescriptions for these drugs are experiencing these moral modifications. Their underlying brain chemistry might be different. As the number of people taking the drugs rises, however, it is important to consider that there may be unexpected side effects. —*Diana Kwon*

DRUG	WHAT IT IS USED FOR NOW	HOW IT WORKS	HOW IT MODIFIES MORAL JUDGMENT	IMPLICATIONS
Propranolol	Treats the physical symptoms of anxiety. Also prescribed for various heart conditions, including hypertension, angina and arrhythmias.	Known as a beta-blocker, it prevents the transmission of neural signals by blocking receptors for stress hormones (adrenaline and nor-adrenaline) located in the peripheral nervous system and various brain regions, including the amygdala. This reduces blood pressure and slows heart rate.	Makes people less willing to endorse utilitarian solutions—such as sacrificing one for the good of the many—when the scenario involves “up close and personal” harm to innocent individuals. Other studies reveal that it can significantly reduce implicit, but not explicit, racial prejudice.	Propranolol reduces emotional arousal, so the results suggest that our aversion to harming others is not driven by emotional arousal—contrary to prominent theories. The racism studies support the notion that there is an emotional component in our subconscious attitudes toward out-groups.
SSRIs (e.g., Prozac, Zoloft, Paxil, Celexa)	Treat depression and anxiety disorders.	Selective serotonin reuptake inhibitors prevent neurons from mopping up serotonin, prolonging the neurotransmitter's effects in the brain.	Researchers have found that SSRIs make people less likely to reject unfair offers and more reluctant to cause harm to themselves and others. (An important exception: when a depressed person first starts taking an SSRI, there is a small but real increase in the risk that he or she will attempt suicide.)	Studies have shown that SSRI treatment can slightly reduce impulsive aggression in those with a history of such behavior and in those with psychopathic traits. Researchers want to find a way to more selectively target the serotonin receptors involved in aggression.
Levodopa	Treats the dopamine deficit in Parkinson's disease.	Drug molecules are chemical precursors of dopamine that cross the blood-brain barrier, where they are converted to dopamine by enzymes in the nervous system.	Boosting dopamine levels seems to reduce hyperaltruistic behavior, the tendency to outweigh others' pain over our own. In some studies, people become more selfish and less averse to harming others for profit. Other studies find potentially conflicting results—another dopamine drug, tolcapone, led people to distribute money more fairly.	A common mechanism could underlie both these effects, namely the desire to reduce inequity—whether it benefits or harms others. Much more research is needed to understand dopamine's complex role in moral decision making. Whatever that role may be, researchers suspect that Adderall and Ritalin, which also raise dopamine levels, could have similar effects.
Oxytocin	Occasionally used to induce uterine contractions during labor; some combination of contraceptive pills and glucocorticoids are known to increase oxytocin levels.	A hormone and neurotransmitter that is naturally produced in the brain and then released into the bloodstream.	Can induce trusting behavior and increase ethnocentrism as well as envy and gloating. Some new studies have seen sex-specific effects: oxytocin can promote self-interest in men but increase altruistic behavior in women.	To date, most studies have been conducted on men because menstrual cycles lead to fluctuation of oxytocin levels in women. But the new sex-specific findings point to the need for further research, considering the fact that women are more likely to be exposed to drug-enhanced oxytocin levels.



## Don't Overuse That Pacifier!

Babies need free tongue movement to learn speech

You might assume that listening and speaking are different processes, but more and more evidence suggests these tasks are inextricably linked. The latest piece of the puzzle comes from a study of babies with teething toys. The findings support a theory that our perception of speech is dependent on brain areas that control mouth movements.

Alison Bruderer, a cognitive scientist at the University of British Columbia, gave six-month-old infants who were not yet starting to talk common teething toys that immobilized their tongue. Then she played recordings of an English *d* sound and a Hindi *d* sound made by moving the tongue farther back on the palate. Babies of this age from any culture reliably notice the difference between these sounds, as indicated by an increase in attention paid when the sound changes. When the babies were using the teething toys, however, they did not appear to notice the difference in sounds. The results suggest that even babies who have not yet started speaking use their tongue to help them understand speech.

Evidence in adults also suggests a link between tongue movement and speech perception. Neurolinguist William Katz of the University of Texas at

Dallas used real-time three-dimensional images to show native English speakers the position of their tongue as they tried to make a made-up sound not found in any known language. Participants were more likely to make the sound correctly when they had this visual feedback. Katz says the technology might help people improve pronunciation in a second language or even relearn speech after a stroke.

Both studies are aligned with the motor theory of speech perception: our perception of speech sounds is in some way dependent on the knowledge of how we would position our lips, teeth and tongue if we were making those sounds ourselves. Yet it is unclear to what degree we rely on that information. The strongest version of the theory suggests that the sound of spoken speech does not matter; it is just another clue as to how a speaker is moving his or her mouth. It is mentally mirroring the speaker's movements that makes us understand, not auditory recognition.



“I would be a little more moderate than that,” Bruderer says. She is curious whether the ability to move our lips and tongue is critical to learning speech—longer-term studies would be needed to determine if the differences in perception she found could cause a delay in language acquisition. She also hopes to investigate whether oral malformations such as cleft palate and tongue-tie affect speech perception. —Meredith Knight

## Why Sleep Deprivation Makes You Crabby

Lack of sleep blunts emotional reactions, especially positive feelings



When you're tired, it can seem as if everything is filtered through a negative lens. That might be because your positive lens is fuzzy when you are sleep-deprived, according to findings of two related studies published last year in the *Journal of Psychosomatic Research*. Two groups of college students completed a series of tests to assess their emotional responses to negative and positive pictures, similar to those often shown on the nightly news. Twenty-eight students completed the test at various points throughout a night of simulated shift work after getting five hours of sleep, and 31 students did the same after staying awake for more than 24 hours. The students completed a short survey to indicate how each picture made them feel.

The researchers found that all subjects' emotional response to the photographs became increasingly dampened as the night wore on, and their reaction to positive stimuli was even more subdued—that is, they grew less likely to feel good in response to uplifting pictures. “The human brain is naturally more attentive to negative events,” perhaps as a survival mechanism that keeps us on the alert for life-threatening situations, says study co-author June J. Pilcher, a psychologist at Clemson University. Yet in modern society, life-threatening events are fairly rare, so instead we find ourselves overreacting to the pile of dirty dishes—especially when we, ourselves, are washed-out. —Tori Rodriguez

## INJECTABLE BRAIN IMPLANTS TALK TO SINGLE NEURONS

By using a fine, flexible mesh, researchers have created implants that will last longer and cause less damage

Brain implants have been around for decades—stimulating motor areas to alleviate Parkinson's disease symptoms, for example—but until now they have all suffered from the same limitation: because brains move slightly during physical activity and as we breathe and our heart beats, rigid implants rub and damage tissue. This means that eventually, because of both movement and scar-tissue formation, they lose contact with the cells they were monitoring.

Now a group of researchers, led by chemist Charles Lieber of Harvard University, has overcome these problems using a fine, flexible mesh. In 2012 the team showed that cells could be grown around such a mesh, but that left the problem of how to get one inside a living brain. The solution the scientists devised was to draw the mesh—measuring a few millimeters wide—into a syringe, so it would roll up like a scroll inside the 100-micron-wide needle, and inject it through a hole in the skull.

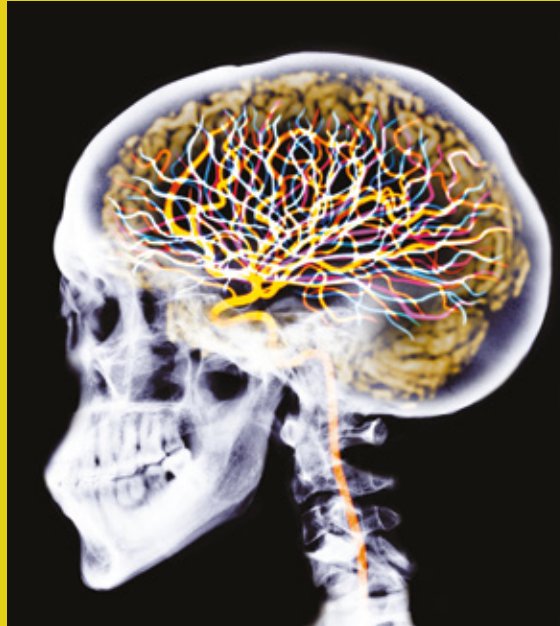
In a study published in *Nature Nanotechnology* last year, the team injected meshes studded with 16 electrodes into two brain regions in mice. The mesh is composed of extremely thin, nanoscale polymer threads, sparsely distributed so that 95 percent of it is empty space. It has a level of flexibility similar to brain tissue. “You’re starting to make this nonliving system look like the biological system you’re trying to probe,” Lieber explains. “That’s been the goal of my group’s work, to blur the distinction between electronics as we know it and the computer inside our heads.”

Once inside, the mesh unfurls (*Illustration at left*)—either enough to meet the sides of brain cavities called ventricles or very slightly if injected into solid tissue—to form a three-dimensional structure. The researchers showed that the implants integrated with tissue to form stable connections, with no inflammation five weeks later. “It’s the dawn of biointegration,”

says Ivan Minev of the Center for Neuroprosthetics at the Swiss Federal Institute of Technology in Lausanne, who was not involved in the work.

The researchers claim the mesh can be positioned with an accuracy approaching the scale of individual neurons. Activity can then be recorded to study the workings of brain circuitry, or neurons can be stimulated for therapeutic applications such as the deep-brain stimulation used to treat Parkinson's disease. One application Lieber envisions is injecting implants into the brains of stroke victims alongside neural stem cells to study how the stem cells grow and alter neural circuitry during recovery. “This opens up unprecedented opportunities, both for fundamental brain science and for any therapeutic applications where you need stability beyond a very short time,” Lieber says. He believes the device could “completely change the picture of what’s possible with electrical brain interfaces.”

—Simon Makin



## Flexible Spinal Implants Help Rats Walk Again

Spinal implants have suffered similar problems as those in the brain—they tend to abrade tissue, causing inflammation and ultimately rejection by the body. Now an interdisciplinary research collaboration based in Switzerland has made a stretchable implant that appears to solve this problem. Like Lieber's new brain implant, it matches the physical qualities of the tissue where it is embedded.

The “e-dura” implant is made from a silicone rubber that has the same elasticity as dura mater, the protective skin that surrounds the spinal cord and brain, explains Stéphanie Lacour, a professor at the school of engineering at the Swiss Federal Institute of Technology in Lausanne. This feature allows the implant to mimic the movement of the surrounding tissues.

Embedded in the e-dura are electrodes for stimulation and microchannels for drug therapy. Ultrathin gold wires are made with microscopic cracks that allow them to stretch. Also, the electrodes are coated with a special platinum-silicone mixture that is stretchable.

In an experiment that lasted two months, the scientists found that healthy rats with an e-dura spinal implant could walk across a ladder as well as a control group with no implant. Yet rats with a traditional plastic implant (which is flexible but not stretchable) started stumbling and missing rungs a few weeks after surgery. The researchers removed the implants and found that rats with a traditional implant had flattened, damaged spinal cords—but the e-dura implants had left spinal cords intact. Cellular testing also showed a strong immune response to the traditional implant, which was minimal in rats with the e-dura implant.

Finally, the researchers implanted the device directly on the spinal cord of paralyzed rats. With a combination of drug therapy and electrical stimulation administered via the e-dura, the rats were able to walk again. Researchers envision the e-dura being used in people with spinal cord injuries, as a brain implant and even to correct nerve damage in other parts of the body.

—Esther Hsieh





## Keeping Up with the Joneses—in Bed

Couples who have sex at least once a week are happiest, perhaps because that rate is thought to be the norm

How much sex is enough? You might question the premise of that query, but new research reports that there's a limit to the benefits of carnal pleasures. Beyond a certain frequency, more sex does not mean more happiness. One possible reason: as long as we are doing it as often as our neighbors are, we're content.

For a recent paper in *Social Psychological and Personality Science*, Amy Muise, Ulrich Schimmack and Emily Impett, all at the University of Toronto Mississauga, analyzed three survey samples comprising more than 30,000 Americans. They found that among couples, sex frequency positively correlated with satisfaction in life, confirming earlier reports. (They found no such link for singles.) The difference in happiness between those who had sex less than once a month and those who had sex once a week was at least as great as that between those earning less than \$15,000 a year and those earning more than \$100,000. Direction of causality is unclear; their analysis suggested that sex frequency increases relationship satisfaction, which increases happiness, but they also found evidence for the reverse pathway, in which general life satisfaction increases relationship satisfaction, which in turn increases sex frequency.

Unlike in previous studies, a subtler pattern also appeared: at frequencies greater than once a week, the happiness graph flattened out. The reason "is an open question that we are exploring," Muise says. Her team thinks one possibility is that people are satisfied when they are doing it as much as they think they should be, a standard set by their peers. Indeed, the average for couples is once a week.

In support of this idea, Tim Wadsworth, a sociologist at the University of Colorado Boulder, reported in 2014 in *Social Indicators Research* that happiness is positively correlated with sex frequency but negatively correlated with the sex frequency of others in the same demographic group, a rate people probably surmise from conversation and media. "How much sex is appropriate, like so many other questions, depends on what we think is 'normal,'" Wadsworth says. One sees the same trend with income: a 2010 paper in *Psychological Science* reported that income rank among peers predicted happiness better than did absolute income.

So if you are worried you and your sweetheart are failing to keep up with the Joneses, there is an easy solution: just tell yourself you're having *better* sex than all those once-a-weekers.

—Matthew Hutson

## Why Whiz Kids Win

Despite professing to value hard work, we all have a soft spot for natural talent



Americans never tire of rooting for the underdog or praising the self-starter who climbs his or her way to the top through blood, sweat and tears. But in our hearts we may prefer naturals over strivers. And understanding people's true preferences could help us navigate the worlds of academics, business and art.

Five years ago Chia-Jung Tsay, a psychologist now at University College London School of Management, reported a "naturalness bias." After listening to two clips from the same classical music recording, subjects said they preferred the clip they were told was performed by a musician who was naturally talented over the one described as having come from a hard worker—even though they explicitly said they valued effortful training over innate ability.

A new paper by Tsay in *Personality and Social Psychology Bulletin* builds on this work by extending it beyond music and also measuring the bias's consequences. Subjects with business experience and novices alike said they preferred business ideas and entrepreneurs when the entrepreneur was described as a natural versus a striver, despite saying earlier that effort was more important than natural talent. This bias was as strong, if not stronger, in business experts; one experiment found that a supposed striver needed 4.5 more years of leadership experience, 28 more IQ points, or \$39,000 more in capital, compared with a natural, to be on equal footing when appealing for investment to business experts.

So why do we have this preference for inborn talent, which Tsay says she has also found in sports and dance? Her data point to a common belief that naturals have more potential for progress. Tsay's interest in this kind of bias derives from her own experience as a pianist competing for prizes. "I saw a lot of this," she says—to the extent that musicians would present themselves as younger than they really were and downplay how hard they practiced.

—Matthew Hutson



## How to Be a Better *interviewee*

As with so many professions, journalism inhabits a small world—and the New York City magazine world in which I worked for most of my career is even smaller. Once you build a solid reputation in the industry, you're often poached by other publications. Long story short: I haven't had a real job interview in a dozen years. So imagine my dismay when I realized that my recent yearnings for a career change will no doubt lead to face-to-face meetings with intimidating hiring managers who have no idea who I am. That's one reason I was excited to dig into the research and talk to experts in the psychology of human resources. Preparation is 90 percent of success (or something like that), right?

### #1 Do a little preinterview cleanup.

Before you even start sending out applications, it's smart to prune prejudicial content (politics talk, margarita selfies, rants about your current boss) from your social-media accounts, says Therese Macan, a professor at the University of Missouri–St. Louis, who studies the process of employee selection and recruitment. “If your Facebook, Twitter, Instagram and other accounts aren't private, the interviewer may build an impression of you before you even walk into the room,” she says. “You should at least Google yourself and see what comes up.”

You might also search LinkedIn to see if anyone else in your field also has your *name* (and a typo-ridden profile). “One of my grad students found out there was somebody else in the Midwest, in a psych department, who had her exact same unusual name and who had a provocative picture on her site. She had to make sure employers knew that wasn't her!”

### #2 Prep a few key answers.

Many companies use so-called structured interviews that focus on asking job seekers to describe past behavior. A couple of examples: “Tell me about a time when you worked with a difficult co-worker and what you did to resolve it” or “Tell me about a tough project you worked on and how you managed it.” Try to give concrete examples of what you did in those situations, Macan says: “To figure out what the questions are



likely to be, think about what the job might entail. Does it require that you work as a team? Does it require that you present in front of people?” Then you might be asked to describe such moments from your past. Another option is one-on-one expert coaching. A few years ago management researchers Todd Maurer and Jerry Solamon found that 91 percent of people who took an interview-training program felt like it helped them do better in their real interviews.

### #3 Picture yourself landing the job.

Visualization has become a training staple for elite athletes—and there's evidence it may work for job seekers, too. Applicants who practiced mental imagery were less stressed and got better evaluations than those who didn't, according to a 2003 study in the *Journal of Managerial Psychology*. The 10- to 20-minute protocol is fairly simple: picture yourself feeling confident and in control during the course of an interview, then envision the entire thing ending in a job offer.

### #4 Channel your inner narcissist.

It's usually pretty obnoxious when

people outright brag about themselves. Yet an interesting 2013 study in the *Journal of Applied Social Psychology* confirmed that being wholeheartedly self-promotional during an interview can be a good thing. About 70 tapes of mock job interviews were viewed and scored by more than 200 raters—applicants who talked a lot, spoke quickly, were self-promotional, and tried to ingratiate themselves by smiling and complimenting their interviewers were given much more positive evaluations than people who acted a bit more modest.

My best friend, Cheri, has been in staffing and recruiting for the past 10 years, and, boy, does she have some stories. Like the woman who gave Cheri way too much information about how diarrhea contributed to losing her last job. And then there was the eager beaver who followed up several days in a row, *in person*. I know better than to cross any of those fairly obvious lines, but in a challenging job market, all of us have to strive to get where we want to be. If that means learning to brag a bit and engage in shameless temporary self-promotion, I'm up for it.

—Sunny Sea Gold



# Clean Teens at Risk for Opioid Abuse

An opioid painkiller prescription predicts later misuse for drug-naïve teenagers

A prescription for an opioid drug such as Percocet or Vicodin can offer pain relief, but it also comes with the potential for abuse and addiction. In the past 20 years the number of overdose deaths from these drugs has more than tripled. In examining whether a legitimate prescription for opioid drugs increases the likelihood of later misuse for teens, a recent study uncovered a surprising trend: it's the drug-naïve teens who are most at risk.

Sociologist Richard Miech of the University of Michigan and his team analyzed data about high school seniors from the ongoing Monitoring the Future

Overall, young adults who had taken opioids with a prescription by 12th grade were 33 percent more likely to misuse the drugs after high school than those who had not been prescribed opioids. But the researchers also broke down the data based on the teens' history of, and attitudes regarding, illicit drug use. Teens with a lot of drug experience were likely to misuse an opioid after high school whether or not they had had a prescription by 12th grade. Instead the risk stemming from a legitimate prescription was concentrated among teens who were previously thought to have a *low* likelihood of misusing opioids.

These teens had very little experience taking illicit drugs, and they disapproved of marijuana use. Yet if the drug-naïve kids had a prescription for opioids by 12th grade, they were three times more likely to misuse them by age 23 than similar teens who never had a prescription.

"These results suggest that we shouldn't overlook kids who are not using drugs when they are younger," Miech



says. Even though the vast majority misused opioids infrequently—no more than five times in a year—being drug-naïve “makes their misuse potentially more dangerous,” Miech says. “They may not realize that taking a couple of opioids after a night of drinking could have lethal consequences.” But on the plus side, “these kids already go into the doctor's office with attitudes against drugs and are likely to listen,” he adds, so doctors and parents should make the effort to inform them of the risks of taking opioids outside of a doctor's care. —Aimee Cunningham

## ABUSE OF PRESCRIPTION OPIOIDS HAS OUTSTRIPPED THAT OF COCAINE, HEROIN AND OTHER ILLEGAL NARCOTICS.

project, an annual survey that tracks the alcohol and drug use of representative samples of eighth, 10th and 12th graders in the U.S. The new study, published in November 2015 in *Pediatrics*, included more than 6,000 12th graders who had been randomly selected for follow-up questions about opioid misuse when they were between the ages of 19 and 23.

## The Problem with Perfect Posture

Slouching might help us concentrate when we are challenged



“Sit up straight!” The exhortation rings through many a primary school classroom and across the family dinner table. A large body of research suggests that controlling your position can be a task like any other, drawing on cognitive resources: simple tasks such as counting backward get harder when you must

also hold a particular pose, and vice versa.

Most of these previous studies of posture, however, focused on standing positions rather than different sitting postures. Now, in a vindication for slouchers everywhere, a small study of seated Japanese fourth graders suggests that a relaxed posture may somehow help us concentrate on mentally challenging math.

In the study, 28 children sat on a backless stool like those used in elementary schools in Japan. They were fitted with electrodes to record the activity of core muscles involved in maintaining upright posture, and after asking the kids to focus on sitting up, the researchers had some sit quietly for two minutes, whereas others were asked to answer first easy math problems orally, then harder ones.

The researchers found that the children doing math relaxed their core muscles. The muscles were the most relaxed when the kids were working on the harder problems, and they did just as well on the hard problems as on the easy ones. That may mean, the researchers speculate, that slouching frees up some cognitive power that would otherwise be tied up in sitting up straight, allowing them to do better on tough problems than they might have otherwise.

The results are suggestive, but they are far from conclusive (sorry, slouchers). To get a clearer picture of what effect posture has, researchers would have to test each child's math skills without having them pay particular attention to posture and then test them again after asking them to focus on sitting up, says Marjorie Woollacott, a neuroscientist studying motor control at the University of Oregon, who was not involved in the research. As it stands (or rather, sits), the exact effects of posture remain a question for future research.

—Veronique Greenwood

## A Safe Drug to Boost Brainpower

Rigorous analysis finds that the drug modafinil significantly enhances cognition during complex tasks

What if you could pop a pill that made you smarter? It sounds like a Hollywood movie plot, but a new systematic review suggests that the decades-long search for a safe and effective “smart drug” (*box below*) might have notched its first success. Researchers have found that modafinil boosts higher-order cognitive function without causing serious side effects.

Modafinil, which has been prescribed in the U.S. since 1998 to treat sleep-related conditions such as narcolepsy and sleep apnea, heightens alertness much as caffeine does. A number of studies have suggested that it could provide other cognitive benefits, but results were uneven. To clear up the confusion, researchers then at the University of Oxford analyzed 24 studies published between 1990 and 2014 that specifically looked at how modafinil affects cognition. In their review, which was published last year in *European Neuropsychopharmacology*, they found that the methods used to evaluate modafinil strongly affected the outcomes. Research that looked at the drug’s effects on the performance of simple tasks—such as pressing a particular button after seeing a certain color—did not detect many benefits.

Yet studies that asked participants to do complex and difficult tasks after taking modafinil or a placebo found that those who took the drug were more accurate, which suggests that it may affect “higher cognitive functions—mainly executive functions but also attention and learning,” explains study co-author Ruairidh Battleday, now a medical doctor and Ph.D. student at the University of California, Berkeley.



But don’t run to the pharmacy just yet. Although many doctors very likely prescribe the drug off-label to help people concentrate—indeed, a 2008 survey by the journal *Nature* found that one in five of its readers had taken brain-boosting drugs, and half those people had used modafinil—trials have not yet been done on modafinil’s long-term effectiveness or safety. Studies of the drug have been “carried out in a controlled scientific environment and usually only looked at the effects of a single dose,” explains Oxford neuropsychologist and review co-author Anna-Katharine Brem—so no one yet knows whether it is safe for long-term use in healthy people. Nor is it known whether modafinil might lose its edge with repeated use, a phenomenon familiar to many coffee drinkers.

Side effects are another important consideration. Modafinil has been shown to cause insomnia, headache and stomachache in some users. Although these kinds of problems may be worth enduring for a drug that treats an illness, “if you don’t have a medical condition, the risks versus benefits change dramatically,” says Sharon Morein-Zamir, a psychologist at the University of Cambridge who studies ethical considerations associated with the use of cognition-enhancing drugs. “For some, the benefits will likely outweigh risks, at least some of the time,” she says, whereas “for others this may not be the case.” A pill you take to ace an exam, for instance, won’t do you much good if it also causes a grueling stomachache.

—Melinda Wenner Moyer

### The Search for an Intelligence Drug

People have been searching for ways to boost their brainpower perhaps for all of history. In the past century scientific efforts have revealed a few promising chemicals, but only modafinil has passed rigorous tests of cognitive enhancement.

**Caffeine:** One of the oldest and most popular stimulants. People recognized caffeine’s stimulant properties hundreds (perhaps thousands) of years ago. It can enhance alertness and attention; however, effects are short-lived, and tolerance builds up quickly.

**Nicotine:** Also a stimulant, used for hundreds of years for a range of medicinal purposes. It is very addictive and has many dangerous side effects.

**Amphetamine (Benzedrine, Adderall):** First synthesized in 1887. Benzedrine was the first drug to treat hyperactivity in children. Amphetamine can enhance attention and memory by increasing levels of norepinephrine and dopamine in the brain, but the compound can be addictive and comes with a range of side effects, including hyperactivity, loss of appetite, disturbed sleep, even psychosis.

**Methylphenidate (Ritalin):** First marketed in 1954 and prescribed in the 1960s for treating hyperactivity. It became popular for ADHD in the 1990s. As with amphetamine, it can improve memory and focus for those with ADHD, but it is also used off-label as a study and work aid. Some individuals build up a tolerance to Ritalin over time.

**Acetylcholinesterase inhibitor (Aricept):** Approved to treat Alzheimer’s disease in the 1990s. It has been shown in some studies to enhance memory and attention in healthy individuals.

**Modafinil:** Originally used to treat narcolepsy. It can also enhance cognitive function, especially when completing difficult tasks. Experts are not quite sure how it works or what long-term effects would look like.

## Should Everyone Take Cognition-Enhancing Drugs?

As is the case with all medications, cognition-enhancing drugs affect different people in various ways. Setting aside the ethical questions about brain boosters, here is a look at groups who may deserve special consideration.

**CHILDREN AND TEENS.** Cognition-enhancing drugs could present unique risks to the developing brain. Several clinical trials found modafinil to be safe when given to children with attention-deficit/hyperactivity disorder (ADHD), but the trials lasted only a few months, making it difficult to ascertain the potential effects of long-term use. In a 2014 review article examining the biochemical effects of modafinil and other common “smart drugs,” researchers at the University of Delaware and Drexel University raised concerns that the use of these drugs could affect the developing brain’s ability to adapt to new situations and might increase the risk for addictive behaviors.

### PEOPLE WITH LOWER IQs.

Research suggests that cognition-enhancing drugs offer the greatest performance boost among individuals with low-to-average intelligence. These findings led University of Oxford researchers to propose in a 2014 paper that if such drugs were selectively given to people who need them most, many ethical concerns about the drugs’ use would be alleviated, and they might even reduce opportunity inequality.

**SENIORS.** Some studies suggest that older adults may not derive much benefit from cognition-enhancing drugs. One study found that methylphenidate (Ritalin), which boosts working memory and attention in young adults, had no effect on performance among healthy elderly volunteers who were asked to perform various cognitive tasks.

—M.W.M.



## Could Childhood Adversity Boost Creativity?

A new finding suggests that the cognitive effects of an unpredictable childhood are not all bad

Childhood adversity is thought by most experts to be bad for cognitive development: for instance, people who grow up in stressful environments tend to score lower on tests of memory and IQ. They also perform worse on tests of impulse inhibition, which in turn predicts success and competence in later life.

Now a new study suggests that the picture of how unreliable environments affect cognition is not purely one of harm. Wondering whether there might actually be benefits, psychologist Chiraag Mittal and his colleagues at the University of Minnesota ran a series of experiments in which they measured both inhibition and task switching.

In the inhibition test, the 103 adult participants had to try to ignore a flash on one side of a screen so they could identify which direction an arrow was facing when it flashed briefly on the other side. The switching test involved categorizing colored shapes by either shape or color, as instructed by a changing word on the screen. Being good at shifting means a person is able to let their responses be guided by the situation rather than an internal goal. It is an aspect of cognitive flexibility, which is thought to underlie abilities such as creativity.

The researchers assessed the participants’ childhoods in terms of both “harshness” (using questions about socioeconomic status) and “unpredictability” (using degree of agreement with statements such as “People often moved in and out of my house on a pre-

ty random basis”). They also included a condition where subjects were prompted to feel uncertainty via reading an unsettling news story, a well-established laboratory technique.

The results show that when participants felt uncertain, those who had experienced unpredictable but not harsh childhoods performed worse at inhibition but better at shifting than those whose childhoods were not unpredictable. The finding makes sense: inhibition is important for pursuing long-term goals and is thus most useful in stable environments, whereas the ability to shift rapidly among different demands would presumably be most useful in changeable environments. The implication is that kids who grow up in adverse environments are not impaired so much as *shaped*. “This is one of the first studies showing that early unpredictability shapes people’s cognition adaptively rather than impairing it,” Mittal says.

There is much we do not yet understand about the mechanisms at work here, cautions Celeste Kidd, a cognitive scientist at the University of Rochester who also studies children’s cognitive development. As a new finding, this study needs replicating, she says, but she is enthusiastic about the approach. “People don’t usually think about these things in terms of adaptive processes,” Kidd says. “This is positing that there are certain abilities that are better developed through unstable environments than stable ones; it’s very cool.”

—Simon Makin



## Animal Magicians

Humans are not the only species to use visual trickery to their advantage

In the forests of Australia and New Guinea lives a pigeon-sized creature that is not only a master builder but a clever illusionist, too. The great bowerbird (*Chlamydera nuchalis*)—a cousin of crows and jays—has an elaborate mating ritual that relies on the male's ability to conjure forced perspective.

Throughout the year he painstakingly builds and maintains his bower: a 60-centimeter-long corridor made of twigs, leading to a courtyard decorated with gray and white pebbles, shells and bones. Some species also add flowers, fruits, feathers, bottle caps, acorns, abandoned toys—whatever colorful knickknacks they can find. The male takes great care to arrange the objects according to size so that the smallest pieces are closest to the bower's entrance



and the largest items are farthest away.

The elaborate structure is not a nest. Its sole purpose is to attract a female for mating. Once construction is complete, the male performs in the courtyard for a visiting female, who—poised like a critical *American Idol* judge—evaluates the routine from the middle of the corridor. He sings, dances and prances, tossing around a few select trinkets to impress his potential mate. Her viewpoint is very narrow, and so she perceives objects paving the courtyard as being uniform in size. This forced perspective makes the choice offerings appear grander and therefore all the more enticing.

The offerings, and the male himself, appear larger than life because of an effect that visual scientists call the Ebbinghaus illusion, which causes an object to look bigger if it is surrounded by smaller objects. In 2012 ecologists Laura Kelley and John A. Endler, both then at Deakin University in Australia, confirmed that among the great bowerbirds in Queensland, how well a male gener-

ates these illusions can predict his mating success.

Visual deception is not unusual in the animal kingdom, which is perhaps why so many cultures have tales of trickster creatures—the wolf in *Aesop's Fables* from ancient Greece, Old Man Coyote from Plains Indian myths and Brer Rabbit stories from the Southern U.S., to name a few. As is often the case, though, reality surpasses fiction. Bowerbirds are just one of many animals that routinely employ visual duplicity to stay alive and reproduce. These adaptations support the case that illusions are not simply errors of perception but can provide significant advantages, too.

Some animals change their environment, as the bowerbird does, but many others transform their appearance or behavior to dupe a potential enemy or unsuspecting meal. Here we review the three main illusions animals use to change their looks—crypsis, masquerade and mimicry—and survey a few of the most spectacular examples of each. **M**



BY SUSANA MARTINEZ-CONDE  
AND STEPHEN L. MACKNIK

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



Send suggestions for column topics to  
[MindEditors@sciam.com](mailto:MindEditors@sciam.com)

## MASQUERADE



Some animals are less appealing to predators because they look like familiar inanimate or inedible objects. For instance, the larva of the giant swallowtail butterfly (*Papilio cresphontes*) (left) masquerades as a bird dropping, as does the orb web spider (*Cyclosa ginnaga*).

The larva of the feathered thorn moth (*Selenia dentaria*) (center) masquerades as a twig. Not only does it resemble a twig in color and shape, it also holds itself at an angle much like those of actual twigs in the host plant. Similarly, birds from the genus *Nyctibius*, with bark-colored plumage, masquerade as tree stumps by sitting motionless during the day.

A few species have the flexibility to match different unappetizing objects in their surroundings. Cuttlefish, like their octopus kin, have remarkable camouflaging talents and can suddenly change their skin color. They can readily disguise themselves as rocks or seaweed. Peppered moth larvae (*Biston betularia*) can also, chameleonlike, vary their coloration to match different twigs in their vicinity.

Some predators make use of this trick, too. The ghost mantis (*Phyllocrania paradoxa*) (right) masquerades as a dead leaf to fool unsuspecting flies.

## CRYPISIS

Some animals blend into their environment to go undetected by predators. This technique, called crypsis, relies on the failure of another animal to perceive the deceiver. (In contrast, masquerading and mimicking creatures are not hard to spot, but the animal that sees them miscategorizes them as another species or inanimate object.)

There are a variety of ways in which cryptic animals, such as this lichen-mimicking katydid (right), avoid detection through camouflage. Thanks to disruptive coloration and patterns in their skin or exoskeleton, many creatures effectively disappear into the background. Others also deploy cryptic behaviors, hiding in burrows or covering themselves in sediment.



## MIMICRY

Eyespots—concentric circles resembling vertebrate eyes—are ubiquitous among moths and butterflies, but they can be small and marginally located or large and central. Smaller eyespots may attract a predator's attention away from the head or other vital body parts. Larger eyespots tend to look like the eyes of a predator's enemy, which suggests they serve to intimidate potential attackers.

In 2014 biologist Sebastiano De Bona of the University of Jyväskylä in Finland and his colleagues concluded that eye mimicry—rather than the conspicuousness of an eyespot—was responsible for averting predators. They showed various images on a computer screen to great tits (*Parus major*), birds that prey on butterflies. The photographs included owls (which prey on great tits), as well as several different butterflies. Some of these butterfly pictures featured natural-looking eyespots, others had none, and a third group showed digitally manipulated spots that had the same color contrast as real spots but looked less like eyes. The birds produced equivalent aversive responses to mimetic eyespots and to the true eyes of owls. They responded less dramatically to the modified eyes.

So-called Batesian mimics are harmless creatures that, by virtue of their sound, appearance, behavior or smell, trick predators into mistaking them for noxious or dangerous species. For example, the syrphid fly mimics the patterns and colors of the honeybee. Predators that have learned to stay away from painful stings will be motivated to leave this mimic alone.

### MORE TO EXPLORE

- **Illusions Promote Mating Success in Great Bowerbirds.** L. A. Kelley and J. A. Endler in *Science*, Vol. 335, pages 335–338; January 20, 2012.
- **Animal Visual Illusion and Confusion: The Importance of a Perceptual Perspective.** L. A. Kelley and J. L. Kelley in *Behavioral Ecology*, Vol. 25, No. 3, pages 450–463; May–June 2014.
- **Predator Mimicry, Not Conspicuousness, Explains the Efficacy of Butterfly Eyespots.** S. De Bona, J. K. Valkonen, A. López-Sepulcre and J. Mappes in *Proceedings of the Royal Society: Biological Sciences*, Vol. 282, No. 1806, Article No. 20150202; May 2015.
- **Masquerade.** J. Skelhorn in *Current Biology*, Vol. 25, No. 15, pages R643–R644; August 3, 2015.



## MENTAL ILLNESS

## Is There a Better Way to Diagnose Psychosis?

A new study opens a door to more biologically based categories of major mental illness

By Thomas R. Insel

If you are unfortunate enough to develop acute chest pain this winter, you will probably be assessed by a clinician who will order a battery of tests to determine if your symptoms result from pneumonia, bronchitis, heart disease or something else. These tests can not only yield a precise diagnosis, they ensure you will receive the appropriate treatment for your specific illness.

If, however, you are unfortunate enough to have a psychotic episode this winter, the process of arriving at a diagnosis will be quite different. In fact, there are not many choices available to you.

Most people with a psychotic disorder are labeled as having either schizophrenia or bipolar disorder. The distinction has been in textbooks for a century: schizophrenia (originally dementia



praecox) is associated with delusions, hallucinations, an absence of affect and a chronic course—meaning that it can become an unyielding condition. Bipolar disorder (originally manic depression) can also involve delusions and hallucinations and, typically, dramatic swings in mood. It has a fluctuating course, which means that it may be more episodic. But outside of textbooks, in the real world of the emergency room or clinic, these distinctions are less clear because many patients do not neatly fit the formal descriptions. Sadly, there are no blood tests or scans to distinguish schizophrenia from bipolar disorder.

While clinicians have become very skilled at assessing symptoms and signs, the absence of such tests poses a serious problem in psychiatry. Do all people with a label of schizophrenia have the same disorder? What about the large number of people who appear to have aspects of both schizophrenia and bipolar? Are

these disorders, diagnosed exclusively by signs and symptoms, identifying distinct biological entities, or could there be many different illnesses with a continuum of psychotic signs and symptoms? These questions are not merely academic. As with chest pain, getting a precise diagnosis is key to selecting the best treatment.

Moving psychiatry into a new era of biologically based diagnosis has been a long-sought goal—and a priority at the National Institute of Mental Health, where I served as director for 13 years. The challenges are many, but a new study published online in December 2015 in the *American Journal of Psychiatry* raises fresh hope.

### Defining Biotypes

The study led by neuroscientist Brett Clementz of the University of Georgia, psychiatrist Carol Tamminga of the University of Texas Southwestern Medical Center in Dallas, and their colleagues at

---

**THOMAS R. INSEL** is a neuroscientist and psychiatrist who served as director of the National Institute of Mental Health from 2002 to 2015. He recently joined Verily, a new life sciences company within Alphabet, the parent company of Google.

---



Send suggestions for column topics to [MindEditors@sciam.com](mailto:MindEditors@sciam.com)



Yale University and Harvard University found distinct “biotypes” of psychosis that can be identified with quantitative biomarkers. In this study, from the Bipolar-Schizophrenia Network on Intermediate Phenotypes (B-SNIP) consortium, 711 people with a diagnosis of schizophrenia, bipolar disorder or schizoaffective disorder (a hybrid of schizophrenia and bipolar disorder) were given a variety of tests assessing brain functions that have been associated with psychosis. These included a battery of cognitive tests, a measure of auditory processing, an assessment of cognitive control, as well as EEGs and studies of eye movements. In addition,

new categories. Second, biotypes differed in social functioning—with people in biotype 1 showing more serious functional impairment relative to the other biotypes. Third, the brain-imaging studies, which were not used in defining the biotypes, showed clear differences in regional gray matter, especially in the frontal, cingulate, temporal and parietal cortices.

Although none of these observations proves that the biotypes are more valid than clinical diagnosis, these findings together encourage a novel approach to the diagnosis of psychotic disorders. Going forward it will be important to know whether genomic variation, functional brain measures or other behav-

are seeing evidence of this in autism and attention-deficit/hyperactivity disorder, as well as depression and anxiety disorders. Autism, for example, is almost certainly a large, loose diagnostic label covering a variety of conditions that are genetically diverse, albeit superficially similar.

The NIMH has proposed a new approach to the diagnosis of mental disorders that calls for the incorporation of biological, cognitive, behavioral and social data, in addition to observed symptoms and signs. Known as the Research Domain Criteria, or RDoC, it has been controversial both because it represents a major break with traditional psychiatry and because some doubt that it is viable. The data from the B-SNIP study provide early evidence for the RDoC approach.

Of course, the real test of the B-SNIP biotypes—or any new method of diagnosis—is whether they will be useful in targeting treatments and predicting outcomes. That will require studies of treatment response. Usually in the U.S., people with schizophrenia receive antipsychotic medication and psychosocial supports such as counseling, vocational training and other forms of help. Physicians treat bipolar disorder with mood stabilizers, antipsychotic drugs, and sometimes antidepressants and psychosocial supports. Treatment remains empirical, with few guides to know which person will respond to a given therapy.

One of the hopes of precision medicine for psychiatry is that the use of biomarkers will provide more predictability so that patients and clinicians can make more informed and precise treatment decisions. Psychotic disorders are among the most disabling conditions in all of medicine—with enormous costs in dollars and suffering for patients and their families. New approaches to diagnosis and treatment are long overdue. **M**

## THE ABSENCE OF DIAGNOSTIC BLOOD TESTS, SCANS AND BIOMARKERS POSES A SERIOUS PROBLEM IN PSYCHIATRY: DO ALL PEOPLE WITH SCHIZOPHRENIA HAVE THE SAME DISORDER?

each subject had an MRI scan of his or her brain.

Ignoring the clinical diagnosis, researchers pooled the data and analyzed them with unbiased, criterion-free statistical methods to look for biotypes. Perhaps it is not surprising that the computer analysis from a large population with three diagnostic categories would find three clusters or biotypes. But the three biotypes have very little relation to the three traditional diagnostic categories. In fact, people with schizophrenia, bipolar and schizoaffective disorders were distributed across the three biotypes. And the biotypes did not differ simply by symptom severity or the presence of mania-related symptoms.

Is there any reason to think that these biotypes are more valid than a clinical diagnosis based on symptoms? A few observations suggest that the B-SNIP investigators may be on to something.

First, some of the biotype differences were also found in first-degree family members, for whom data were also collected, suggesting a genetic basis for the

biotype differences. Second, biotypes differed in social functioning—with people in biotype 1 showing more serious functional impairment relative to the other biotypes. Third, the brain-imaging studies, which were not used in defining the biotypes, showed clear differences in regional gray matter, especially in the frontal, cingulate, temporal and parietal cortices.

### More Precise Treatment

Precision medicine has become a buzzword to describe the diagnostic revolution in cancer and other diseases. The concept is simply that the tools of modern biology, including genetics and imaging, can deconstruct current diagnostic categories to yield more precise disease groups—sometimes at the level of a specific genetic variation—that can be matched to more personalized treatments.

For mental disorders, where laboratory tests have not been used in the clinic, precision medicine could be a disruptive innovation, revealing that many of the current diagnostic categories are imprecise and biologically heterogeneous. We

#### MORE TO EXPLORE

■ **No One Is Abandoning the DSM, but It Is Almost Time to Transform It.** Ferris Jabr in *Brainwaves* blog, *ScientificAmerican.com*. Published online May 7, 2013.

■ **Identification of Distinct Psychosis Biotypes Using Brain-Based Biomarkers.** Brett A. Clementz et al. in *American Journal of Psychiatry*. Published online December 7, 2015.

NEUROPATHOLOGY

## Sleep without End

A long-forgotten epidemic teaches us about the science of slumber

*Unity Kinkaid finds it harder and harder to stay awake. She now sleeps for almost 20 hours a day. She used to dream; to shift in her sleep, muttering and sighing, locked in half-remembered fantasies ... Now she lies unmoving, breath shallow and silent, lost to the world. Unity sleeps.*

—Neil Gaiman, *The Sandman: Preludes & Nocturnes*, 1991

In the above-cited comic, a necromancer imprisons Morpheus, an immortal who is master of sleep and dreams. Consequently, people are unable to stay awake, sleeping the days, months and years away, until Morpheus escapes and restores the natural order. The chilling real-life inspiration for this compelling serialized comic was an epidemic that swept the world between 1916 and 1926. A hundred years after the first cases of “sleepy sickness” came to the attention of the medical community, we still do not know what agents were responsible for this disease.



**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.



It emerged from the cold, wet plains and trenches of northern France and Belgium, the battlefields of World War I, shorn apart and denuded of trees by the endless barrage of explosions from artillery, mines and machine-gun fire, a landscape crowded with millions of young men living under atrocious and unsanitary conditions at close quarters. Indeed, one of the most famous victims of the disease may have been Adolf Hitler, who was wounded at the Battle of the Somme.

Two physicians from opposing sides, Jean-René Cruchet in Paris and Baron

Constantin von Economo in Vienna, identified the condition's principal manifestation—its profound effect on sleep, that restorative period during which the body is at rest and the brain disconnects from the external environment. It was the clinical acumen of the aristocratic von Economo, a professor of psychiatry and neurology of Greek origin, whose masterful monographs on the subject gave us the best description of the disease and its underlying pathology of encephalitis, an inflammation of the brain.

Encephalitis lethargica (EL), epidemic encephalitis or von Economo disease

JEFFREY ALAN LOVE

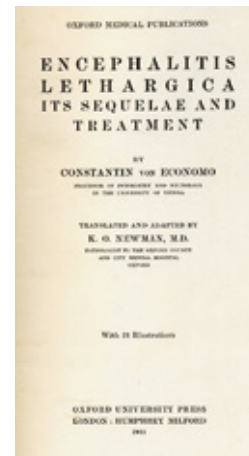
starts with sore throat, nausea, headache, joint pain and fever—the general malaise associated with flu. From there the illness progresses to abnormal eye movements (which often cause double vision as the two eyes are no longer coordinated), drooping eyelids, an inability to open the eyes, and an irresistible need to sleep, day and night. This lethargy lasts for weeks, even in some cases for a year or more. Eleanore Carey, an eloquent young woman living in New York City, fell into a Sleeping Beauty–like trance in February 1923. Many years later she described these symptoms in a magazine article:

*After two months of illness I was in little pain, in fact, I was very comfortable, provided they did not prod me nor stand me on my head, turn me over in bed nor dash cold water on my face to waken me. It was so heavenly just to be allowed to sleep, but these people around me seemed determined to prevent my being comfortable! When the idea finally crept through my sleeping brain that I must waken, it seemed to be a physical impossibility. I wanted to be obliging, but I just could not. It seemed to me to be just as difficult to come to consciousness as it would have been had I been buried in a pit as deep as the center of the earth, where the circular walls about me were of shiny, polished marble. There were no crevices for*



*my fingers on its sides nor any places to put my feet, but I must climb out of that pit with my bare hands!... Perhaps it will give the reader a vague inkling of the dreadful lethargy which completely overpowers the victim of this disease and renders him impotent to make the effort to help himself.*

These periods experienced by Carey and others came replete with vivid dreams, hallucinations and nightmares. When patients were woken up by calling their name or shaking them, they responded intelligently before quickly succumbing to somnolence again, often before they could fully provide answers to



The aristocratic Viennese physician Baron Constantin von Economo composed masterful monographs on a condition that began with a sore throat, progressed to abnormal eye movements, and ended with a lethargy that could last for a year or more.

questions asked. The victims could not feed or clean themselves. In severe cases, they were stuporous or even comatose.

EL is a protean disease with some victims showing the opposite pattern, suffering from extreme insomnia or from inverted sleep—drowsy and lethargic during the day but delirious at night.

Mortality in this acute phase of the disease ran as high as 30 to 40 percent. Medical science was powerless to intervene and had to let the disease run its natural course. Hand in hand with EL's impact on sleep were its variegated effects on motor behavior, with patients displaying a menagerie of tics, motor and linguistic compulsions, tremors, rigidities and unconscious activities known as automatisms.

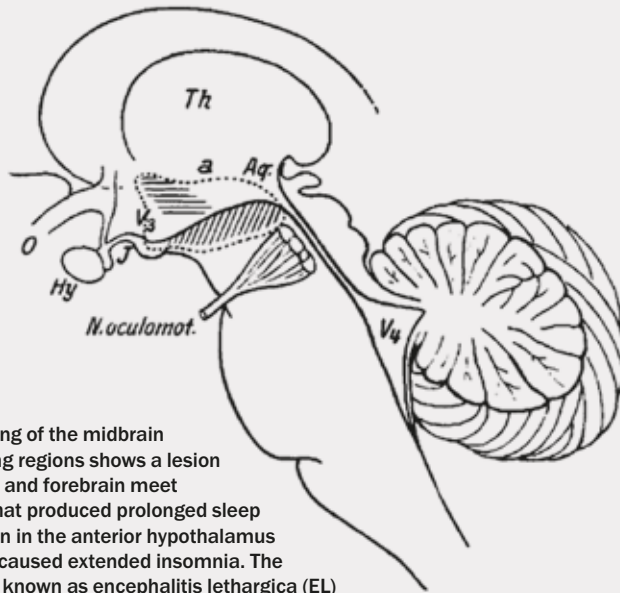
From Europe the disease spread to the Americas by way of New York and other port cities on the Atlantic coast. Estimates for the number of people worldwide who contracted EL ranged from about 52,000 reported cases upward to one million. The uncertainty derives from not knowing how many infected people experienced mild and short-lasting symptoms of EL that went unreported.

AN ELOQUENT YOUNG WOMAN LIVING  
IN NEW YORK CITY IN 1923  
DESCRIBED THE SYMPTOMS OF  
ENCEPHALITIS LETHARGICA AS AKIN TO  
**A SLEEPING BEAUTY–LIKE TRANCE.**

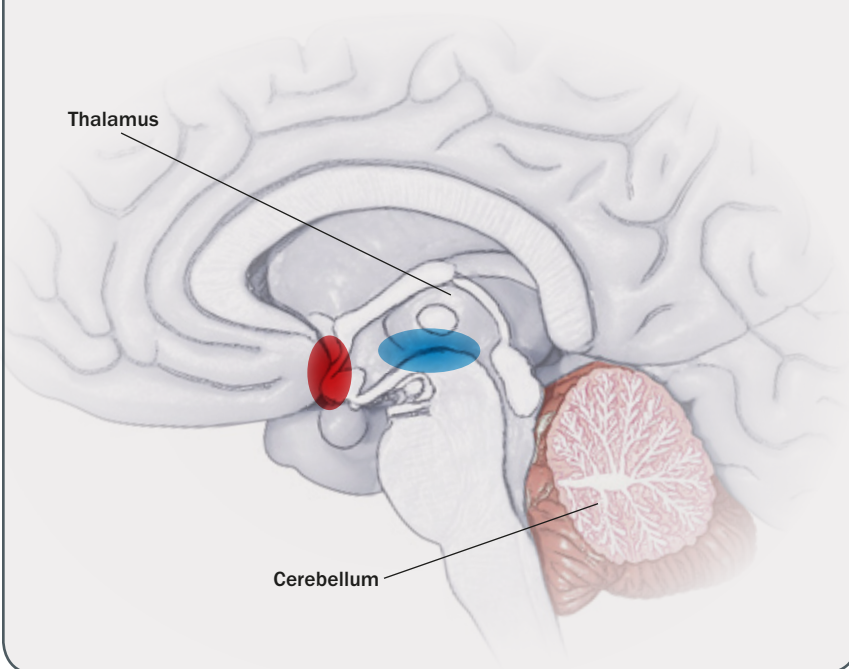


## Anatomy of a Trance

In 1916 neurologist Constantin von Economo encountered his first patients afflicted with a form of encephalitis in areas of the midbrain that are involved with the regulation of sleep and wakefulness.



Von Economo's drawing of the midbrain (right) and surrounding regions shows a lesion where the brain stem and forebrain meet (diagonal hatching) that produced prolonged sleep in a patient. The lesion in the anterior hypothalamus (horizontal hatching) caused extended insomnia. The condition came to be known as encephalitis lethargica (EL) or von Economo disease. More advanced methods have confirmed that the areas identified by von Economo (depicted below) are indeed essential elements of the sleep-wake regulatory system. The horizontal blue ellipse highlights a key region involved in wakefulness; the vertical red one corresponds to a critical area that regulates sleep.



Why the epidemic strain of EL disappeared 10 years later as abruptly as it did remains unknown. Since then, only a handful of sporadic cases have been reported. Medical sleuthing has revealed previous instances of outbreaks of an EL-like disease, in particular in Tübingen, Germany, in 1712 (where it was dubbed *die Schlafkrankheit*) and in northern Italy in 1890 (*la nona*).

It is disconcerting that to this day, the culprit responsible for EL remains unknown and, presumably, at large. As epidemic encephalitis partially overlapped with the 1918–1920 epidemic of influenza—the H1N1 or “Spanish flu” that killed an estimated 50 million people—some consider the former a consequence of the latter. Yet no concrete causal evidence of any such link to influenza has surfaced. Nor did pathologists isolate from the brains of EL patients any bacteria or viruses that could be identified as the responsible agents.

A currently popular hypothesis suggests that the initial cold or flu virus triggered an inappropriate immune response. If true, EL would join an ever growing list of autoimmune afflictions. This hypothesis, however, fails to explain how the epidemic form of EL could burst onto the world stage, affect tens of thousands and then vanish. Most likely multiple factors were responsible, a set of antecedents that might in time converge again under the appropriate conditions to haunt humankind.

Unfortunately, worse was in store for some of the patients who survived the acute phase of EL. They subsequently developed Parkinson's disease to a varying degree, including an extreme form of akinesia, in which they remained immobile for decades, frozen statues locked away in nursing homes or wards for the terminally demented. These long-forgotten postencephalitic parkinsonian patients were the ones that neurologist Oliver Sacks awakened with L-DOPA drug therapy in the late 1960s, as famously described in his 1973 master-

FROM “SLEEP AS A PROBLEM OF LOCALIZATION,” BY C. V. ECONOMO, IN *JOURNAL OF NERVOUS AND MENTAL DISEASE*, VOL. 71, NO. 3; MARCH 1930 (top); SCIENCE SOURCE (bottom)

piece *Awakenings*. The book became an eponymous movie with Robin Williams playing a character based on Sacks and an amazing, heart-wrenching performance by Robert De Niro portraying the patient Leonard L.

### Sleep Is Actively Regulated

Historically the clinic has always served as the most fecund source of insight about the brain and the mind. EL remains a case in point. Most of von Economo's patients had eye-movement abnormalities and slept excessively. When

existence of a structure in the midbrain that keeps the overlying thalamus and the neocortex in an activated, awakened state. This ascending arousal system sends fibers upward to the forebrain.

A smaller number of von Economo's EL patients showed the opposite reaction. They were able to sleep fitfully only for a few hours, beset by drowsiness most of the day but thwarted from sleep at night. These insomniacs had lesions in the gray matter of the anterior hypothalamus (literally, "below the thalamus"), extending into the basal ganglia. The

within three dozen or more highly heterogeneous nuclei with idiosyncratic cell structures housed within the brain stem (that is, the medulla, the pons and the midbrain), as well as the hypothalamus and the basal forebrain.

It is a complex system that uses a variety of neurotransmitters: acetylcholine, noradrenaline, GABA, histamine, serotonin and orexin. Collectively they implement something akin to a bistable flip-flop, a type of electronic circuit in which two intrinsically excitatory networks mutually inhibit each other—when one is "on," the other one is "off," and vice versa. The system can be in one of two states—awake or asleep—with relatively abrupt transitions between the two.

When we lose the ability to sleep, to mercifully slip into its oblivion and forget our daily toils and troubles, we realize how utterly dependent we are on Morpheus' power. Indeed, forced sleep deprivation is rightfully considered a form of torture.

Let me end with Haruki Murakami, who perfectly captures the sensations of falling asleep in the final phrase of his 2013 novel *Colorless Tsukuru Tazaki and His Years of Pilgrimage*:

*The rear light of consciousness, like the last express train of the night, began to fade into the distance, gradually speeding up, growing smaller until it was, finally, sucked into the depth of the night, where it disappeared. All that remained was the sound of wind slipping through a stand of white birch trees.*

Sleep well tonight. **M**

## SLEEP, VON ECONOMO ARGUED, IS NOT THE PASSIVE RESPONSE OF A RUN-DOWN BODY. RATHER IT IS TIGHTLY CONTROLLED BY SPECIFIC ORGANS TO CHOREOGRAPH THE SLEEP-WAKE CYCLE.

awakened, they interacted relatively normally with their environment but soon returned to sleep. That is, EL has specific symptoms that reflect that the underlying disease does not destroy gray matter willy-nilly but selectively attacks particular sites for unclear reasons.

Postmortem examination of brains of patients invariably reveals discrete lesions in the midbrain, a structure that aptly describes its own whereabouts. It lies above the pons and just below the thalamus, the quail-egg-shaped structure that is the gateway to the neocortex, the ruffled outer layers responsible for perception, memory, thought and consciousness. The damage often includes the oculomotor nucleus in the midbrain, explaining the pronounced eye-movement dysfunctions characteristic of EL.

Damage also occurs in another deep-brain structure, the substantia nigra, part of the basal ganglia, an explanation for the patients' behavioral and motor pathologies. Von Economo proposed the

physician inferred the existence of another center controlling the onset and depth of sleep. He argued that sleep is not just the passive response of a run-down body, tired after a day's work, ready to replenish itself. Rather it is an active state initiated and controlled by the tightly synchronized activity of specific organs in the central nervous system that are responsible for the daily choreography of our sleep-wake cycle.

Refined animal and clinical research over the past 80 years since von Economo published his work has validated his ideas and deepened our understanding of sleep and waking. We now know that there are two quite distinct forms of sleep, rapid eye movement (REM) and non-REM (or deep sleep). We know that circadian rhythms present in every cell in our body drive this system and are synchronized by the waxing and waning of daylight. The notion of a monolithic activating system has given way to the realization that sleep and arousal are controlled by activity

#### MORE TO EXPLORE

- **Hypothalamic Regulation of Sleep and Circadian Rhythms.** Clifford B. Saper, Thomas E. Scammell and Jun Lu in *Nature*, Vol. 437, pages 1257–1263; October 27, 2005.
- **Encephalitis Lethargica: During and after the Epidemic.** Edited by Joel A. Vilensky. Oxford University Press, 2010.







**IN  
SEARCH  
OF  
THE  
OPTIMAL  
BRAIN  
DIET**

The field of nutritional psychiatry is taking off as scientists home in on the ingredients for good mental health and cognitive staying power

**BY BRET STETKA**

Carolyn feels great these days. She exercises. She's socially active. She spends as much time with her four grandchildren as possible. But it wasn't always that way. A retired radiology film librarian from Pittsburgh, she began feeling apathetic and isolated seven years ago. "I'd just lost my mother, and my two sons had moved away," recalls Carolyn, now 75. She also struggled with excess weight, diabetes and chronic lung disease. She was grieving, eating a worrisome amount of junk food and slipping into what looked a lot like depression.

A few years later a friend told Carolyn about a depression-prevention study at the University of Pittsburgh. She signed up immediately. All 247 participants were, like her, older adults with mild depressive symptoms—people who without treatment face a 20 to 25 percent chance of succumbing to major depression. Half received about five hours of problem-solving therapy, a cognitive-behavioral approach designed to help patients cope with stressful life experiences. The rest, including Carolyn, received dietary counseling. Guided by a social worker, she discovered that she liked salmon, tuna and a number of other "brain-healthy" foods—which quickly replaced all the chips, cake and candy she was eating.

When the trial concluded in 2014, the results came as a surprise—to the researchers at least. The dietary counseling was not meant to have any substantial effect; Carolyn's group was the experiment's control. And yet psychiatrist Charles Reynolds and his colleagues discovered that both interventions had significantly reduced the risk of depression—by approximately the same amount. When they reviewed the data, all the patients scored on average 40 to 50 percent lower on the Beck Depression Inventory test, a common measure of depressive symptoms, 15 months after their ses-



Evidence links stereotypical Western diets, which are heavy in processed and fatty foods, to higher rates of depression and anxiety. Unhealthy diets most likely contribute to a range of neuropsychiatric disorders by increasing inflammation.

sions ended. What is more, only about 8 percent, regardless of the therapy they received, had fallen into major depression.

It cannot be ruled out that a placebo effect contributed to the improvements seen in both groups. Meeting with a health care professional and being proactive about getting better in and of itself may have helped participants feel more upbeat. In Carolyn's view, however, she had reversed her downward spiral largely by changing how she ate.

She is not alone in making that connection. Among scientists and clinicians there is a growing appreciation of the critical interplay between diet and brain health. The evidence is preliminary, and it is hard to tease out cause and effect. Perhaps people who eat well are also apt to have other healthy brain habits, such as regular exercise and good sleep routines. Or maybe depressed people tend to self-medicate with Oreos. But the data continue to accumulate. Every year the list of correlations between certain foods and mental well-being grows: fish and other sources of omega-3 fatty acids might help fend off psychosis and depression; fermented foods such as yogurt, pickles and sauerkraut seem to ease anxiety; green tea and an-

#### FAST FACTS

##### PRESCRIPTION HAPPY MEALS

- 1 Research indicates that traditional diets from the Mediterranean, Scandinavia and Japan help to preserve our psychological and cognitive well-being.
- 2 These diets all feature fish, one of the best sources of omega-3 fatty acids—nutrients that play a vital role in promoting neuronal health and that may have helped drive the evolution of the human brain.
- 3 Studies indicate that diet changes may alleviate a range of psychiatric symptoms, and mental health practitioners may start to complement therapy and pharmaceutical treatments with recommended eating plans in the near future.

## A STUDY OF MORE THAN 12,000 HEALTHY SPANIARDS FOUND THAT THOSE WHO CLOSELY FOLLOWED A MEDITERRANEAN DIET HAD A 30 PERCENT REDUCED RISK OF DEPRESSION.

tioxidant-rich fruits may help keep dementia at bay. And so on.

There is probably no single ingredient, no happy seed from the jungles of beyond, that is sure to secure a better mood or mental acuity into old age. But there do appear to be specific dietary patterns—calibrated by millions of years of human evolution—that boost our cognitive and psychological fitness. Within the nascent field of nutritional psychiatry, consensus is building about just what types of diets are best. And perhaps most exciting is the prospect that dietary intervention could serve as a valuable adjunct to medication and other therapies for mental disorders—just as it does in so many other areas of medicine.

### Good Diet, Bad Diet

When it comes to promoting brain health, the diet supported by the strongest data draws on traditional eating patterns from Italy, Greece and Spain. The so-called Mediterranean diet consists primarily of fruits, vegetables, nuts, whole grains, fish, lean meats in moderation, olive oil and maybe a little red wine. In 2011 public health expert Almudena Sánchez-Villegas of the University of Las Palmas de Gran Canaria and her colleagues assessed the relation between this diet and depression in more than 12,000 healthy Spaniards over the course of a median of six years each. They found that compared with people who did not eat a Mediterranean diet, those who did were significantly less likely

to succumb to depression. For the subjects who followed the diet most closely, the risk dropped by a substantial 30 percent.

Sánchez-Villegas later confirmed the association in another large trial. The PREDIMED (Prevention with Mediterranean Diet) study—a multicenter research project evaluating nearly 7,500 men and women across Spain—initially looked at whether a Mediterranean diet, supplemented with extra nuts, protects against cardiovascular disease. It does. But in 2013 Sánchez-Villegas and other investigators also analyzed depression data among PREDIMED's participants. Again, compared with subjects who ate a generic low-fat diet, those who adhered to the nut-enriched Mediterranean diet had a lower risk for depression. This was especially true among people with diabetes, who saw a 40 percent drop in risk. Perhaps these patients, who cannot adequately process glucose, benefited the most because the Mediterranean diet minimized their sugar intake.

Indeed, a central feature of the diet is that it is low in sugar, as well as processed foods and fatty meats, which are commonplace on most Western menus. Leading nutritional psychiatry researcher Felice N. Jacka of Deakin University and the University of Melbourne in Australia was one of the first to demonstrate an association between stereotypical Western diets and depression and anxiety. Most recently, she has drawn another link between poor diet and, quite literally, a shrinking brain. In

## Traditional Diets for Healthy Brains

### MEDITERRANEAN

Research consistently finds the dietary patterns of cultures hugging the Mediterranean Sea to be among the healthiest in the world. Ingredients common to Greek, Italian, Spanish and Middle Eastern cuisine (*below*) are linked with improved cardiovascular, mental and neurological function.

Olive oil

> **Omega-3-rich fish (sardines, tuna, salmon)**

Antioxidant-rich fruits and vegetables (tomatoes, peppers, eggplant)

Whole grains

Legumes

Moderate amounts of lean meat and red wine

Limited sugar and processed food

### OKINAWAN

According to the World Health Organization, the Japanese have the highest life expectancy in the world—in part thanks to the population of Okinawa. Staples of the island group's traditional diet (*below*) include the nutrient-rich purple sweet potato, often eaten in place of rice. Indeed, Okinawans tend to eat less fish, meat, rice and sugar—and fewer calories overall—than do those in other parts of the country.

> **Antioxidant-rich vegetables (Okinawan purple sweet potatoes)**

Seaweed

Some fish

Some meat

Limited sugar and white rice intake

### SCANDINAVIAN

Swedish meatballs aside, Scandinavians cook, collect and cultivate a host of foods that together constitute the new Nordic diet, one of the world's healthiest. It is associated with reduced inflammation and decreased risk for cardiovascular disease and diabetes, both of which can influence brain health. Of particular note, Scandinavians tend to cook with canola oil, also called rapeseed oil, which contains far more omega-3 fatty acids than olive oil.

Fruits (lingonberries)

Vegetables (potatoes)

Nuts/whole grains (rye breads very common)

Seafood

Moderate amounts of meat and dairy

> **Canola (rapeseed) oil**



September 2015 she and her colleagues discovered that older adults who consumed a Western diet for four years not only suffered higher rates of mood disorders but also had a significantly smaller left hippocampus on MRI scans. The hippocampus, composed of two seahorse-shaped arcs of brain tissue deep underneath our temples, is critical to memory formation. Jacka focused on the hippocampus because animal studies have also noted diet-related changes there.

Scientists have proposed a number of possible mechanisms to explain this damage. Jacka's findings parallel other research revealing that high-sugar diets can prompt runaway inflammation and trigger a cascade of other metabolic changes that ultimately impair brain function. Ordinarily inflammation is part of our immune system's arsenal to fight infection and encourage healing, but when it is misdirected or overly aggressive, it can destroy healthy tissues as well. According to numerous studies, inflammation plays a role in a range of brain disorders—from depression and bipolar disorder to possibly autism, schizophrenia and Alzheimer's disease.

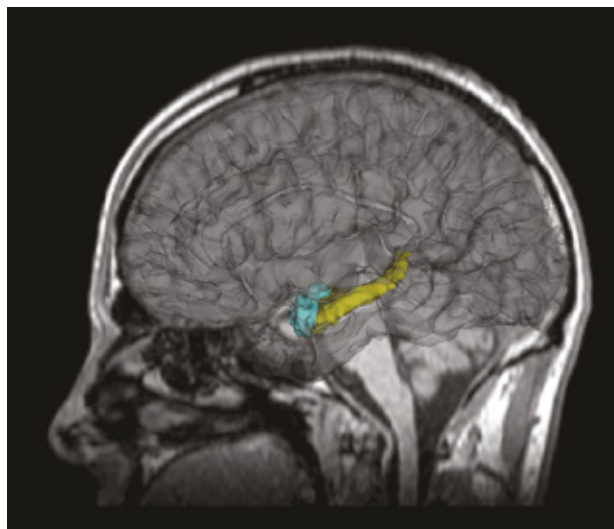
Two meta-analyses from 2010 and 2012 collectively reviewed data from 53 studies and reported significantly elevated levels of several blood markers of inflammation in depressed patients. And numerous studies have reported increased or altered activity of immune cells called microglia—which play a key role in the brain's inflammatory response—in patients with psychiatric disorders, including depression and schizophrenia. It is not clear whether inflammation causes mental illness in some cases, or vice versa. But the evidence suggests that many if not most known risk factors for psychiatric disorders, especially depression, promote inflammation; these include abuse, stress, grief and certain genetic predilections.

Jacka's work repeatedly points to traditional diets such as Mediterranean, Japanese and Scandinavian ones—all of which tend to be noninflammatory—as being best for our neurological and mental health. "There is no doubt that stress and uncomfortable emotions can cause us to reach for the biscuit tin—they don't call them comfort foods for nothing!" she admits. "But consistently the data show that the main constituents of a healthy brain diet include fruits, vegetables, legumes, nuts, fish, lean meats and healthy fats such as olive oil."

### Brain-Building Fatty Acids

Increasingly, researchers are finding that the power of these more traditional diets extends beyond just supplanting bad food with good. Last summer neuroscientists Amandine Pelletier, Christine Barul, Catherine Féart and their colleagues at the Uni-

versity of Bordeaux in France discovered that a Mediterranean diet may actually help physically preserve neuronal connections in the brain. They used a highly sensitive neuroimaging analysis technique called voxel-based morphometry to identify subtle changes in brain anatomy over time. And last September nutritional epidemiologist Martha C. Morris of Rush University and her co-workers reported that the MIND diet—a hybrid of the Mediterranean and the high-nutrient, low-salt DASH diet—may help slow cognitive decline and possibly even help prevent Alz-



In both animal and human studies, typical unhealthy Western diets appear to cause damage to the hippocampus (yellow on MRI scan above), a brain structure that plays an essential role in learning and memory. In one recent study, older adults who had consumed poor-quality diets over the course of four years had a smaller left hippocampus compared with peers who ate more healthfully.

heimer's. When they tested cognitive ability in 960 older adults, those who had followed the MIND diet for roughly five years achieved scores matching those of people 7.5 years younger.

Our evolutionary backstory could explain these neuroprotective effects. Sometime between 195,000 and 125,000 years ago, humans may have nearly gone extinct. A glacial period had set in that probably left much of the earth icy and barren for 70,000 years. The population of our hominin ancestors plummeted to possibly only a few hundred in number, and most experts agree that everyone alive today is descended from this group. Exactly how they—or early modern humans, for that matter—managed to stay alive during recurring glacial periods is less clear. But as terrestrial resources dried up, foraging for marine life in reliable shellfish beds surrounding Africa most likely became essential for survival. Graduate student Jan De Vynck of Nelson Mandela Metropolitan University in South Africa has shown that one person working those shellfish beds can harvest a staggering 4,500 calories an hour.

---

#### THE AUTHOR

**BRET STETKA** is an editorial director at Medscape (a subsidiary of WebMD) and a frequent contributor to *Scientific American Mind*. His writing has appeared in *Wired* and online for the *Atlantic* and NPR.

COURTESY OF NICOLAS CHERBUIN

## By Land or by Sea?

Experts debate how human ancestors found enough fatty acids to build better brains

Omega fatty acids, including docosahexaenoic acid, or DHA, are key to brain health and most likely helped to drive the evolution of the modern human brain. But how did early humans access these vital nutrients? The answer is a matter of some debate.

For nearly two decades archaeologist Curtis W. Marean, associate director of Arizona State University's Institute of Human Origins, has overseen excavations at a site called Pinnacle Point on South Africa's southern coast, near where a newly discovered early human species, *Homo naledi*, was recently unearthed. His work there suggests that sometime around 160,000 years ago, during a glacial period known as Marine Isotope Stage 6 (MIS6), humans made a significant shift in their eating habits, moving from foraging for terrestrial plants, animals and the occasional inland fish to relying on the rich, predictable shellfish beds in the area.

Marean believes this change occurred when early humans learned to exploit the bimonthly spring tides. And to do so, he says, our brains were already fairly well evolved. "Accessing the marine food chain could have had huge impacts on fertility, survival and overall health, including brain health," Marean explains, in part because of the high return on omega-3 fatty acids. But before MIS6, he speculates, hominins would have had access to plenty of brain-healthy terrestrial nutrition, including by feeding on animals that consumed omega-3-rich plants and grains.

Others disagree, at least in part. "I'm afraid the idea that ample DHA was available from the fats of animals on the savanna is just not true," says psychiatrist Michael A. Crawford of Imperial College London. "The animal brain evolved 600 million years ago in the ocean and was dependent on DHA and compounds essential to the brain such as iodine, which is also in short supply on land. To build a brain, you would need building blocks that were rich at sea and on rocky shores."

His early biochemical work focused on showing that DHA is not readily accessible from the muscle tissue of land animals. Using DHA tagged with a radioactive isotope, Crawford and his



Even before early humans began foraging for seafood, they may have incorporated nutrient-rich fish from lakes and rivers into their diets, helping them to build healthy brains.

colleagues also demonstrated that "ready-made" DHA—such as that found in shellfish—is incorporated into the developing rat brain with 10-fold greater efficiency than plant-sourced DHA.

Crawford's colleague and collaborator, physiologist Stephen Cunnane of the University of Sherbrooke in Quebec, also feels that aquatically sourced food was crucial to human evolution. But he believes that before MIS6, inland hominins had already incorporated fish from lakes and rivers into their diet for millions of years.

He suggests that it was not just omega-3s but a cluster of nutrients found in fish (including iodine, iron, zinc, copper and selenium) that contributed to our big brain. "I think DHA was hugely important to our evolution and brain health, but I don't think it was a magic bullet all by itself," Crawford says.

All three researchers are confident that higher intelligence evolved gradually over millions of years as mutations inched the cognitive needle forward, conferring survival and reproductive advantages. But advantages such as, say, figuring out how to shuck oysters—as well as track the spring tides—threw open the Darwinian floodgates. Cunnane comments: "Once we were able to access the coastal food chain in Africa—far more rich and reliable than inland sources of fish—brain and cultural evolution exploded." —B.S.

The archaeological record corroborates the idea and indicates that our ancestors depended on a diet heavy in shellfish and cold-water fish—both rich sources of omega-3 fatty acids. These fats may have driven the evolution of our uniquely complex brains, which are 60 percent fat in composition. One omega-3 in particular, docosahexaenoic acid, or DHA, is arguably the single nutrient most strongly associated with brain health.

In 1972 psychiatrist Michael A. Crawford, now at Imperial College London, co-published a paper concluding that the brain

is dependent on DHA and that DHA sourced from the sea was critical to mammalian brain evolution, especially human brain evolution. For more than 40 years he has argued that the rising rates of brain disorders are a result of post-World War II dietary changes—especially a move toward land-sourced food and, subsequently, the embrace of low-fat diets. He feels that omega-3s from seafood were critical to the human species' rapid neural march toward higher cognition [see box above].

Many studies have confirmed DHA's importance to the de-



Cold-water fish, such as salmon, tuna and sardines (above), are rich sources of DHA, a fatty acid that contributes to the growth, structure and function of nerve cells.

velopment, structure and function of the human brain: it is a component of neuronal cell membranes, facilitates neuron-to-neuron communication, and is also thought to boost levels of brain-derived neurotrophic factor, a protein that supports the growth and survival of brain cells. Given the starring role this and other omega-3 fatty acids play in shaping and maintaining our most complex organ, it makes intuitive sense that incorporating more of them into our diet—by emphasizing seafood—might, as the nutritional data suggest, protect the brain from going haywire. Also of note, DHA appears to decrease chronic brain-harming inflammation.

Fatty acids aside, there is another important link between our ancestors' diets, inflammation and mental health. As we evolved, the 100 trillion bacteria, fungi and other microorgan-

isms that colonize our bodies and constitute 90 percent of our cells came along for the ride. This so-called microbiota—and its collective genes, the microbiome—makes a critical contribution to the formation and function of our digestion and immune system. A growing number of findings now suggest that disrupting it through poor eating habits comes at a cost to the brain.

### A Blow to the Gut

In one striking (if slightly nauseating) experiment in 2014, then 23-year-old student Tom Spector wiped out about a third of the bacterial species in his gut by limiting his diet to McDonald's fast food. It took only 10 days. Spector played the guinea pig for two reasons: as a project to complete his genetics degree and to provide data for his father, Tim, a genetic epidemiology professor at King's College London, who studies how processed diets affect gastrointestinal bacteria. The Spector family's research did not assess specific health consequences—they were measuring only the drop in floral diversity in Tom's gut—but Tom did report feeling lethargic and down after days of burgers, fries and sugary soda. The decline in species was so drastic that Tim sent the results to three laboratories for confirmation.

Diet-induced shifts in the microbiota of the kind Spector brought on himself can rapidly ratchet up inflammation in the gut. On top of the ill effects just described, gastrointestinal inflammation can deplete our supply of serotonin, a neurotransmitter long tied to depression and other psychiatric disorders. About 90 percent of our serotonin is produced in the gut when certain microbes interact with cells lining the gastrointestinal tract (some microbes even produce a portion of our serotonin themselves). But by-products of inflammation convert serotonin's metabolic precursor, tryptophan, to a compound that generates neurotoxic metabolites linked with depression, schizophrenia and Alzheimer's.

The good news is that dietary changes can not only wreck our microbial diversity, they can boost it, reducing gastrointestinal inflammation in the process. In 2015 a group at the University of Pittsburgh conducted a study in which 20 African-Americans from Pennsylvania swapped diets with 20 rural black South Africans. In place of their usual low-animal-fat, high-fiber diet, the Africans consumed burgers, fries, hash browns, and the like. The Americans eschewed their normal fatty foods and refined carbohydrates for beans, vegetables and fish. After just two weeks the Americans' colons were less inflamed, and fecal samples showed a 250 percent spike in butyrate-producing bacterial species. Butyrate is thought to reduce the risk of cancer. The South Africans, on the other hand, underwent microbial changes associated with increased cancer risk.

"Dietary changes are the easiest way to alter your microbiome and help to control inflammation," says psychiatrist Emily Deans of Harvard Medical School. She believes diet is every bit as important as pills and psychotherapy in managing mental illness—a view informed by her own clinical practice. "I discuss nutrition with just about all of my patients," she adds, "and



## DIET MAY BE “AS IMPORTANT TO PSYCHIATRY AS IT IS TO CARDIOLOGY, ENDOCRINOLOGY, AND GASTROENTEROLOGY,” SAYS A 2015 REPORT IN THE *LANCET PSYCHIATRY*.

I think it can really help in managing conditions like depression, at least in some people.” Deans also feels that timing of meals can influence mood, and research suggests that eating on a regular schedule can improve mental health.

Deans acknowledges that science has a long way to go before we fully understand the brain-diet relation. She is also wary of the massive probiotic industry that has, like the supplement industry in general, barreled ahead of the minimal but growing scientific evidence suggesting that probiotics might be effective in preventing or treating mental illness. “You can do studies with, for example, certain vitamins, and some might turn out positive and others negative,” she explains. “But the truth is vitamins exist in all sorts of different chemical states in food and in just one state in supplements.” This difference in form between nutrients in food versus pills explains why the data tend to favor nutrition through diet rather than supplementation. “I think we can safely say that certain dietary patterns seem to promote a healthy microbiome,” Deans speculates, “like the Mediterranean diet and diets that include lots of fiber, fermented foods and fish.” And a healthy microbiome may be essential for a healthy brain.

### Food for Thought

For seven years now Carolyn has been eating better—focusing on seafood and cutting back on sugar. She has lost weight, and her diabetes is under control. “It’s part of a whole new way of life,” she glows, “knowing that what I eat can affect how I feel.” That awareness is building momentum among patients and practitioners alike. In March 2015 a large team of clinicians and researchers published a report in the *Lancet Psychiatry* on behalf of the International Society for Nutritional Psychiatry Research—an organization Jacka co-founded in 2013. Citing modest therapeutic gains yielded by many psychiatric drugs, the authors called for the integration of nutrition-based approaches into mental health care. “The emerging and compelling evidence for nutrition as a crucial factor in the high prevalence and incidence of mental disorders,” they wrote, “suggests that diet is as important to psychiatry as it is to cardiology, endocrinology, and gastroenterology.”

Thanks to our evolutionary lineage (and plenty of fish), attention to our diets may prove critical to reversing the rising rates of mental illness around the world; lowering the proportion of people struggling with various forms of dementia; and staving off milder psychiatric symptoms and disorders. There is little doubt that eating right can help shuttle us through tough times—just as it may have done 160,000 years ago for a small group of humans huddled in coastal African caves.

One of the leading proponents of leveraging diet to better brain health, Jacka is encouraged that interventional studies—in which patients are actually “prescribed” a particular diet and tracked over time—are finally getting under way. Such research will be able to offer more definitive proof of the connection between diet and mental and cognitive well-being. Jacka’s own group is now conducting a randomized controlled investigation to assess the effectiveness of dietary changes in adults with major depression. “Our current trial is the first to attempt to directly address the question: ‘If I improve my diet, will my depression improve?’” she says, adding, “The preliminary results look very exciting.” Her team hopes to have answers later this year.

In the meantime, many doctors and patients are beginning to see dietary interventions as a beacon of hope after several decades of disappointing psychiatric drug development. Too many patients suffering from mental illness or dementia do not respond adequately to existing medications, if at all. For example, selective serotonin reuptake inhibitors such as Prozac—one of the most commonly prescribed drug classes for treating depression—appear effective only in severe cases; they are often no better than placebo for mild to moderate disease. As scientists learn more about the pathologies behind mental and cognitive disorders, new and promising therapeutic targets will surely emerge. But it is clear that nutrition-based treatment plans—free from side effects and low in cost—will also figure prominently in the future of dementia and psychiatric care. **M**

### MORE TO EXPLORE

- **Mediterranean Dietary Pattern and Depression: The PREDIMED Randomized Trial.** Almudena Sánchez-Villegas et al. in *BMC Medicine*, Vol. 11, Article No. 208; September 20, 2013.
- **Early Intervention to Preempt Major Depression among Older Black and White Adults.** Charles F. Reynolds et al. in *Psychiatric Services*, Vol. 65, No. 6, pages 765–773; June 2014.
- **The Origins and Significance of Coastal Resource Use in Africa and Western Eurasia.** Curtis W. Marean in *Journal of Human Evolution*, Vol. 77, pages 17–40; December 2014.
- **Nutritional Medicine as Mainstream in Psychiatry.** Jerome Sarris et al. in *Lancet Psychiatry*, Vol. 2, No. 3, pages 271–274; March 2015.
- **Western Diet Is Associated with a Smaller Hippocampus: A Longitudinal Investigation.** Felice N. Jacka et al. in *BMC Medicine*, Vol. 13, Article No. 215; September 8, 2015.

From Our Archives

- **The Most Invasive Species of All.** Curtis W. Marean; August 2015.
- **Brain Food.** Dina Fine Maron; The Science of Health, September 2015.



BUZELLI



**Like so many momentous events in the lives of young women,** this one began with a missed period. Julia\* had been on oral contraceptives for years, but when she went off the pill, her period did not start up again. Her doctor told her this was not unusual, but months later she still was not menstruating and had begun to experience hot flashes. Hormone levels showed she had a condition called primary ovarian insufficiency—in other words, premature menopause. She was 22 years old.

Julia's primary doctor referred her to a specialist in reproductive endocrinology, who told Julia there was only a 2 percent chance she would ever have children. "It was such a heartbreaking shock for me," she says. "I overcompensated by feeling I had to be perfect, look perfect, be a perfect woman because a core part of my femininity had been taken away." She was still single and imagined that men would not want to have anything to do with a woman who could not have children.

Meanwhile Julia had begun to notice that something was off with her father, David. In his early 60s and recently retired, David had always been an avid fisherman whose steady hands had reliably tied flies for decades. But he had developed a tremor and was having trouble rising from a chair. His movements were growing slower. These changes were gradual and might

---

# THE CARRIERS

---

A genetic anomaly—the fragile X premutation—puts millions of people at risk for infertility and a neurodegenerative disorder they have probably never heard of  
**By Anne Skomorowsky**

---

have gone unnoticed had it not been for Julia's own startling discovery. Her endocrinologist ordered a genetic test to better evaluate her menopausal symptoms and in the process discovered an explanation for both Julia's infertility and her father's tremor: they were carriers of fragile X.

In this age of heightened autism awareness, many people have heard of fragile X syndrome as the most common known genetic cause of autism and intellectual disability. Fragile X children have a number of characteristic physical features such as an elongated face, prominent ears and low muscle tone. Many have symptoms of autism, and many struggle with severe anx-

*\*All patient names in this story—excepting the case study—are pseudonyms.*



ity and disturbed behavior in addition to cognitive impairment. But no one in Julia and David's family is intellectually disabled. They are instead carriers of a genetic trait known as the fragile X premutation, an alteration to the X chromosome that puts them at *risk* of having a child with fragile X syndrome.

Although the syndrome is rare, the premutation is surprisingly common—with a prevalence of around one in 150 women and one in 450 men in the U.S. In addition to causing infertility, the mutation can affect the brain, altering mood and behavior and in some cases causing a devastating movement disorder and dementia. Some evidence has linked it to a variety of autoimmune conditions, fibromyalgia and neuropathic pain, obstructive sleep apnea and restless legs syndrome, among others. But very few doctors are aware of the premutation, and most carriers have no idea they are affected.

That may be about to change. A small group of scientists is intent on uncovering the full consequences of the premutation. To do so, they are reversing the usual order of genetic research: rather than seeking the genetic roots of an established disease, they are using a known gene defect to characterize a new condition, by sharing information about people carrying the premutation. In the process, they are illuminating how a gene that scientists thought was silent may have been shaping the stories of countless families.

### Molecular Anomaly

Suzanne is a journalist who covers women's health, but she drew a blank when her ob-gyn told her that prenatal testing showed she was a carrier of fragile X syndrome. "I said, 'What are fragile eggs?'" she recalls. Her doctor explained that Suzanne was a fragile X premutation carrier and suggested she consider amniocentesis to evaluate her unborn child.

What exactly is a premutation? To understand that, one has to know something about the inheritance of fragile X syndrome. In 1991 researchers identified and sequenced the *FMR1* gene, which codes for a protein needed for normal brain function. The FMR1 protein regulates many processes in the brain. Although its exact role is unknown, this much is clear: children who lack the protein are born with fragile X syndrome.

The *FMR1* gene lies on the X chromosome. Like many genes, it contains a certain amount of noncoding DNA, so

Compared with a normal X chromosome (left), an X chromosome affected by the fragile X mutation (right) actually looks fragile—as if a piece is about to snap off. This reflects an abnormal amount of noncoding DNA on the *FMR1* gene.



called because it does not represent any particular protein. In the case of the *FMR1* gene, this consists of repeated triplets of cytosine, guanine and guanine (CGG repeats), basic components of DNA. It is normal to have these CGG repeats; most people have around 30 on their *FMR1* genes.

Premutation carriers, however, have between 55 and 200 repeats, which makes the gene unstable. The "pre" in "premutation" refers to the way that CGG repeats on an unstable *FMR1* gene can expand over generations. Within a generation or two the gene could be burdened with more than 200 CGG repeats, the threshold number for the *full* fragile X mutation. At that point, the gene stops functioning, and the FMR1 protein cannot be made. The result is fragile X syndrome, a name

---

**Fragile X syndrome is rare, but the premutation is common—affecting one in 150 women and one in 450 men in the U.S. Yet few doctors are aware of it or its impact.**

---

derived from the fragile appearance of the X chromosome, which looks as if a piece were about to fall off.

Because this is an X-linked mutation, its prevalence in men and women differs. Girls have two X chromosomes—one each from their mother and father—so they usually have a healthy X to balance out the defective one. Boys have only one X chromosome, which they inherit from their mother. As in other X-linked conditions, such as hemophilia and color blindness, fragile X syndrome is therefore much more pronounced in boys, and girls are more likely to be carriers.

In 1943, when British physicians first described what came to be known as fragile X syndrome, geneticists believed that carriers had only one thing to worry about: the possibility of having a developmentally disabled child. But now we know otherwise. In the late 1990s a behavioral pediatrician, Randi Hagerman, working in concert with geneticists—including her

---

#### FAST FACTS

##### A MUTATION MYSTERY

- 1 Roughly one in 150 women and one in 450 men are fragile X premutation carriers—that is, people at risk for having children with fragile X syndrome.
- 2 In the past two decades researchers have begun to discover that the premutation itself is associated with certain health outcomes, including infertility in women and a neurodegenerative condition known as fragile X–associated tremor/ataxia syndrome (FXTAS).
- 3 As scientists study carriers, they are beginning to conclude that the premutation itself can be classified as a disease state—generally mild but in some cases involving more serious consequences.

husband, Paul Hagerman, their colleague, biochemist Flora Tassone, and a genetic counselor, Louise Gane—described a new syndrome associated with fragile X. The research team, all of whom (excepting Gane, who recently retired) are now associated with the MIND Institute at the University of California, Davis, studied and treated fragile X kids. Randi Hagerman and Gane followed fragile X children from diagnosis to adulthood and developed close relationships with the mothers of their patients.

They noticed that many of these women had concerns about their own fathers. These grandfathers of kids with fragile X syndrome had begun to develop tremor, trouble walking and even personality changes. At an event for fragile X families in 2000, Hagerman and Gane asked mothers to raise their hands if they thought their fathers were impaired. The researchers were stunned when a third of the audience raised hands.

They began to study the grandfathers of their fragile X patients and to characterize what they dubbed fragile X-associated tremor/ataxia syndrome (FXTAS). Claudia Greco, a MIND Institute neuropathologist, discovered the underlying cause when she was able to obtain four grandfathers' brains at autopsy. It turns out that the premutation is not just a "lite" version of the full mutation but has a completely different mechanism. Because the premutation carrier has extra CGG repeats, he or she makes an abnormal amount of associated RNA—the molecule that directs the synthesis of proteins from DNA. The excess RNA binds necessary proteins, which pile up "like a scrum in rugby," as Paul Hagerman describes it. These "scrum" of RNA and protein are called inclusion bodies, and the FXTAS brains that Greco studied were full of them. The toxic clumps lead to tremor and ataxia in late midlife and to more severe symptoms later on.

In 2010 Tassone and Elizabeth Berry-Kravis, a neurologist at Rush University in Chicago, further described the brain differences in FXTAS patients. Among the most notable are changes in white matter, detectable by MRI, in the middle cerebellar peduncles (MCPs), structures that connect the brain's hub for motor control, the cerebellum, to the upper brain stem. This signature is highly specific to FXTAS and is now a diagnostic criterion. Randi Hagerman notes that it was not until this so-called MCP sign was established that the medical community embraced FXTAS as a real entity.

Damage to the cerebellum and frontal lobes also helps to explain the behavioral changes seen in individuals with FXTAS.

---

## A Mutation's Many Maladies

Researchers have already identified three disorders connected to the fragile X mutation and premutation. The best known is fragile X syndrome, which causes intellectual disability. Fragile X-associated tremor/ataxia syndrome (FXTAS) is a neurodegenerative condition that affects balance, movement and behavior. And fragile X-associated primary ovarian insufficiency (FXPOI) can involve early menopause and infertility. In addition, fragile X premutation carriers may be at risk for dozens of other conditions, including:

- ◆ Thyroid disease
- ◆ Hypertension
- ◆ Fibromyalgia
- ◆ Migraine
- ◆ Neuropathy
- ◆ Vestibular difficulties
- ◆ Impotence
- ◆ Restless legs syndrome
- ◆ Obstructive sleep apnea
- ◆ ADHD

James Bourgeois, a psychiatrist at the University of California, San Francisco, describes the personality change associated with FXTAS as one of "executive dysfunction." Coordination between the cerebellum and the frontal lobes is essential for planning and organizing behavior, as well as maintaining attention and focus long enough to carry out a planned behavior. Put simply, the cerebellum organizes movements, and the frontal lobes keep the activity on track by strengthening impulse control, thereby inhibiting deviations from the plan.

Julia's father, David, has early signs of FXTAS, which is causing his tremor, a swaying gait and tendency to fall. He feels "tippy" when he gets up too fast, and a couple of years ago, he broke his wrist falling down stairs. Of more concern is his emotional reactivity. He describes his emotions as "amplified by 10 percent." In particular, he gets angry: "Sometimes the rage is more than I've ever experienced." David was always passionately engaged in creative work as an artist and teacher, but in the past year or two he has let it drop. He does

not find that disturbing—calling it just a new phase of life—but his friends and family do. What seems to his friends to be a crucial part of his identity is no longer that important to him.

---

## A New Disease

In 2015 at the Second International Conference on the *FMR1* Premutation, 80 researchers and clinicians from all over the world came together in Sitges, Spain, to discuss the phenotype of the premutation—not the carrier's genes, but how they manifest in the individual. This tiny group of researchers is engaged in fully describing the symptoms and behaviors of people who carry the premutation. As they share findings, they are, in a sense, defining a new disease.

FXTAS is just one part of this condition. Another component is infertility: 20 percent of female premutation carriers, like Julia, will develop primary ovarian insufficiency by the time they are 40 years old. A long list of other medical issues recur in the community of carriers [see box above]. By gathering more and more data from carriers, the scientists hope to sift through whether and how these conditions relate to the premutation.

---

### THE AUTHOR

**ANNE SKOMOROWSKY** is an assistant professor of psychiatry at Columbia University Medical Center.





*Pictured, from left:*  
Cheryl Davidson,  
Chrystie Shubert,  
Braden Shubert,  
Alyssa Shubert,  
Bowen Thibodeaux,  
Brayson Thibodeaux  
and Michele Hansen.

Evidence presented at the conference suggests that the pre-mutation may affect mood, anxiety and personality, in both male and female carriers. But such links can be difficult to untangle. For example, many parents of fragile X kids suffer from depressed mood and anxiety, and some have true anxiety disorders such as phobias and obsessive-compulsive disorder. Historically the presence of depression and other psychiatric conditions has been attributed to the stress of raising a child with fragile X syndrome. As early childhood expert Don Bailey of the nonprofit Research Triangle Institute pointed out at the confer-

ence, the most difficult challenge faced by pre-mutation carriers is management of their children's disruptive or autistic behaviors. Most mothers attributed their anxiety to chronic stress.

Yet psychiatrists and behavioral pediatricians who work with mothers of fragile X children wondered if something else was going on. All mothers of fragile X children are themselves pre-mutation carriers, which leaves open the possibility that some of the psychological patterns in this group reflect genetics. Support for the latter idea came from findings in childless sisters of fragile X mothers—pre-mutation carriers who were

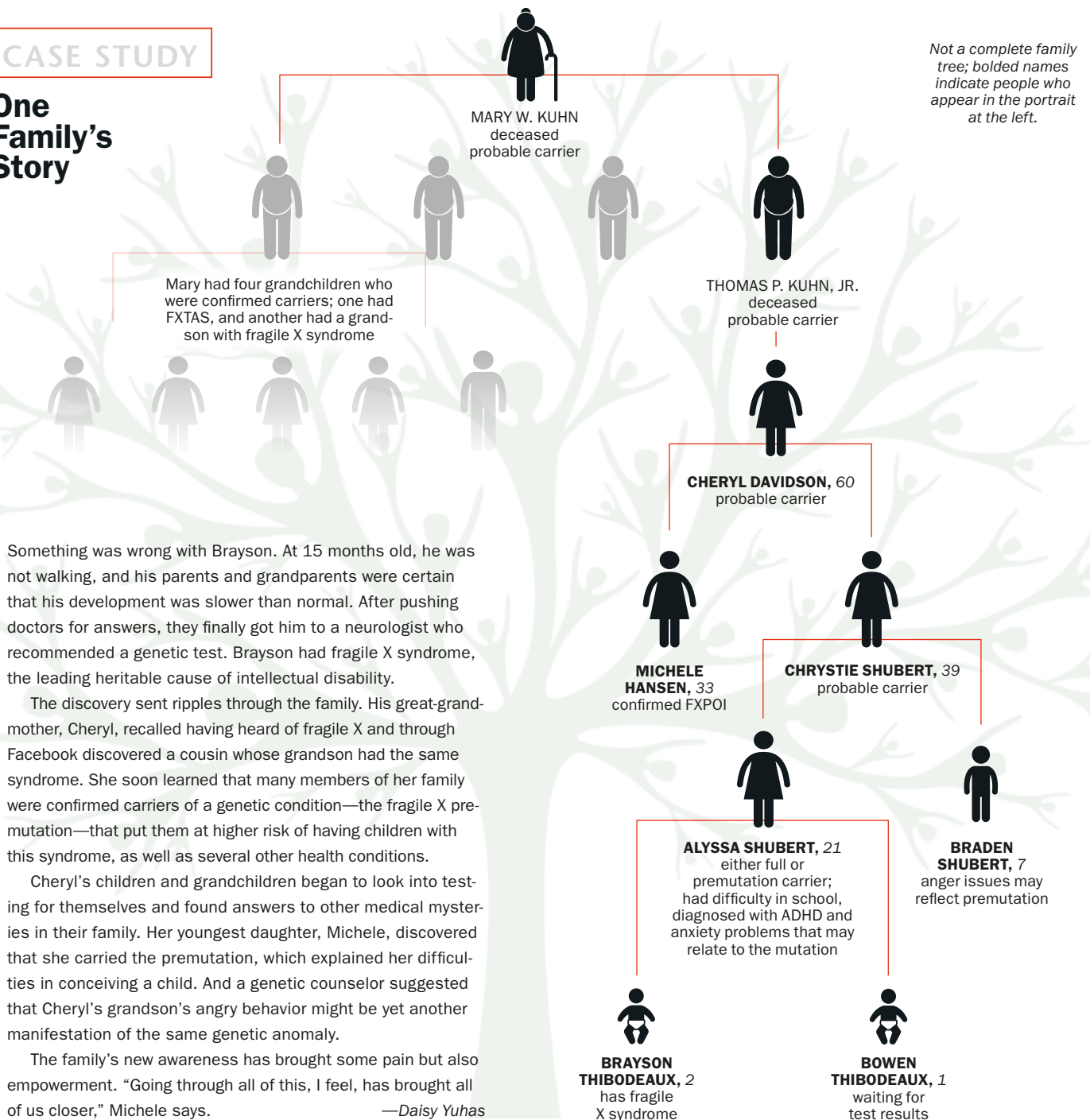
PHOTOGRAPH BY EDMUND FOUNTAIN



## CASE STUDY

### One Family's Story

Not a complete family tree; bolded names indicate people who appear in the portrait at the left.



Something was wrong with Brayson. At 15 months old, he was not walking, and his parents and grandparents were certain that his development was slower than normal. After pushing doctors for answers, they finally got him to a neurologist who recommended a genetic test. Brayson had fragile X syndrome, the leading heritable cause of intellectual disability.

The discovery sent ripples through the family. His great-grandmother, Cheryl, recalled having heard of fragile X and through Facebook discovered a cousin whose grandson had the same syndrome. She soon learned that many members of her family were confirmed carriers of a genetic condition—the fragile X pre-mutation—that put them at higher risk of having children with this syndrome, as well as several other health conditions.

Cheryl's children and grandchildren began to look into testing for themselves and found answers to other medical mysteries in their family. Her youngest daughter, Michele, discovered that she carried the pre-mutation, which explained her difficulties in conceiving a child. And a genetic counselor suggested that Cheryl's grandson's angry behavior might be yet another manifestation of the same genetic anomaly.

The family's new awareness has brought some pain but also empowerment. "Going through all of this, I feel, has brought all of us closer," Michele says.

—Daisy Yuhas

not raising fragile X kids—who also had a higher than average incidence of depression and anxiety. Furthermore, the mothers of children with autism *not* caused by fragile X syndrome, who therefore faced similar parenting challenges but did not carry the pre-mutation, were found to have a lower incidence of mental disorders than fragile X moms.

As genetic testing became more sophisticated, researchers were able to show that the presence and severity of psychiatric symptoms was related to the number of CGG repeats. In a study published in 2015 Danuta Loesch, a neurologist and ge-

neticist at La Trobe University in Australia, and her colleagues studied a sample of 299 adult female carriers and found that those women with midrange expansions—60 to 80 repeats—were more symptomatic than those with larger or smaller numbers of repeats.

Further, in a 2012 study a team of researchers, including Marsha Mailick of the University of Wisconsin–Madison, looked at the biological response to stress in 82 mothers of children with fragile X syndrome. Mothers with midsize repeats produced more of the stress hormone cortisol when confronted

## Counting Up the Risks

The risk for fragile X syndrome stems from the repetition of a specific genetic sequence—in this case, CGG (cytosine-guanine-guanine)—in a gene called *FMR1* on the X chromosome. Fewer than 45 repeats is considered stable, with no adverse effects; more than 200 repeats indicates the full mutation, which causes fragile X syndrome. The health consequences vary for those with between 55 and 200 repeats, and because men have only one X chromosome, the impact differs for males and females.

Number of Repeats	Mutation Type and Risks
<45	Unaffected: Gene is considered stable
45–54	Intermediate: CGG repeats may expand
55–200	Premutation: <ul style="list-style-type: none"> <li>Women face several risks associated with repeat length (<i>right panel</i>), and up to 17 percent may develop FXTAS</li> <li>Men have a 40 percent risk for FXTAS that increases to 75 percent in males older than 80; they also pass the premutation to their daughters</li> </ul>
>200	Full mutation: Boys will have fragile X syndrome; in girls, the outcome is variable

55–79	<b>In women:</b> <ul style="list-style-type: none"> <li>10 percent chance of developing FXPOI, a common cause of infertility</li> <li>3–31 percent chance child will have full mutation if he or she inherits a mutated X chromosome</li> </ul>
80–99	<ul style="list-style-type: none"> <li>30 percent chance of developing FXPOI</li> <li>60–80 percent chance child will have full mutation if he or she inherits a mutated X chromosome</li> </ul>
>100	<ul style="list-style-type: none"> <li>20 percent chance of developing FXPOI</li> <li>95–100 percent chance child will have full mutation if he or she inherits a mutated X chromosome</li> </ul>

with stressful life events. Why women with midrange expansions have a bigger stress response than those with more CGG repeats is a counterintuitive finding that remains unexplained.

Beyond parents of kids with fragile X syndrome, the psychological changes associated with the premutation are most clearly established in FXTAS. These patients primarily show problems with behavior, which may be vulgar or socially inappropriate (in contrast to Alzheimer’s dementia, for example, which can involve behavioral changes but is primarily characterized by memory deficits). Some, like David, may become emotionally labile or lose interest in formerly loved pursuits. Psychiatrist James Bourgeois notes that most of the time, psychiatric symptoms precede tremor and ataxia in patients with FXTAS, and dementia follows the onset of the movement disorder. Even among carriers who never develop the worst-case scenario of FXTAS, he has observed anecdotally that many premutation carriers have “an avoidant, deferential character style” and may be drawn toward isolated pursuits.

Randi Hagerman, the world’s foremost authority on the premutation, sees patients who travel from all over to consult her team at U.C. Davis’s MIND Institute. Thus self-selected, they tend to be educated and competent—doctors, lawyers, rabbis and more than one jet pilot. Even so, Hagerman notes that many patients, especially women, have told her they need to work really hard to maintain eye contact. At the conference, Molly Losh, a psychologist at Northwestern University, spoke of premutation carriers’ greater tendency than noncarriers to perceive standardized faces as “untrustworthy.” Jane Roberts, a psychologist at the University of South Carolina, presented unpublished evidence that even infants with the premutation

had mild autistic features. These may represent the avoidant phenotype described by Bourgeois.

On the other hand, David Hessl, a psychologist at the MIND Institute, cautioned that people need to know that many premutation carriers have no symptoms at all. About 40 percent of male carriers will develop FXTAS, with varying degrees of severity, sometime between their 50s and their 80s, as will a small percentage of females. Carriers without FXTAS, Hessl believes, may have a higher risk of psychiatric disorders, but it is probably not *much* higher, and it is only a risk, not a given.

Scientists say they are limited by the fact that they do not have enough patients to study—a recurring theme at the conference in Spain. There was a sense of urgency about the need to share tissue samples and data. Maureen Leehey, a FXTAS neurologist at the University of Colorado School of Medicine, estimated that there are as few as 500 known FXTAS patients in the U.S. Yet according to the Centers for Disease Control and Prevention, 320,000 U.S. males are premutation carriers, and of these more than 100,000 are likely to develop FXTAS during their lifetime. The problem is that most people do not know they are carriers.

### Genetics Revolution

For-profit genetic-testing laboratories can now screen women for more than 100 genetic conditions, including the fragile X premutation, with a saliva sample patients can mail from home. Such testing programs may lead to the identification of thousands of premutation carriers in the next few years. The profits go to genetic-testing companies, but it is a potential gold mine for subject-starved researchers as well. Meanwhile patients who test positive for the premutation will want to know what to do about it.

For women who learn of their carrier status during pregnancy, as was the case for Suzanne, prenatal testing such as amniocentesis can reveal whether or not the fetus is affected. In Suzanne's case, it showed that her baby carried the premutation, not the full mutation. Today Ruby is a healthy eight-year-old. When she is old enough, Suzanne will let her know about the risks conferred by the premutation, and when she is of reproductive age, she will have her own choices to make.

Virginia, who has almost 200 repeats, is a recently married 28-year-old carrier who designs software. Her younger brother and sister both have the full fragile X syndrome, and she has always known and embraced the fact that someday she would be responsible for their care. "Having grown up watching my parents struggle, it's not something I would take on, knowing it could be avoided in a way I feel comfortable with," she says. Before the wedding, she and her husband-to-be talked frankly about adoption, abortion and other possibilities.

Virginia does not have ovarian failure, but with nearly 200 repeats, her chance of bearing a child with fragile X syndrome is close to 100 percent if the fetus inherits the mutated X. Fortunately, there is a 50 percent chance the baby will inherit her normal X chromosome. If Virginia decides to start a family, she has a handful of choices: not having her own children, using a donated egg, having early chromosomal analysis followed by termination if the fetus has the full mutation, and in vitro fertilization with preimplantation diagnosis. In that procedure, eggs are harvested and fertilized in the lab; then the embryos are evaluated for the presence of the fragile X chromosome and only the healthy ones implanted.

Virginia considers the necessity for premarital family planning a great opportunity, a reckoning that all young couples could benefit from. She is nothing like the anxious, deferential type described by Bourgeois, and she gets her spunk from her premutation-carrier mother. "My mom's badass," Virginia says. She adds that if her husband did not want to be with someone who was open about fragile X syndrome, the premutation and pregnancy, "he should have married somebody else."

The question of who should be screened, and when, is an active area of research in the fragile X community. Virginia and her husband have surely benefited from their knowledge of her family history. Yet the American Congress of Obstetricians and Gynecologists does not currently endorse universal testing for fragile X syndrome. Universal screening of newborns for fragile X has been proposed but is controversial. The MIND Institute's Flora Tassone reviewed the risks and benefits of newborn screening in 2014, noting that such screening would identify premutation carriers, who would then require further evaluation and treatment by an infrastructure that does not yet exist. There is currently no approved treatment for FXTAS. On the other hand, premutation carriers could benefit by making lifestyle changes to protect their health, such as avoiding nicotine and other toxic substances, treating high blood pressure and other conditions that can damage the brain, and seeking treatment for depression and anxiety.

---

**“Geneticists are starting to question the very notion of carrier genes. The fragile X premutation could be a vanguard case for this kind of revolution.”—Sociologist Daniel Navon, U.C. San Diego**

---

Research on the fragile X premutation is challenging some of geneticists' most basic assumptions. As University of California, San Diego, sociologist Daniel Navon explains, our understanding of the fragile X premutation has changed from its being seen as simply a "carrier" gene, to a gene that confers a high risk of two adult-onset conditions, and now to a common, generally mild genetic condition that manifests from infancy. "I know a lot of geneticists are starting to question the very notion of carrier genes, and the fragile X premutation could be a vanguard case for this kind of revolution," Navon says. If seemingly unaffected carriers of other genetic diseases turn out to be mildly affected in ways that have not yet been noticed, then genetic disorders are more common than we ever suspected.

Today, five years after her diagnosis, Julia has more on her mind than the premutation. She is prone to introspection; some experts might say this is part of the premutation carrier phenotype. Cognitive-behavioral therapy has helped her manage her anxiety and restore her healthy self-esteem. She has gone back to school to pursue a long-held dream and says she has made peace with her condition: "It's part of who I am, but it doesn't define who I am." Sometimes she shares in the family worry about what may lie ahead for herself and her father, but for now, she says, "I'd rather focus on the present." **M**

---

#### MORE TO EXPLORE

- **The Fragile-X Premutation: A Maturing Perspective.** Paul J. Hagerman and Randi J. Hagerman in *American Journal of Human Genetics*, Vol. 74, No. 5, pages 805–816; May 2004.
  - **Advances in Clinical and Molecular Understanding of the FMR1 Premutation and Fragile X-Associated Tremor/Ataxia Syndrome.** Randi Hagerman and Paul Hagerman in *Lancet Neurology*, Vol. 12, No. 8, pages 786–798; August 2013.
  - **Health and Reproductive Experiences of Women with an FMR1 Premutation with and without Fragile X Premature Ovarian Insufficiency.** Anne C. Wheeler et al. in *Frontiers in Genetics*, Vol. 5, Article No. 100. Published online September 8, 2014.
  - National Fragile X Foundation: <https://fragilex.org>
- From Our Archives*
- **What Really Causes Autism.** Simon Makin; November/December 2015.







# The Fantasy Advantage

**New findings hint that children absorb some lessons better when they are wrapped in magic and imagination**

By Deena Weisberg

JOHN LUND Getty Images



In J. M. Barrie's classic stage play, *Peter Pan*, the Darling children embark on an adventure with Peter, a puckish young boy who refuses to grow old. In magical Never Land they meet fairies, battle pirates and encounter mystical creatures. The tale, which has inspired youngsters for generations to play similar games, seems to hint that one can remain young at heart forever by indulging in the wonders of imagination.

Nearly all children enjoy getting lost in fantastical worlds. But why they use their imagination so much is a question that has puzzled scientists studying human behavior for decades.

In the early 20th century psychologists suspected that imaginative activities were frivolous—fun but without any real purpose. Kids, they reasoned, would need to leave fantasy behind to fully develop into mature thinkers. More recently, a different viewpoint has emerged. Far from being useless, play is now seen as crucially important for children's development. When kids play, for instance, they can reenact events that scared or confused them as a way of making sense of these experiences. Through the scenarios presented in stories and embodied in play, youngsters learn about the world around them and explore their own place within it. Today advocates for “free play” argue that unstructured time for imaginative activities can help kids be happier and more creative and sociable.

In one particular area, however, imaginative play has seemed unhelpful: education. Decades of research have shown that for the purposes of in-

struction, the context for learning something new should be as similar as possible to the situation in which we apply it. By this logic, make-believe is best for learning when it is as true to life as possible. For example, in a 1989 investigation of hospitalized children at a Scott & White Clinic in Texas, children who engaged in therapeutic play, such as role-playing with medical scenarios and props, showed fewer hospital-related fears than those who engaged in other kinds of play.

It is easy to see how playing doctor might be useful for learning information about the body or health care. What has been less clear is whether a child gains anything by pretending to be a mermaid or superhero. But a new line of research suggests that such whimsical moments may, in fact, have educational value. Psychologists are finding that unrealistic situations can be surprisingly good for helping children learn. As evidence accumulates, it could lead to new approaches in early education that incorporate elements of fantasy—and may eventually illuminate the benefits of adult immersion in fictional worlds.

### Dragons vs. Ducks

In 2015 my colleagues and I published a study in which we enrolled 154 children from low-income preschools in a two-week educational program. We read half of them realistic books on themes such as cooking and farming and the other half fantasy stories with elements such as dragons and castles. In the course of reading, we also taught the children new vocabulary.

After each reading session, we gave the students the opportunity to engage in pretend play with toys that represented characters or objects in the books. For example, there were shovels and ducks for the realistic books and swords and dragons for the fantastical ones. We tested their knowledge of the new words before the start of the program and after it ended, allowing us to measure how much knowledge the preschoolers had gained from these activities.

Overall, the program was a success. Both groups learned the new words that we taught. But kids who heard the fantastical stories were better able to tell researchers about the meanings of the new words than those who had heard realistic tales, showing important growth in their productive vocabulary.

Admittedly, each group was exposed to different words, so it is possible that something about the vocabulary in the fantasy tales was of higher interest than the other new words, but a study from another research team hints that we have stumbled on a broader pattern. In findings presented at the 2013

#### FAST FACTS

#### FLIGHTS OF FANCY

- 1 For a long time psychologists had assumed that role-playing and other imaginative games would be most conducive to learning when the situation was as realistic as possible.
- 2 New research suggests that a fantastical context may actually improve a child's learning outcomes in some cases, leading to a so-called fantasy advantage.
- 3 This advantage may reflect the fact that from infancy, we are primed to pay extra attention in situations that do not conform to ordinary patterns.





For many years psychologists assumed play helped kids test-drive real situations. Pretending to be a doctor, for example, might be useful for learning information about the body or health care. Recent research hints that fantasy play can also powerfully influence learning.

Biennial Meeting of the Society for Research in Child Development, Emily Hopkins and Angeline Lillard, psychologists at the University of Virginia, reported on having read 100 children different kinds of stories, one-on-one. In each narrative, the protagonist was faced with a problem. For instance, a female character needed to get food into a dog's bowl on the other side of a fence with slats too narrow for her hand. She solved the problem by rolling newspaper into a tube, slipping it between the slats and passing bits of kibble through the tube, one at a time, into the bowl.

As in my study, some of the kids heard about a problem and solution in the course of a realistic story. But another group heard about the problem and its solution in the course of a narrative that incorporated some violations to the laws that govern reality, such as characters who could fly or walk through walls.

After telling the children the story, experimenters presented them with a real-world analogue of the problem: they needed to move some marbles into a bowl that was placed inside a box with narrow slats. The subjects received a variety of materials for solving the problem. Some were irrelevant, but others could be used to re-create the solution in the story. For instance, one of the materials was a magazine they could roll into a tube, just like the fictional character had done with a newspaper. Children who had heard the fantastical tale were more

likely to transfer this solution from the story to reality than those who had heard the realistic one.

### Explaining the Impossible

These studies reveal that fantasy can help children learn but do not explain why an unusual context would be better than a realistic one in helping kids acquire real-world knowledge. A possible explanation emerges when we consider research with infants.

Recent work by Aimee Stahl and Lisa Feigenson, both psychologists at Johns Hopkins University, suggests that the fantasy advantage may have its roots in very early development. In a 2015 study, they tested the ability of 110 11-month-old infants to learn while watching a simple series of actions take place on a small stage in front of them, such as a ball rolling down a slide. In one scenario, half of the infants saw an ordinary event: the ball rolled down the slide and was stopped at the bottom by a wall. The other half saw the ball roll down the slide and then appear to roll through a solid wall before stopping at the bot-

---

#### THE AUTHOR

**DEENA WEISBERG** is a faculty member in the department of psychology at the University of Pennsylvania, where she is also affiliated with the Institute for Research in Cognitive Science and the Annenberg Public Policy Center.

When something extraordinary is happening in a story or game, kids may pay closer attention. This not only adds to the appeal of an activity such as make-believe, it can also help children learn more from a given situation.



tom. (Similar magic tricks have been used extensively in developmental psychology studies, and even very young babies know that the first kind of event is ordinary and that the second kind is surprising.)

Next the infants observed a demonstration that revealed the ball's hidden property—that it squeaked when shaken. Researchers then tested the infants' memory for this property by showing them the ball and a new object and moving both while playing the squeaking sound. The simultaneous motion made it unclear which object was making the sound.

Babies who had seen the ball magically disappear looked more at it when presented with this test than infants who had seen the toy roll to a stop at the wall. In other words, the infants who had just seen an impossible event were more attentive to the squeaky ball, which suggests that they had absorbed the lesson of which toy squeaked—just as youngsters seemed to learn more from a fantastic story rather than a realistic one.

In the same study, Stahl and Feigenson further found that infants would investigate the aspect of an object that had just violated their expectations. For instance, when they played with a car they had previously seen floating in midair, they tended to drop it, as if to test its response to gravity.

These situations suggest that these infants were especially attentive to the source of the violation and open to receiving new information about it. If

this is the case, then fantasy helps children to learn because it engages their full focus and attention in a way that reality does not. This interpretation is based on the *mise en place* theory, which my colleagues and I proposed in 2014. It describes the way in which aspects of the environment set the stage for particular kinds of thoughts and behaviors. When the environment is realistic, children know that they should not expect anything out of the ordinary and can proceed as usual. But fantastical scenarios signal that kids need to pay attention because things in that environment do not necessarily follow the typical script. As a result, children feel drawn to engage more deeply, mentally preparing them to learn in a more focused way.

The attention infants gave to the ball hints at a second reason for fantasy's power in learning. Surprising and unrealistic scenarios may require us to try to make sense of what has just happened. Along these lines, a 2010 study by Cristine Legare of the University of Texas at Austin and her colleagues involved teaching 80 preschoolers about special machines and objects, each with a unique purpose. Then, during a test trial, one of the objects worked as expected (for example, a “starter” object caused a machine's lights to turn on, just as it should), and one of the objects did not (a “do-nothing” object, which ought to have no effect, also turned the light on).

When asked to talk about what had happened

during the trial, the children chose to explain the unexpected outcome first. The strange situation seemed to trigger a need to understand what had happened and to seek additional information. In other words, the unexpected scenario was especially ripe for learning.

This study suggests that perhaps unrealistic scenarios help children see the possibilities inherent in reality. As University of California, Berkeley, psychologist Alison Gopnik and I proposed in 2013, fantasy may facilitate learning in the same way that baby talk fosters speech. We do not talk to babies in an exaggerated, high-pitched way because that is how we want them to speak. Rather baby talk highlights important aspects of speech, such as word boundaries, and helps infants to zoom in on key elements of language. It is therefore possible that when children seek out impossible events, it is not because they use them as a direct guide to reality. Instead thinking about unrealistic possibilities can help create informative contrasts with how reality does and does not work, bringing to light the structure of the real world.

### Tapping the Power of Fantasy

Naturally, the results from this small set of studies do not negate the body of previous work showing that similarity is helpful for learning and transfer of information. Similarities between educational and real-world contexts do enhance learning.

There are even a few cases where fantasy may backfire and send a mixed message. A 2014 study by University of Toronto psychologist Patricia Ganea found that preschoolers who heard stories with anthropomorphized animals were left with less realistic expectations about the mental states of these creatures as compared with children who had heard realistic tales. Although the kids in the former group seemed to understand that birds and rodents cannot talk, they were more likely than the latter group to extend humanlike characteristics to the way these animals could think and experience the world.

Nevertheless, the new findings hint at the fact that we have too long underestimated the power of a child's flights of fancy. And there could be educational contexts that are particularly ripe for the fantasy advantage. Much of physics, for instance, relies on testing the natural world's limits. Children and infants alike are captivated by an object's ability to seemingly defy gravity. And imaginative thinking is requisite for older students grappling with complex scenarios such as particles invisible to the naked eye that might travel at nearly the speed of light.

In fact, reality is often unintuitive, forcing scientists to grapple with unlikely possibilities for how the

world works. Fictional worlds that bear less resemblance to reality may help throw reality into sharper relief, making it easier for children to understand and hence learn new information.

In the meantime, parents and teachers can encourage children's engagement with fantasy. If, as our research is finding, fantastical elements are especially helpful to learning, it could encourage children's fantasy-based play and provide them with stories that deliberately break the laws of reality. It may also be useful to nudge kids to notice the impossible aspects of these games and stories; getting them to understand what can and cannot happen in reality may set the stage for future learning. Children's attraction to superheroes, dragons and wizards offer perfect opportunities to ask young learners: "Could dragons be real?" or "What would happen if you could become invisible?"

It may be too soon to speculate on how fantasy's educational power plays out in older children or adults, but it certainly seems likely that the same advantage would remain to some degree. Literature that takes place in fantastic landscapes can help us think deeply about our own world. Consider the science fiction of Ursula K. Le Guin, whose book about a planet without gender prompts us to rethink our assumptions about men and women. And counterfactual history books can make us reconsider present circumstances by inviting us to reimagine the past. These texts demonstrate how fiction can bring unique insights and may even inspire new solutions. Ultimately a little fantasy could do us all a lot of good. **M**

Thinking about unrealistic possibilities can help create informative contrasts with how reality does and does not work, bringing to light the structure of the real world.

#### MORE TO EXPLORE

- **Effects of Fantasy Contexts on Children's Learning and Motivation: Making Learning More Fun.** Louise E. Parker and Mark R. Lepper in *Journal of Personality and Social Psychology*, Vol. 62, No. 4, pages 625–633; April 1992.
- **The Real Reason Children Love Fantasy.** Alison Gopnik in Slate. Published online December 20, 2005.
- **Strange Concepts and the Stories They Make Possible: Cognition, Culture, Narrative.** Lisa Zunshine. Johns Hopkins University Press, 2008.
- **Revisiting the Fantasy-Reality Distinction: Children as Naïve Skeptics.** Jacqueline D. Woolley and Maliki E. Ghossainy in *Child Development*, Vol. 84, No. 5, pages 1496–1510; September/October 2013.
- **Shovels and Swords: How Realistic and Fantastical Themes Affect Children's Word Learning.** Deena Skolnick Weisberg et al. in *Cognitive Development*, Vol. 35, pages 1–14; July–September 2015.

From Our Archives

- **The Serious Need for Play.** Melinda Wenner; February/March 2009.



# The Invisible Girls

**New research suggests that autism often looks different in females, many of whom are being misdiagnosed and missing out on the support they need**

By Maia Szalavitz





hen Frances was an infant, she was late to babble, walk and talk. She was three before she would respond to her own name. Although there were hints that something was unusual about her development, the last thing her parents suspected was autism. “She was very social and a very happy, easy baby,” says Kevin Pelphrey, Frances’s father.

Pelphrey is a leading autism researcher at Yale University’s world-renowned Child Study Center. But even he did not recognize the condition in his daughter, who was finally diagnosed at about five years of age. Today Frances is a slender, lightly freckled 12-year-old with her dad’s warm brown eyes. Like many girls her age, she is shy but also has strong opinions about what she does and does not want. At lunchtime, she and her little brother, Lowell, engage in some classic sibling squabbling—“Mom, he’s kicking me!”

Lowell, seven, received an autism diagnosis much earlier, at 16 months. Their mom, Page, can recall how different the diagnostic process was for her two children. With Lowell, it was a snap. With Frances, she says, they went from doctor to doctor and were told to simply watch and wait—or that there were various physical reasons for her delays, such as not being able to see well because of an eye condition called strabismus that would require surgical treatment at 20 months. “We got a lot of different random little diagnoses,” she recalls. “They kept saying, ‘Oh, you have a girl. It’s not autism.’”

In fact, the criteria for diagnosing autism spectrum disorder (ASD)—a developmental condition that is marked by social and communication difficulties and repetitive, inflexible patterns of behavior—are based on data derived almost entirely from studies of boys. These criteria, Pelphrey and other researchers believe, may be missing many girls and adult women because their symptoms look different. Historically the disorder, now estimated to affect one out of every 68 children in the U.S., was thought to be at least four times more common in boys than in girls. Experts also believed that girls with autism were, on average, more seriously affected—with more severe symptoms, such as intellectual disability. Newer research suggests that both these ideas may be wrong.

Many girls may, like Frances, be diagnosed late because autism can have different symptoms in females. Others may go undiagnosed or be given diagnoses such as attention-deficit/hyperactivity disorder (ADHD), obsessive-compulsive disorder (OCD) and even, some researchers believe, anorexia. As scientists study

how this disorder plays out in girls, they are confronting findings that could overturn their ideas not only about autism but also about sex and how it both biologically and socially affects many aspects of development. They are also beginning to find ways to meet the unique needs of girls and women on the spectrum.

### It’s Different for Girls

Scientists in recent years have investigated several explanations for autism’s skewed gender ratio. In the process, they have uncovered social and personal factors that may help females mask or compensate for the symptoms of ASD better than males do, as well as biological factors that may prevent the condition from developing in the first place [see box on page 54]. Research has also revealed bias in the way the disorder is diagnosed.

A 2012 study by cognitive neuroscientist Francesca Happé of King’s College London and her colleagues compared the occurrence of autism traits and formal diagnoses in a sample of more than 15,000 twins. They found that if boys and girls had a similar level of such traits, the girls needed to have either more behavioral problems or significant intellectual disability, or both, to be diagnosed. This finding suggests that clinicians are missing many girls who are on the less disabling end of the autism spectrum, previously designated Asperger’s syndrome.

In 2014 psychologist Thomas Frazier of the Cleveland Clinic and his colleagues assessed 2,418 autistic children, 304 of them girls. They, too, found that girls with the diagnosis were more likely to have low IQs and extreme behavior problems. The girls also had fewer (or perhaps less obvious) signs of “restricted interests”—intense fixations on a particular subject such as dinosaurs or Disney films. These interests are often a key diagnostic factor on the less severe end of the spectrum, but the examples used in diagnosis often involve stereotypically “male” interests, such as train timetables and numbers. In other words, Frazier had found further evidence that girls are being missed. And a 2013 study showed that, like Frances, girls typically receive their autism diagnoses later than boys do.

Pelphrey is among a growing group of researchers who want to understand what biological sex and gender roles can teach us about autism—and vice versa. His interest in autism is both professional and personal. Of his three children, only his middle child is typical. Kenneth, Pelphrey jokes, has classic “middle-child syndrome” and complains that his siblings “get

#### FAST FACTS

##### AUTISM IN GIRLS

- 1 One in 68 children in the U.S. is affected by autism—but new research suggests that current diagnostic methods overlook girls, meaning even more kids may be on the spectrum.
- 2 Behavioral and preliminary neuroimaging findings suggest autism manifests differently in girls. Notably, females with autism may be closer to typically developing males in their social abilities than typical girls or boys with autism.
- 3 Girls with autism may be harder to diagnose for several reasons, including criteria developed specifically around males and overlapping diagnoses such as obsessive-compulsive disorder or anorexia.





JAIME MONFORT Getty Images

away with murder because they can blame it on their autism.”

Pelphrey is now leading a collaboration with researchers at Harvard University, the University of California, Los Angeles, and the University of Washington to conduct a major study of girls and women with autism, which will follow participants over the course of childhood through early adulthood. The researchers want “every bit of clinical information we can get because we do not know what we ought to be looking for,” Pelphrey says. Consequently, they are also asking participants and family members to suggest areas of investigation because they know firsthand what is most helpful and most problematic.

Girls in the study will be compared with autistic boys, as well as typically developing children of both sexes, using brain scans, genetic testing and other measures. Such comparisons can help researchers tease out which developmental differences are attributable to autism, as opposed to sex, as well as whether autism itself affects sex differences in the brain and how social and biological factors interact in producing gender-typical behaviors.

Already Pelphrey is seeing fascinating differences in autistic girls in his preliminary research. “The most unusual thing we keep finding is that everything we thought we knew in

terms of functional brain development is not true,” he says. “Everything we thought was true of autism seems to only be true for boys.” For example, many studies show that the brain of a boy with autism often processes social information such as eye movements and gestures using different brain regions than a typical boy’s brain does. “That’s been a great finding in autism,” Pelphrey says. But it does not hold up in girls, at least in his group’s unpublished data gathered so far.

Pelphrey is discovering that girls with autism are indeed different from other girls in how their brain analyzes social information. But they are not like boys with autism. Each girl’s brain instead looks like that of a typical boy of the same age, with reduced activity in regions normally associated with socializing. “They’re still reduced relative to typically developing girls,” Pelphrey says, but the brain-activity measures they show would not be considered “autistic” in a boy. “Everything we’re looking at, brain-wise, now seems to be following that pattern,” he adds. In short, the brain of a girl with autism may be more like

**The old idea that there is only one girl on the autism spectrum for every four boys with the disorder is almost certainly wrong, as is the notion that autism is more severe in girls.**

the brain of a typical boy than that of a boy with autism.

A small study by Jane McGillivray and her colleagues at Deakin University in Australia, published in 2014, provides behavioral evidence to support this idea. McGillivray and her colleagues compared 25 autistic boys and 25 autistic girls with a similar number of typically developing children. On a measure of friendship quality and empathy, autistic girls scored as high as typically developing boys the same age—but lower than typically developing girls.

Pelphrey is finding that autism also highlights normal developmental differences between girls and boys. Sex hormones, he says, “affect just about every structure you might be interested in and just about every process you might be interested in.” Although boys generally mature much later than girls do, the differences in brain development appear to be quite big—far larger than the differences in behavior.

### Masking Autism

Jennifer O’Toole, an author and founder of the Asperkids Web site and company, was not diagnosed until after her husband, daughter and sons were found to be on the spectrum. On the outside, she looked pretty much the opposite of autistic. At Brown University, she was a cheerleader and sorority girl whose boyfriend was the president of his fraternity.

But inside, it was very different. Social life did not come at all naturally to her. She used her formidable intelligence to become an excellent mimic and actress, and the effort this took often exhausted her. From the time she started reading at three and

Researchers suspect that comparing boys and girls on the spectrum will reveal more about autism, as well as the ways in which gender affects typical development.

**“Everything we thought was true of autism seems to only be true for boys.”**

*—Psychologist Kevin Pelphrey,  
Yale University*

throughout her childhood in gifted programs, O’Toole studied people the way others might study math. And then, she copied them—learning what most folks absorb naturally on the playground only through voracious novel reading and the aftermath of embarrassing gaffes.

O’Toole’s story reflects the power of an individual to compensate for a developmental disability and hints at another reason females with autism can be easy to miss. Girls may have a greater ability to hide their symptoms. “If you were just judging on the basis of external behavior, you might not really notice that there’s anything different about this person,” says University of Cambridge developmental psychopathologist Simon Baron-Cohen. “It relies much more on getting under the surface and listening to the experiences they’re having rather than how they present themselves to the world.”

O’Toole’s obsessive focus on reading and finding rules and regularities in social life is far more characteristic of girls with autism than boys, clinical experience suggests. Autistic boys sometimes do not care whether they have friends or not. In fact, some diagnostic guidelines specify a disinterest in socializing. Yet autistic girls tend to show a much greater desire to connect.

In addition, girls and boys with autism play differently.

Studies have found that autistic girls exhibit less repetitive behavior than the boys do, and as the 2014 findings from Frazier and his colleagues suggest, girls with autism frequently do not have the same kinds of interests as stereotypical autistic boys. Instead their pastimes and preferences are more similar to those of other girls.

Frances Pelphrey’s obsession with Disney characters and American Girl dolls might seem typical, not autistic, for example. O’Toole remembers compulsively arranging her Barbie dolls. Furthermore, although autism is often marked by an absence of pretend play, research finds that this is less true for girls.

Here, too, they can camouflage their symptoms. O’Toole’s behavior might have seemed like typical make-believe to her parents because she staged Barbie weddings just like other little girls. But rather than imagining



GALLERY STOCK



she was the bride, O'Toole was actually setting up static visual scenes, not story lines.

Also, unlike in boys, the difference between typical and autistic development in girls may lie less in the nature of their interests than in its level of intensity. These girls may refuse to talk about anything else or take expected conversational turns. "The words used to describe women on the spectrum come down to the word 'too,'" O'Toole says. "Too much, too intense, too sensitive, too this, too that."

She describes how both her sensory differences—she can be overwhelmed by crowds and is bothered by loud noise and certain textures—and her social awkwardness made her stand out. Her life was dominated by anxiety. Speaking broadly of people on the spectrum, O'Toole says, "There is really not a time when we're not feeling some level of anxiety, generally stemming from either sensory or social issues."

As she grew up, O'Toole channeled her autistic hyperfocus into another area to which culture frequently directs women: dieting and body image, with a big dollop of perfectionism. "I used to have a spreadsheet of how many calories, how many grams of this, that and the other thing [I could eat]," she says. The resulting anorexia became so severe that she had to be hospitalized when she was 25.

In the mid-2000s researchers led by psychiatrist Janet Treasure of King's College London began to explore the idea that anorexia might be one way that autism manifests itself in females, making them less likely to be identified as autistic. "There are striking similarities in the cognitive profiles," says Kate Tchanturia, an eating disorder researcher and colleague of Treasure's at King's College London. Both people with autism and those with anorexia tend to be rigid, detail-oriented and distressed by change.

Furthermore, because many people with autism find certain tastes and food textures aversive, they often wind up with severely restricted diets. Some research hints at the connection between anorexia and autism: in 2013 Baron-Cohen and his colleagues gave a group of 1,675 teen girls—66 of whom had anorexia—assessments measuring the degree to which they had various autism traits. The research found that women with anorexia have higher levels of these traits than typical women do.

No one is suggesting that the majority of women with anorexia also have autism. A 2015 meta-analysis by Tchanturia and her colleagues puts the figure at about 23 percent—a rate of ASD far higher than that seen in the general population. What all of this suggests is that some of the "missing girls" on the spectrum may be getting eating disorder diagnoses instead.

Further, because autism and ADHD often occur together—and because people diagnosed with ADHD tend to have higher levels of autism traits than typical people do—girls who seem easily distracted or hyperactive may get this label, even when autism is more appropriate. Obsessive-compulsive behavior, rigidity and fear of change also occur in both people with autism and those with OCD, suggesting that autistic females might also be hidden in this group.



Girls with autism tend to show a higher interest in socializing and learning the rules of interaction than boys. This can make them more adept but also makes social exclusion especially painful.

## Double Standards

Even when young women are comparatively "easy" to diagnose, they still face many challenges in the course of development—particularly social ones. This was the case for Grainne.

Her mother, Maggie Halliday, had grown up in a large Irish family and could see early on that her third child, Grainne, was different. "I knew from when she was a couple of months old that there was something not right," Halliday says. "She didn't like to be held or cuddled. She could make herself a dead weight and just—you couldn't pick her up."

Although Grainne's IQ tests are in the low normal range, the results do not capture either her abilities or her disabilities well. Today the teenager's intense interests are boy bands and musical theater. Despite being extremely shy, she blooms on stage and loves to sing. "The play she's in, when they deliver the script, within a week, she has everybody's part memorized and every song in the score memorized," Halliday says.

Because of a genetic condition, Grainne is short: 4'7"—and a half, she insists. And although she is laconic and does not tend to initiate conversation, she is also bubbly and smiles frequently, clearly interested in connecting. She weighs what she does say very carefully. For example, when asked whether she thinks autistic girls are more social than boys with autism, Grainne says, "Some might be," not wanting to generalize.

---

### THE AUTHOR

**MAIA SZALAVITZ** is a journalist and author or co-author of seven books. Her latest, *Unbroken Brain: A Revolutionary New Way of Understanding Addiction*, will be published in April by St. Martin's Press.



Of course, adolescence is difficult for most kids, but it is especially challenging for autistic girls. Many can cope with the far simpler world of elementary school friendships, but they hit a wall with the “mean girls” of junior high and the subtleties of flirting and dating. Moreover, puberty involves unpredictable changes such as breast development, mood swings and periods—and there are few things that autistic people hate more than change that occurs without warning. “She would like to have a boyfriend—that’s why she loves the boy bands,” says Halliday, adding that she thinks Grainne may not understand what such a relationship would really mean.

Unfortunately, the autistic tendency to be direct and take things literally can make affected girls and women easy prey for sexual exploitation. O’Toole herself was the victim of an abusive relationship, and she says the problem is “endemic” among women on the spectrum, particularly because so many are acutely aware of their social isolation. “When you feel

you’re too difficult to love, you’ll love for crumbs,” she says.

In this way, autism may be more painful for women. Autistic people who do not seem interested in social life probably do not obsess about what they are missing—but those who want to connect and cannot are tormented by their loneliness. A study published in 2014 by Baron-Cohen and his colleagues found that 66 percent of adults with the milder form of ASD (so-called Asperger’s) reported suicidal thoughts, a rate nearly 10 times higher than that seen in the general population. The proportion was 71 percent among women, who made up about one third of the sample.

Until very recently, few resources have been available to help autistic girls through these difficulties. Now researchers and clinicians are starting to fill these gaps. For example, Rene Jamison, an assistant clinical professor at the University of Kansas Medical Center, runs a program in Kansas City called Girls Night Out. Aimed at helping affected girls navigate ado-



## The Protected Sex

Simon Baron-Cohen, a professor of developmental psychopathology and director of the University of Cambridge’s Autism Research Center, has helped develop several of the major theories that are guiding current thinking about autism. One of these hypotheses, which he is continuing to test, is the “extreme male

brain” theory, which first appeared in the literature in 2002. The idea is that autism is caused by fetal exposure to higher than normal levels of male hormones, such as testosterone. This occurrence shapes a mind that is more focused on “systemizing” (understanding and categorizing objects and ideas) than “empathizing” (considering social interactions and other people’s perspectives).

In other words, autistic minds may be stronger in areas where male brains, on average, tend to have strengths—and weaker in areas where females, again, speaking broadly, are the superior sex. (When it comes to individuals, of course, these averages do not say anything about a particular man or woman’s ability or capacity—nor do the differences necessarily reflect immutable biology rather than culture.)

Numerous recent studies have supported Baron-Cohen’s idea. In 2010 he and his colleagues found that male fetuses exposed to higher levels of testosterone in amniotic fluid during pregnancy tend to grow up to have more autism traits. A 2013 study he co-authored, led by his Cambridge colleague Meng-Chuan Lai, found that the brain-scan differences seen in children with autism occurred most often in regions that tend to vary by gender in typical children.

In 2015 Baron-Cohen and his colleagues published results

of an analysis of a large group of amniotic fluid samples from Denmark that are linked to population registries of mental health. They found that in boys, having an autism diagnosis was linked with higher levels of fetal testosterone and various other hormones, but the first cohort tested had too few girls with autism, so they are analyzing later births to see if the same results will be found. Further evidence came from a large Swedish study, also published last year, that found a 59 percent increased risk of giving birth to a child with autism among women with polycystic ovary syndrome—an endocrine disorder involving elevated levels of male hormones.

Few scientists—including Baron-Cohen—think that the extreme male brain theory is the whole story. A second idea emerges when looking at the typical strengths of women. If having female hormones and a female-type brain structure increases the ability to read the emotions of others and makes social concerns more salient, it might take a greater number of genetic or environmental “hits” to alter this capacity to the level where autism would be diagnosed. This idea is known as the “female protective” hypothesis.

Along these lines, several studies have shown that in families with affected daughters, there are higher numbers of mutations known as copy-number variations than there are in families where only boys are affected. A 2014 study by geneticist Sébastien Jacquemont of the University of Lausanne in Switzerland and his colleagues found that there was a 300 percent increase in harmful copy-number variants in females with autism, compared with males.

If either—or both—of these hypotheses is correct, then there will always be more boys than girls on the spectrum. “I imagine that once we’re very good at recognizing autism in females, there will still be a male bias,” Baron-Cohen says. “It just won’t be as marked as four to one. It might be more like two to one.”

—M.S.



New programs are helping young and adult women with autism master skills that are crucial to greater independence and confidence, including socializing and self-care.

ing to address such “superficial” concerns can cause serious life problems and restrict independence.

Even many highly intelligent girls on the spectrum have difficulties with washing their hair, wearing deodorant and dressing appropriately, Jamison says. Some of this behavior is linked to sensory issues; other aspects of the problem are related to difficulty following the appropriate sequence of behavior when doing something you think is unimportant. “When Grainne was in seventh grade, I had to tell her it was against the law not to wear a bra,” Halliday says of her daughter, who found bras uncomfortable. Grainne also did not want to wear deodorant—saying, almost certainly accurately, that the boys smelled worse.

The Girls Night Out group does fun activities, ranging from having manicures to playing sports. Typical girls who get school credit for volunteering provide mentoring and talk about boys and other issues the girls might not want to discuss with adults. “One of the things that we really work on is getting them to try new things to figure out what they might like,” Jamison says.

In New York City, Felicity House, which its founders tout as the world’s first community center for women on the spectrum, opened in 2015. Funded by the Simons Foundation, it occupies several floors of a spectacular Civil War-era mansion near Gramercy Park and offers classes and social events so autistic women can get to know and support one another. Five of the autistic women who helped to found Felicity House met a few weeks before it opened to talk about life on the spectrum. Only two had been diagnosed as children—one with Asperger’s and another with what she said was “ADHD with autistic tendencies.” Of the other three women, two had struggled with depression before their diagnosis as adults.

lence, it focuses on specific issues such as hygiene and dress. Although this emphasis might seem trivial or a concession to gender stereotypes, in fact, fail-

Emily Brooks, 26, is a writer studying for her master’s in disability studies at City University of New York. She identifies as gender queer and believes gender norms cause many problems for people on the spectrum. She noted, to broad agreement, that boys are allowed far greater leeway to deviate from social expectations. “If a guy does something that is considered socially inappropriate . . . his friends may sometimes encourage some of those behaviors,” she said, adding that “teen girls will shut you down if you do anything that’s different.”

Leironica Hawkins, an artist who has created a comic book about Asperger’s, also has to contend with social cues about race. “It’s not just because I’m a woman on the spectrum. I’m a black woman on the spectrum, and I have to deal with social cues that [other] people can afford to ignore,” she said. She added that she thought women “are probably punished more for not behaving the way we should. I’ve always heard women are socially aware to the needs of others, and that’s not me, most of the time . . . I feel like I get pressured to be that way.”

Because of these expectations, there is less tolerance for unusual behavior—and not just in high school. Many of the women report having difficulty keeping—but not getting—jobs, despite excellent qualifications. “You can see that in a faculty meeting even at the high-level academic departments,” Yale’s Pelphey says. “The guys still get away with much, much more.”

As awareness of autism grows, women and girls are already increasingly likely to be diagnosed; this generation clearly has significant advantages over those past. But much more research will need to be done to design better and more gender-appropriate diagnostic tools. Perhaps in the interim, the experiences of women with autism should teach us to be more tolerant of socially inept behavior in women—or less tolerant of it in men. Either way, it is clear that a greater understanding of autism in girls is needed to recognize this condition. And in the process it could illuminate new facets of typical behavior and the way that gender shapes the social world. **M**

#### MORE TO EXPLORE

- **Thinking in Pictures: My Life with Autism.** Expanded edition. Temple Grandin. Vintage, 2006.
- **Aspergirls: Empowering Females with Asperger Syndrome.** Rudy Simone. Jessica Kingsley Publishers, 2010.
- **The Autistic Brain: Thinking across the Spectrum.** Temple Grandin and Richard Panek. Houghton Mifflin Harcourt, 2013.
- **Seeking Precise Portraits of Girls with Autism.** Somer Bishop in Spectrum. Published online October 6, 2015. <https://spectrumnews.org/opinion/seeking-precise-portraits-of-girls-with-autism>
- **The Lost Girls.** Apoorva Mandavilli in Spectrum. Published online October 19, 2015. <https://spectrumnews.org/features/deep-dive/the-lost-girls>

From Our Archives

- **Taking Early Aim at Autism.** Luciana Gravotta; January/February 2014.
- **Autism Grows Up.** Jennifer Richler; January/February 2015.

# Can Kids *Really* Learn to **COOPERATE?**

**Yes—especially if frazzled parents steal  
a few lessons from game theory**

By Paul Raeburn and Kevin Zollman

ILLUSTRATIONS BY EMMA HANQUIST



Adapted from *The Game Theorist's Guide to Parenting: How the Science of Strategic Thinking Can Help You Deal with the Toughest Negotiators You Know—Your Kids*, by Paul Raeburn and Kevin Zollman, by arrangement with Scientific American/Farrar, Straus and Giroux, LLC (US), Commonwealth Publishing (Taiwan) and Grand China Publishing House (China). Copyright © 2016 by Paul Raeburn and Kevin Zollman.





# Sibling rivalry?

We talk about it all the time, but what we're really concerned with is the incessant squabbling that can turn a happy home into what feels like a battleground. That's not rivalry—it's conflict. After repeatedly separating our kids and reminding them for the thousandth time that they should *try to be a little nicer to one another*, many of us begin to think we will never put an end to the fighting. But reducing the number and intensity of these conflicts is possible—if we strike the right bargain.

Here's where a little knowledge of human behavior and game theory comes in handy. Psychologists have found that how children approach negotiations—and whether they share or turn spiteful—depends in large part on notions of fair play. And game theorists have devised various ways to approach any negotiation—some of which are more likely to result in fair outcomes than others. Some schemes require an authority figure—like a parent—to enforce them, but others are designed to structure the bargaining so that no enforcer is needed. What that means is, with the right incentives, kids can be taught to reach fair agreements all on their own.

Everyone wins when children figure out for themselves that cooperation beats conflict—and decide to cooperate without threats from the parental authorities. The key is not that the kids will cooperate every time; they won't. But if they know they must meet in negotiation again—possibly even five minutes later to, say, decide which movie they are going to watch—they might figure out that cooperating this time could win them better treatment from a sibling next time around.

## Learning to Cooperate

Cooperation is part of our biology. It is not limited to adults or even to humans. It occurs within many species—from fish and bats to birds and monkeys. Harvard University psychologist Elizabeth S. Spelke, a pioneer in the study of infant cognition, has examined how children learn to cooperate. She notes that human adults prefer to share with three groups of people: close relations; people who have shared with us, whom we want to reward by being generous in return; and people who have shared with others because we like to reward generosity even if it is not directed at us (game theorists call this “indirect reciprocity”). The problem is that we don't know how we ac-

quired those preferences. Are they encoded in our development? Do we learn them through our experience of others' generosity, our religious education or our families?

In 2008 Spelke and psychologist Kristina R. Olson, now at the University of Washington, ran a series of experiments to try to answer those questions. First, they investigated kids' willingness to share with family members. Working with a group of 20 boys and girls around four years old, Spelke and Olson represented each child using a doll, which they called the protagonist. They gave each child their protagonist doll and gave the doll resources to share—plastic bananas and oranges, rubber ducks, candy, and more—with other dolls, which were described to the kids as sisters, friends or strangers. Even at this young age, the children directed their protagonist dolls to give more gifts to siblings than to friends and more to friends than to strangers.

In a similar experiment, the scientists read the children a story, in which some of the other dolls gave presents to their

Be sure that the benefits of cooperation are in equal balance. If one child stands to gain more than another, then spite might rear its ugly head.

protagonist doll. In turn, the children then directed their protagonist doll to distribute more resources to dolls that had given more to them—demonstrating reciprocity. In one final experiment, the kids gave more resources to dolls that had been generous to others as compared with dolls that had not been generous to anyone.

The studies, taken together, “provide evidence that three specific principles governing complex, mature cooperative networks emerge early in childhood,” Olson and Spelke concluded. Children do not appear to learn these principles from adult experience or from religious or moral instruction. Instead they may arise through their intrinsic development or their interactions with other children. More important, they could also be learning these principles from their family environments.

This kind of generosity—and the special concern for siblings—is related to children's interest in cooperation and sense of fair play. “Probably fairness evolved to support cooperation in some way. We don't know exactly how that works yet,” says psychologist Katherine McAuliffe, now at Boston College. But she and her colleagues have several hunches. One idea is that

### FAST FACTS

#### PLAYING NICE

- 1 Even kindergartners have a sense of fair play and will share more with specific groups—family, friends and people who have been generous with them.
- 2 Parents can tap this notion of fairness to encourage children to cooperate with one another and avoid spiteful behavior.
- 3 Using classic strategies from game theory, kids can learn to establish fair agreements on their own, without any intervention from a parent or other authority figure.



we need to know what we are going to get from cooperating, relative to what we are putting out, she explains: “You want to avoid situations where you’re being exploited.” If we are each trying to maximize our gain in any situation, then we are more prepared to cooperate when it makes sense for us.

### Establishing Fair Play

Consider the pickup dilemma: Putting away the Legos, puzzles, costumes and My Little Pony collection that accumulate on the kids’ bedroom floor. (Where did we *get* all this stuff?) It’s time to clean up, but neither of your kids will budge. Each is waiting for the other to start. Cooperation seems as remote as kids asking for a handful of kale as an after-school snack.

Success in this kind of scenario typically comes only after siblings have negotiated repeatedly with one another over a period of years, honing their notion of what is fair. To get there, you need to put in place a variation on the game theory classic the Prisoner’s Dilemma, which we’ll call the Repeated (or Iterated) Prisoner’s Dilemma. In the Prisoner’s Dilemma, two prisoners are separated and given the option of confessing or saying nothing. If they both say nothing, they both get shorter sentences for a minor crime. If one confesses and the other doesn’t, the confessor goes free, and the other gets a longer term. If both confess, they get equal, intermediate sentences. Silence by both would be best for both—they would only get short sentences. But one of the first and most lasting achievements of game theory has been to show that both will always confess. Without

knowing what the other will do, they have no choice. Each prisoner wants to guard against receiving a stiffer sentence.

In the Repeated Prisoner’s Dilemma, the two prisoners—or let’s say siblings—face the opportunity again and again to keep silent or tell on the other one (confess). Now the game becomes more interesting. Your son might choose to tell on your daughter; she might respond by telling on him, too. But if your son keeps silent, maybe the next time your daughter will offer him the same consideration in return. Why? Because she sees that kindness can be good for both of them. If we can get siblings started along this path, cooperation will most likely increase, with the good behavior of one reinforcing the other.

Game theorists have proved this to be true. They call the strategy “tit for tat.” We realize that tit for tat might sound like the last thing we want to encourage. But in game theory, it means that if your son begins with a cooperative move, your daughter can cooperate, by staying silent, or she can defect, by

---

#### THE AUTHORS

**PAUL RAEBURN** is an award-winning author of four books, including *Do Fathers Matter?* His articles have appeared in *Discover*, the *New York Times Magazine* and many other publications. **KEVIN ZOLLMAN** is a game theorist and an associate professor of philosophy at Carnegie Mellon University.



telling on her brother—but whatever she does, he will do exactly the same thing she does from then on. If she cooperates, he cooperates again. If she defects, so does he. See the logic? Tit for tat is game theorists' version of the Golden Rule.

One of the leaders in research on cooperation is Robert Axelrod, a professor of political science at the University of Michigan. Whereas some say children will never cooperate in the absence of authority, Axelrod has a more optimistic view of human nature. He believes that people can cooperate even if they are not concerned about the welfare of others or the welfare of their group as a whole. Around 1980 he demonstrated this point by creating a simulated computer competition in which game theorists play the Repeated Prisoner's Dilemma game against one another. He asked actual game theorists to offer the strategies they thought would be most successful. Fourteen experts stepped up.

When he ran his computer simulation using those first 14 entries, tit for tat—submitted by the now late mathematical psychologist Anatol Rapoport of the University of Toronto—beat all the other more complex strategies, “to my considerable surprise,” Axelrod wrote. It was the most effective at encouraging cooperation in the Prisoner's Dilemma. This was big news. Cooperation was emerging in the absence of any threat from above. Or, as Axelrod put it, “cooperation based solely on

reciprocity seemed possible.” To be sure of the findings, he ran the computer tournament again. This time he got 62 entries from computer geeks, biologists, physicists, and others. The entries included all kinds of fancy mathematical strategies. Rapoport once again submitted tit for tat. Once again, it won.

So when your kids face the pickup dilemma, each one has an incentive to defect, as in the Prisoner's Dilemma. But in the Repeated Prisoner's Dilemma—as in the playroom—they soon meet again, when the stuffed animals have migrated to the center of the floor like a herd of wildebeest gathering on the African savanna.

The mathematically proven best parent tactic is to encourage your kids to adopt tit for tat. Your daughter and son alternate putting the toys away one at a time until the room is clean. They have both contributed equally to the work, and you can reward both with ice cream. Keep the game going, keep track of whose turn it is and be scrupulously fair. Each child has the incentive to clean up the room because doing so will encourage the other one to do the same.

### Beyond Tit for Tat

If you think that this approach won't work with *your* kids, think again. Axelrod points out that it has worked in situations that are far more volatile and dangerous than sibling relationships.

One of the most improbable appearances of cooperation appeared in Europe during the bloody trench warfare of World War I. Frontline soldiers, with orders to kill their opponents, devised a kind of tit for tat that considerably reduced the bloodshed. In what is referred to as the live-and-let-live scenario, soldiers on one side would refrain from shooting to kill—if the other side reciprocated.

So which of your kids will lay down arms first? You can try to initiate cooperation by taking turns with one child until a recalcitrant sibling jumps in. Or you might try the opposite strategy: You become the person who refuses to cooperate. It works like this: When the kids refuse to pick up the toys, you say you will step in and pick them up yourself. And neither of the kids will get ice cream. Often they quickly realize that they should cooperate before you clean up and they lose their reward.

Your efforts to harshly disrupt the game prompt your kids to cooperate. And remember the next time the situation arises, your children might very well decide to clean up the clutter before you can intervene, having learned that cooperation



can be easier—and lead to more ice cream—than defecting.

Axelrod has taken this a tactic even further, adding in the concept of generosity. Suppose your son grabs the first handful of Lego bricks. Your daughter grabs the next. And so it goes until she decides that she's tired and doesn't want to continue. According to tit for tat, your son should stop, too—the rule is that he does whatever she does. But suppose he believes that she will step up again and finish the job. Then he should continue to pick up the Legos, giving her a chance to change her ways and once again pitch in. This is what Axelrod calls *generous* tit for tat. Your son allows your daughter to slack off a bit now and then.

Or the opposite could happen. Your daughter refuses to take her turn picking up bricks, and your son stops picking up, too. Your daughter, sorry that she has destroyed the coopera-

When kids realize that they have to negotiate repeatedly with one another, they figure out that cooperating this time could win them better treatment from a sibling next time around.

tion, decides to pick up another handful of Legos, and your son reciprocates. This is what Axelrod calls *contrite* tit for tat. “A strategy like generous tit for tat is likely to be effective,” he writes, as can contrite tit for tat “because it can correct its own errors and restore mutual cooperation almost immediately.”

But this doesn't always work. Spite—the shady relative of cooperation (to paraphrase game theorists Rory Smead of Northwestern University and Patrick Forber of Tufts University)—can kill cooperation. We're talking here about the psychological definition of spite—being willing to pay a cost so that someone else has to endure a greater cost. Spite can destroy sibling cooperation faster than anything, but until recently, little was known about whether children would act out of spite. A few years ago McAuliffe explored that very question.

### The Power of Spite

We know that humans are unique in one respect—they cooperate with complete strangers. Animals don't usually do this. This cooperation probably relates to humans' sense of fairness and aversion to inequity. This aversion appears in kids around age four or five. McAuliffe and her collaborators conducted much of the research that established this. But what McAuliffe

wanted to ask beyond that was: *Why* do kids reject inequity? Why are they sometimes willing to forgo their own resources to deprive somebody else of a richer reward?

To find out, in 2014 McAuliffe and her colleagues recruited pairs of children, ranging in age from four to nine, and compared them with pairs of adults in an experiment designed to see who would act out of spite versus frustration. They doled out either fair or unfair shares of candy to the pairs and found that even young children would act out of spite if they got the raw end of the deal, preferring that no one get any candy to letting another child win. That is, they didn't simply reject their unfair share (that's frustration); they wanted to cause a little pain to the party that got the sweeter deal. Interestingly, the adults did not act out of spite, possibly because they were “more worried than children about not appearing resentful or jealous over candy in front of another adult,” McAuliffe and her colleagues wrote. In these trials, spite tended to disappear around age eight, when kids begin to feel uncomfortable if they receive more candy than another child.

What, then, is the takeaway message for parents? First of all, young children tend to be angry when they get less than their fair share of anything—candy, stickers or screen time. And the research suggests that four- and five-year-olds just aren't capable of anything else. So make sure that the benefits of cooperation are divided equally between the kids. If one stands to gain a lot more from cooperation than the other, spite might just rear its ugly head and destroy the utopia you are trying to create.

Second, although it might seem obvious to us that getting too much candy isn't fair and that we should give some back, it's not obvious to kids, at least until they are in the fourth or fifth grade. As McAuliffe and her team write, “Our findings suggest that young children show a sophisticated capacity to maintain their competitive standing relative to others, with older children in addition showing concerns about fairness.” If they show that concern for fairness at the appropriate age, you're on the right track. You're raising kids who are going to be fair and generous—which prepares them to enter that crazy world out there, where these qualities will serve them well.

And third, children can be taught to cooperate. It will take patience and sometimes the resolve to deny them treats when they haven't cooperated in picking up Legos. But hang tough. This can work. Game theory proves it. **M**

#### MORE TO EXPLORE

- **The Evolution of Cooperation.** Robert Axelrod. Basic Books, 2006.
- **Foundations of Cooperation in Young Children.** Kristina R. Olson and Elizabeth S. Spelke in *Cognition*, Vol. 108, No. 1; pages 222–231; July 2008.
- **Children Reject Inequity Out of Spite.** Katherine McAuliffe, Peter R. Blake and Felix Warneken in *Biology Letters*, Vol. 10, No. 12. Published online December 24, 2014.

*From Our Archives*

- **One for All.** Frans de Waal; *Scientific American*, September 2014.





# STATUS UPDATE:

STRESSED,

ANGRY,

AT RISK?

**Using powerful new tools, scientists are mining social media to assess mental and physical health from afar**

By Johannes C. Eichstaedt

**L**ate one night in 2010 after the annual Google Zeitgeist conference had wrapped up, psychologist Martin Seligman, a featured speaker that year, found himself in a huddle with some of the biggest names in technology. Google had just broken ground using search-engine queries to monitor the spread of influenza in the U.S., and Google Maps was taking the world by storm. The potential applications for such tools seemed limitless, so Seligman, a founding father of positive psychology, and Google co-founder Larry Page, among others, began to explore the possibilities.

What if something like Google Flu Trends could be developed to chart psychological health in America? Specifically, they wondered if a computer algorithm could accurately predict happiness and well-being across time and space by tracking the language that people used on social media.

In a matter of months Seligman, along with me and a few others at the University of Pennsylvania, launched the World Well-Being Project (WWBP), initially in collaboration with Google.org, the company's philanthropic arm. Since then our cross-disciplinary team of psychologists, computer scientists, statisticians and app developers has grown rapidly. It now includes 13 staff scientists pursuing 45 sub-projects with collaborators in governments and organizations around the world.

In January 2015 my colleagues and I published an important proof-of-concept result. We evaluated more than 100 million tweets from some 1,300 counties across the U.S., a sample of public data available from Twitter. We discovered that the preponderance of negative tweets—particularly those expressing anger or hostility—in a given location reliably predicted rates of death from heart disease there. Many other findings have piled up that reveal associations between the language in tweets or Facebook posts and traits that include age, gender, personality and income level, as well as mental illness and physical ailments.

These results make it clear that social media data are a rich resource that psychologists, sociologists, epidemiologists and others can mine to make valuable communitywide health forecasts and even individual diagnoses. The opportunity may be huge, but this fast-growing field has a dark side, too. Analyses of how people use language on social media are based solely on statistical patterns. But they can be so revealing that intelligence agents, political candidates and businesspeople—from marketers to insurance actuaries—are just as interested as scientists in their application. Indeed, few people realize just how much information algorithms can cull from their routine activity on Facebook and Twitter.

## What Words Can Reveal

Before the WWBP team began testing tweets to spot health trends, Google had taken an intriguing first step. In 2008 physician Roni Zeiger, then the firm's chief health strategist, and his co-workers launched Google Flu Trends. The program spotted Google searches on terms related to flu symptoms and remedies and noted where geographically those searches were entered. In this way, they could plot the spread of infection in real time. Remarkably, their tracking of the flu season matched the statistics collected by the Centers for Disease Control and Prevention—only Google had the information first because they did not need to wait for doctors and hospitals to report each outbreak. Google discontinued Flu Trends last year, but the program demonstrated that search queries offered a viable way to monitor the spread of specific conditions, and it kick-started the field now called digital epidemiology. Newer endeavors are exploring search queries as a means to surveil not just influenza but dengue fever, malaria and sexually transmitted diseases.

Understanding the psychological states of entire populations, as our project strives to do, can be a little more nuanced than tracking illness: no one Googles “I am happy” in the way they search for remedies when they feel unwell. So we have had to take a less direct

route, analyzing what people write on social media instead of their search terms. Decades of research have found that the words people choose in everyday conversation can reveal a great deal about their underlying psychology. And there are countless links between a person's mental state and physical well-being. Stress, negativity, anxiety and depression can impair our immune and cardiovascular systems, for example. Likewise, positive emotions and optimism appear to have a protective effect, reducing the risk of many diseases, including atherosclerotic heart disease, and increasing life expectancy.

Beginning in the 1990s, social psychologist James Pennebaker, now Regents Centennial Professor at the University of Texas at Austin, and his colleagues made a series of intriguing discoveries about the link between words and well-being. They were investigating why people who write about a trauma after the fact—a technique called expressive writing—are less likely to become physically ill, compared with people who keep disturbing experiences secret. To evaluate what their subjects penned, they used a computer program to quickly tally the words and concepts these essays contained.

Much to their surprise, they found that the actual content of the writing—whether it included positive or negative language and ideas—revealed less about a participant's mental health than functional parts of speech did. For example, they

The language people use in tweets and Facebook posts can indicate their age, gender, personality, income, mental state and physical health.

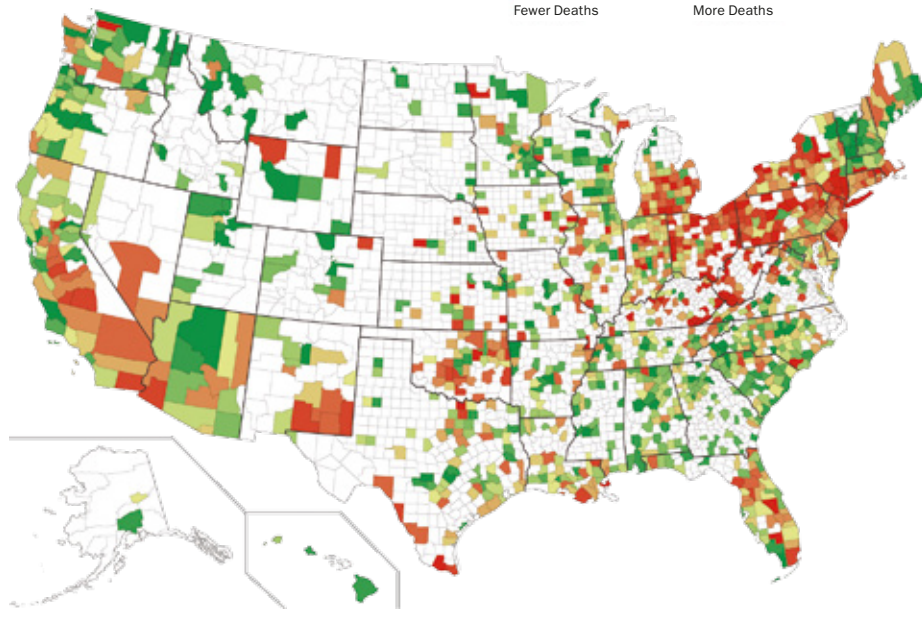
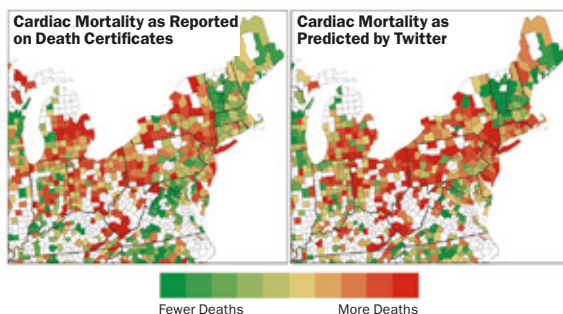
### FAST FACTS

#### USING SOCIAL MEDIA TO MAKE DIAGNOSES

- 1 Social media feeds offer psychologists, sociologists and epidemiologists, among others, a new resource for tracking health and well-being at a distance.
- 2 Algorithms that make use of machine learning can analyze the language people use online to craft detailed psychological profiles of individuals and entire communities.
- 3 Using these methods, researchers are finding a wide range of revealing associations between social media posts and personality, mental health, and even physical conditions such as heart disease.

## Twitter's Powerful Predictions

Actual rates of death from atherosclerotic heart disease (*left inset*), based on CDC data, matched predictions (*right inset*), based on the tenor of tweets from some 1,300 U.S. counties. Specifically, the preponderance of angry or hostile tweets (those containing curses or words such as “hate”) in a given location accurately forecast the mortality rates there (*map below*).



found that people in the throes of depression did not necessarily write about sad things, but they did reliably use more first-person-singular pronouns: I, me, mine. Depressed patients tend to ruminate and are often heavily preoccupied with their own suffering. They found that the symptoms of trauma frequently lifted when participants started using more causal words (because, therefore, but) and complex language in their writing. These patterns appeared to signal that a patient was starting to make sense of the trauma and integrate it into a coherent narrative.

As Facebook, Twitter and similar applications have taken off during the past decade, the amount of language data available for analysis has expanded dramatically, offering psychologists a vast new window into the mental health of social media users. (In general, we work with anonymized data and request permission from Facebook users.) Of course, people present a version of themselves online, playing up good behaviors, traits and events—a skew that researchers refer to as a social desirability bias. But such biases are often less distorting than you might think. The fact that people are Facebook friends with their real friends usually helps to keep them fairly honest

online. Real-world acquaintances know that their life is not all picnics and parties. Moreover, because these biases tend to affect everyone equally, algorithms can still tease out key differences among people. In support of this idea, when we compare the predictions from our methods against data collected in traditional ways (phone surveys, hospital reports, and so on, which sample the population more representatively), we have often been surprised by just how close the two are.

### Needles in a Haystack of Tweets

The language on social media feeds—filled with slang and emoticons—presents a challenging set of data to parse. We are only able to extract meaningful patterns from it today thanks to breakthroughs in natural-language processing during the past 30 years. With exponential growth in computing power, it has become increasingly possible to process language using statistical pattern-recognition algorithms, also called machine learning. These tools have matured dra-

matically in recent years and enable applications such as Apple's Siri and Google's analytics programs, which drop those eerily appropriate ads alongside your e-mail's in-box.

Before these advances, language analysis in psychology was based on simpler dictionary-based approaches that linked emotional states to predetermined lists of words. For instance, if the word “happy” appeared in a text, it was taken as a sign of positive emotion. This method sometimes yielded confusing results because language is inherently ambiguous. When early work in this area applied a psychologist-made “positive emotion” dictionary to social media feeds, it erroneously indicated that there were huge spikes in happiness on New Year's Day—simply because people were wishing one another a “happy” new year.

Modern machine-learning approaches avoid these errors.

#### THE AUTHOR

**JOHANNES C. EICHSTAEDT** is a data scientist pursuing a Ph.D. in psychology at the University of Pennsylvania, where he co-founded the World Well-Being Project in 2011.



## How Twitter Language Reflects the Risk of Heart Disease

### Risk



### Protective



In an analysis of public tweets by U.S. county, we found that words associated with negative topics (shown in red on left) were correlated with higher rates of death from heart disease. More optimistic subjects (shown in green on right) were more often tweeted from communities with lower rates. We found the strongest language correlations with atherosclerosis, a leading cause of death in the U.S., often thought to be closely linked to psychological factors.

They start out agnostically—that is, they make no assumptions whatsoever about which words indicate what emotions or traits—and then they cluster, count, score and isolate words to “learn” psychological associations from scratch. One shortcoming is that these methods work only on data sets with at least 5,000 to 10,000 users. Indeed, the more entries, the more accurate the results because additional input allows us to isolate even faint signals amid all the noise of daily posts. Fortunately for us, most social media sites now have hundreds of millions of users.

In 2013 H. Andrew Schwartz, now at Stony Brook University, Seligman and I, along with our colleagues, published a study in which we had applied a machine-learning method to 700 million words, phrases and topics gleaned from the Facebook messages of 75,000 volunteers, who also took personal-

ity tests. To date, it was the largest study linking language and personality, by an order of magnitude. Once the algorithms had the status updates of so many Facebook users and knew how these users scored on a personality test, they could correlate words to personality traits.

Using the results, we created word clouds to show the words that best distinguished extroversion from introversion and neuroticism from emotional stability. We found that some words are rarely used, but when they are, they are highly predictive of a psychological trait. For example, the use of “depressed” is a powerful, if seldom seen, marker of neuroticism.

Many of the associations made sense, but some were surprising. You may have predicted that extroverts more often use the word “party” and introverts “computer,” but would you have guessed that the word “apparently” is used far more often by people who score high in neuroticism? Or that people who are emotionally stable write more frequently about sports? Or that introverts show a greater interest in Japanese media, such as anime, and emoticons? In a follow-up study led by our colleague Gregory Park, we applied the algorithms to another set of Facebook posts to actually predict users’ personalities using only their feeds. Remarkably, the algorithms did as well as or better than friends who filled out personality surveys about the subjects. In a sense, the algorithms wound up knowing these people better than their friends did! We took this result as a good sign that we had a handle on desirability biases.

My colleagues and I then used this same approach on Twitter to estimate an average “psychological profile” for some 1,300 U.S. counties,

without having to knock on anyone’s door [see box at left]. The counties whose tweets expressed more negative emotion, anger and hostility—filled with words such as “hate” and curse words—had the most heart disease deaths, too, according to CDC data on causes of death, based on actual death certificates. Optimistic counties had lower heart disease–related mortality rates. When we drilled down further into the data, we realized that our method had worked particularly well at predicting deaths from atherosclerosis, more so than for other forms of heart disease. Atherosclerotic heart disease is a leading cause of death in the U.S. and, not surprisingly, the kind of cardiac disease thought to be most associated with psychological causes.

Curiously, the people tweeting were not the people dying. Our method said nothing about anyone’s individual risk for atherosclerosis. Rather the overall tenor of the tweets—typical-

ly from people too young to have heart problems—appear to have captured a snapshot of the psychology of the community at large. It is possible that these tweets detected an elusive quality of communities sociologists often refer to as social cohesion, loosely defined as the willingness of community members to cooperate and help one another. Research indicates that the more cohesive a community, the more its members tend to enjoy good mental and physical health. At present, we are extending our analysis to look for words and language patterns predictive of all the leading causes of death, including cancer and stroke. But we expect that here, too, more positive—and presumably more cohesive—communities will fare better.

Using only the language on Facebook feeds, researchers can predict people's personalities—sometimes better than their friends can.

### Creating Health Dashboards

Our Twitter-based prediction of communitywide deaths from heart disease proved more accurate than any made using government statistics for known risk factors, including obesity, diabetes, smoking and hypertension. The result was so robust, in fact, that our language variables could predict rates of heart disease even after we controlled for strong classical predictors, such as education and poverty.

As more people make use of social media, our predictions may become even better. Ten years ago only certain segments of the population were Facebook users—mostly teens and young adults. As of October 2015, though, the Pew Research Center reported that 65 percent of American adults use social media sites regularly—a 10-fold increase since 2005. Fully 90 percent of younger adults use social media, and rates among those older than 65 have more than tripled since 2010. The median age of Twitter users is 32—only six years younger than the median age of the U.S. population.

Compared with the CDC's Behavioral Risk Factor Surveillance System or Gallup polls—which take into account much smaller samples at far greater cost—Twitter- or Facebook-based health assessments may offer a faster, cheaper dashboard indicator of communitywide well-being. My colleagues and I have now consulted with colleges in the U.K., the state government of South Australia and Mexican authorities who, with aspirations of tracking health trends via Twitter, may begin asking for people's social media handles in their next national census. It is, in many ways, a natural step in a world in which increasingly fewer people are reachable to survey via landlines.

Analyses of language on social media might also be applied to help clinicians treat individual patients. Lyle Ungar and others from our project recently teamed up with Raina Merchant and other Penn Medicine colleagues to put iPads in the Hospital of the University of Pennsylvania's emergency room. We asked ER patients to voluntarily sign in to Facebook and give permis-

sion for their status updates to be analyzed. Using our machine-learning methods, we then correlated all the language patterns with their medical records. Looking at the data, we have discovered an array of potential language markers for various diseases—including depression. In the future, doctors might be able to analyze social media posts for a disease's linguistic red flags and follow up with patients appropriately.

Indeed, it seems entirely conceivable that phone apps analyzing the narrative of our lives could help physicians deliver better care across different contexts. Imagine a psychotherapist who receives an automatic daily mood reading from his or her depressed patients and can then

text them a critical reminder, insight or urgent recommendation. Or a doctor monitoring social media feeds for signs of depression among heart attack patients, for whom depression is a big risk factor for having a repeat crisis. In 2013 a team at Microsoft Research used tweets to predict postpartum depression among 376 new mothers. Their model was 71 percent accurate when it analyzed only prenatal posts and about 80 percent accurate when it also included tweets from the first few weeks following birth.

These are far better uses than, say, an insurance provider or loan shark surreptitiously using social media analytics to deny services or increase rates. In our research, we always obtain permission to analyze participants' online feeds and follow strict privacy guidelines. But few Facebook users realize that giving access to their statuses—or even just their “likes”—can supply a corporation with a fairly fine-grained personality profile. Societies have a way of co-evolving along the lines of their most powerful technologies—and it will take many of us across science, policy and industry to get this one right. The more we realize the potential of social media analytics to better our health and well-being, though, the more we can join in efforts to craft our future in ways that are conscious, ethical and even lifesaving. **M**

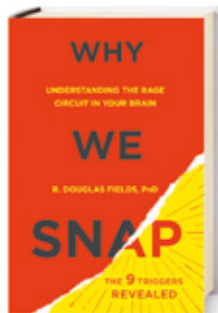
#### MORE TO EXPLORE

- **Personality, Gender, and Age in the Language of Social Media: The Open-Vocabulary Approach.** H. Andrew Schwartz et al. in *PLOS ONE*, Vol. 8, No. 9, Article No. e73791; September 25, 2013.
  - **Psychological Language on Twitter Predicts County-Level Heart Disease Mortality.** Johannes C. Eichstaedt et al. in *Psychological Science*, Vol. 26, No. 2, pages 159–169; February 2015.
  - **Linking Social Media and Medical Record Data: A Study of Adults Presenting to an Academic, Urban Emergency Department.** Kevin A. Padrez et al. in *BMJ Quality & Safety*. Published online October 13, 2015.
- From Our Archives*
- **A Digital Safety Net.** Roni Jacobson; November/December 2014.

SEEING RED

**Why We Snap: Understanding the Rage Circuit in Your Brain**

by R. Douglas Fields. Dutton, 2016 (\$28; 416 pages)



Everyone gets angry. We curse under our breath when another driver cuts us off. Or grumble about our neighbors when they make a lot of noise. But what causes tempers to erupt with such intensity that we lash out beyond all reason? What makes some people

“go postal” and become homicidal seemingly within seconds? In *Why We Snap*, neuroscientist and *Scientific American Mind* advisory board member Fields takes readers on a journey into the brain’s so-called rage circuit to untangle how this emotion works.

The book opens with an adrenalin-packed scene in which Fields and his daughter cross paths with a pickpocket in Barcelona. In almost superhuman fashion, Fields slams the thief onto the pavement, retrieves his wallet and flees through unfamiliar streets. He was so surprised by the violence and speed of his response that he spent the next four years exploring what caused it.

After combing through news headlines, case studies and research reports, Fields homes in on nine fundamental triggers of rage: we are more prone to lose it, he says, when called to defend life and limb, honor, family, our freedom of movement, or our larger social groups, territory, mates, resources or social justice. *Why We Snap* describes how each of these potentially incendiary situations can “initiate an automatic rage response” and delves into the science of the fear and aggression at its root.

Perhaps Fields’s most sobering conclusion is that, under the right circumstances, absolutely anyone, from grandmothers to ex-cons, can lash out violently thanks to our evolutionary past. The neural circuits that helped ancient humans protect themselves and survive also recognize and respond to dangers in our modern environment. When we sense a threat—be it a saber-toothed tiger or a social media troll—we experience flight or fight. In

these moments, adrenaline floods our body, prompting a variety of physical responses that ready us to either attack or escape.

A range of brain areas, including the amygdala (our emotional center), mediates this reaction. In some, these regions become overactive or hypersensitive. Chronic stress or trauma, in particular, “literally rewires the rage circuits,” Fields writes, making those affected more likely to snap, even at minor provocations. Interestingly, he notes that the brain circuitry behind rage behaviors can also prove beneficial. U.S. Navy SEALs, for instance, are trained to harness the emotional rushes associated with rage to pull off heroic feats in the face of imminent danger.

Throughout the book, Fields recounts a steady stream of attention-grabbing, gruesome stories of enraged individuals. About a third of the way in, he begins to jump back and forth between these anecdotes and scientific explanations—a structure that can make the book feel disjointed. Also, the book’s title misleadingly refers to a single “rage circuit,” which Fields himself explains is not the reality—numerous brain regions regulate our anger response. But for those craving an action-packed account of what scientists currently know about how rage works, this book delivers. —Diana Kwon

SURPRISING WAYS TO BE WISE

**The Wisest One in the Room: How You Can Benefit from Social Psychology’s Most Powerful Insights**

by Thomas Gilovich and Lee Ross. Free Press, 2015 (\$26; 320 pages)



To appreciate how good this book is, you need to know a bit about social psychology—the rock-star branch of psychology that has produced a long list of headline-grabbing research, including Stanley Milgram’s classic 1960s experiments at Yale University showing how

easily people in lab coats can pressure average citizens into apparently shocking innocent people to death. Speaking of stars, these experiments were dramatized in a 1976 movie featuring William Shatner as Milgram and again last Octo-

ber in *Experimenter*, which starred Peter Sarsgaard and Winona Ryder.

Social psychology is all about psychological processes that become evident only when people are in social situations. It seeks to discover general principles of human behavior by conducting what are often fiendishly clever experiments with small groups. Unfortunately, many of these principles turn out to be obvious in retrospect, and some of the most famous experiments have proved hard to replicate. One of the highest-profile social psychology experiments of all time—the Stanford Prison Experiment (also now a major motion picture)—doesn’t meet even minimal standards of good scientific research. It lacked a control group, for example.

Now that you know the discipline’s dark side, dig deeply into this new volume by prominent social psychologists Gilovich of Cornell University and Ross of Stanford University. In nine very readable chapters, they have mined their field for the gold nuggets—surprising, practical principles derived from many of the best studies in their specialty.

The book sparkles with examples, but here are just three: If you want people to develop a genuine interest in something, give them only small rewards for their participation; big rewards get people more interested in the rewards than in the activity. If you want people to be more honest, have them sign an honesty statement before they begin a task; pledging truthfulness at the completion of a task—like we all do on our tax returns—has little effect. And if you want to influence which candidate people will vote for, it matters greatly whether those people focus on whom to select versus whom to reject. Even though I’ve taught psychology courses for decades, the authors surprised me repeatedly with these kinds of practical guidelines, all supported by experiments they describe in clear, nontechnical terms.

On the downside, the end of the book gets political, even preachy, when Gilovich and Ross start to apply their principles to specific issues, such as Middle East conflicts and climate change—topics on which, they admit, they have strong personal views. But even here there are surprises. Social psychology suggests, for example, that extreme tactics by environmentalists are “misplaced.” Instead of dire warnings about our great-grandchildren’s fate, “gentle nudges and modest incentives” are the real keys to controlling climate change. Read, be surprised and become wiser. —Robert Epstein



## ROUNDUP

**Think Smart**

**Two books examine the art of thinking clearly**

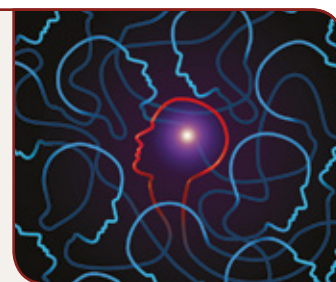
What if we could anticipate well in advance the outcome of an election or the impact of a natural disaster? Psychologist Philip E. Tetlock and journalist Dan Gardner explore how well we can foretell the future in their provocative new book **Superforecasting: The Art and Science of Prediction** (Crown, 2015; 352 pages).

According to Tetlock, most people are pretty bad at judging future events. But

decades of research have led him to recognize special individuals he calls “super-forecasters.” They tend to be open to new ideas, flexible thinkers and okay with getting things wrong. The good news, he reveals, is that it may be possible for everyone to improve their forecasting prowess: ultimately the art of prediction may be less about getting the right answer and more about understanding *why* that answer is right or wrong.

But how can we make good predictions if our reasoning skills are inherently flawed?

**In Phishing for Phools: The Economics of Manipulation and Deception** (Princeton University Press, 2015; 288 pages), Nobel Prize-winning economists George A. Akerlof and Robert J. Shiller argue that we frequently make decisions that are not in our best interests. They define “phishing” as the ability to artificially lure and deceive others and “phools” as victims of phishing. In psychological terms, phools come in two flavors: psychological phools fail to follow common sense, whereas informational ones misinterpret reality and act on



that misinformation. Using compelling examples of flawed decision making from advertising, health care and personal finances, the authors identify our rational weak spots and arm readers with the ability to resist manipulation. —Victoria Stern

**Q&A: JAMIE HOLMES**

### A technology policy expert discusses his new book on the upside of uncertainty

Moments of confusion can be pretty memorable—and not in a good way. How is this thing supposed to work? What is the teacher’s point? Where am I? But confusion is greatly underrated, Jamie Holmes argues in his new book, *Non-sense: The Power of Not Knowing* (Crown, 2015; 336 pages). Our discomfort with not knowing, he writes, can lead us to bad solutions or to brilliant options we would have otherwise never spotted. If we could learn to embrace uncertainty, we would all be better prepared for modern life. Holmes answered questions from contributing editor Gareth Cook. The full interview appears online in *Mind Matters* ([www.ScientificAmerican.com/mind-matters](http://www.ScientificAmerican.com/mind-matters)). An edited transcript follows.

#### How did you become interested in this unusual topic?

My childhood was full of jarring experiences—jarring in a good way—that felt at once bizarre, confusing, challenging and enlightening. The social world of the south side of Chicago, where I started high school, was much more diverse than the one in Cambridge, Mass., where I finished high school. My father threw me into a German school in Berlin, with two weeks of language lessons, when I was 11 years old. I went to high school in Budapest when I was 15. I taught high school classes in Romania after college. So I’ve always found it really intriguing how someone’s worldview changes when it’s challenged by

radically unusual experiences and how difficult and rewarding those time periods can be. Psychologist Dean Keith Simonton calls them “diversifying experiences.” One major theme of the book—what happens when beliefs collide with unexpected or unclear situations—is very personal to me.

#### You write about our “need for closure.” Where does this come from?

Our need for closure is our natural preference for definite answers over confusion and ambiguity. Psychologist Arie Kruglanski co-developed the need-for-closure scale in the early 1990s, although forerunners of the concept appeared after World War II, as psychologists struggled to understand Nazism. Every person has his or her own baseline level of need for closure. It most likely evolved via natural selection. If we didn’t have some capacity to shut down thinking, we’d deliberate forever. Much of the book focuses on the dangers of a high need for closure, strategies for lowering it and ways to learn from ambiguity.

#### Can you give a specific example?

In hiring, for instance, a high need for closure leads people to put far too much weight on their first impression. It’s called the urgency effect. We all know that important decisions shouldn’t be rushed. The problem is that we don’t keep that advice in mind when it matters. In experiments, psychologists lower people’s need for closure by telling them, right before participants are about to make various judgments, that they’ll have to defend their decisions later on, or that they’ll be accountable in some way for them, or that their judgments will have serious consequences. One strategy is to formalize

these reminders. Before making important decisions, write down the pros and cons and what the consequences could be.

Both fiction and multicultural experiences, maybe surprisingly, also help. Reading short stories, as opposed to essays, has been shown to reduce our need for closure. Because fiction, in a nonthreatening way, invites us inside the heads of characters, it makes us more open to thinking about other ideas and possibilities. One fantastic experiment published in 2012 showed, similarly, that merely having subjects write about a time they’d lived abroad, or friends they’d met from different cultures, or diverse musical or culinary experiences also lowered their need for closure. Reading fiction also makes us more empathetic. So, as a bonus, the things that lower our need for closure not only help us make better decisions in daily life—they also make us nicer.

#### Why is there so much interest in ambiguity now?

One area where there is growing interest in ambiguity is among entrepreneurs, simply because the future in many business sectors is highly ambiguous. Last year Thomas Friedman wrote an op-ed in the *New York Times* about disorder in the business world. Uber is one of the biggest taxi companies in the world, he pointed out, yet it has no cars. Facebook doesn’t create media, Alibaba has no inventory, and Airbnb doesn’t own any of the real estate it uses. So the communications platforms we’re using are revolutionizing a range of industries. It’s not in the book, but businesspeople have an acronym, VUCA, or volatility, uncertainty, complexity and ambiguity. It’s a VUCA world.



## Does creativity decline with age?

—Rowena Kong via e-mail



**Dean Keith Simonton,**

Distinguished Professor of Psychology at the University of California, Davis, responds:

This question has attracted scientific research for more than a century. In fact, the first empirical study of this issue was published in 1835. Thus, I can offer a confident answer: not quite! At least not if creativity is assessed by productivity or by making original and valuable contributions to fields such as science and art. By that measure, output first *increases* in our mid-20s, climaxes around our late 30s or early 40s, and then undergoes a slow decline as we age. A person's single best work tends to appear at roughly the same age as their output peaks. But their expected creative productivity at 80 will still be about half of what it was at that high point. Whether you view that as a significant drop or not depends on whether you see the glass as half empty or half full.

That said, this thumbnail summary is based on statistical averages, and averages always have exceptions. That is why scientists put error bars on graphs. Many of the exceptions in this instance can be explained using three empirical principles.

First, the precise relation between age and creativity depends on the domain. Some creative types—such as lyrical poets and mathematicians—tend to have early peaks and relatively rapid declines, whereas others—among them, historians and philosophers—are prone

to later peaks and gradual, even negligible declines.

Second, creative people vary greatly in total lifetime productivity. At one extreme are the one-hit wonders, who make single contributions; their creativity is almost over before it begins. At the other end of the spectrum are highly prolific creators who make dozens, if not hundreds, of contributions and who are often still going strong well

into their 60s and 70s, if not beyond.

Third, career age has more bearing on someone's creative trajectory than chronological age. Hence, early bloomers who start young will have their peak shifted forward, whereas late bloomers who start older will have their pinnacle delayed. Some late bloomers do not truly hit their stride until their 60s or 70s. They often drudged away in uninspiring jobs for decades before discovering their true passion.

One striking implication of these results is that it seems unlikely that creative declines are caused simply by aging brains. If that were the case, it would be hard to explain why the creative path differs by domain, lifetime output, or the time someone embarks on his or her career. After all, late bloomers reach creative peaks at ages when early bloomers are past their prime. So the good news is that it is possible to stay creative throughout one's life span.

## Do dogs have mirror neurons?

—Betty Sue Easton, Me.



**Ádám Miklósi,** head of both the

Family Dog Project and the department of ethology at Eötvös Loránd University

in Budapest, replies:

The short answer is that dogs very likely possess mirror neurons, but we have no concrete proof just yet. Neuroscientist Giacomo Rizzolatti of the University of Parma in Italy and his colleagues discovered mirror neurons by accident during the 1990s, when they were studying motor neurons in rhesus monkeys. Rizzolatti and his co-workers found that certain neurons in the frontal and parietal cortex became active both when a monkey watched another monkey take food and when the monkey grabbed the food itself. They adopted the term "mirror neuron" to reflect the fact that these neurons fire in patterns that mimic others' actions.

Using functional brain imaging, neuroscientists have located brain areas with similar mirror function in humans. They believe that these neural structures may help us understand the intentions of another, to imitate and empathize with others, and perhaps even to process language. Additional evidence suggests that mirror neurons are not exclusive to primates or even mammals. Researchers have found dedicated mirror neurons in the brain of songbirds that fire both when the animal sings a particular tune and when it hears another songbird crooning a similar melody.

The presence of mirror neurons in other animals suggests that they may have an ancient evolutionary origin and play an important role in communication. So it seems entirely reasonable to hypothesize that dogs have mirror neurons, too. Dogs appear to imitate other dogs. And mirror neurons in dogs may support communication with humans; we will have to study dogs' brains more closely to find out.

## Does confessing secrets improve our mental health?

—Christine Blint via e-mail



**James W. Pennebaker,**  
Regents Centennial Professor  
of Psychology at the University  
of Texas, answers:

Any type of open and truthful disclosure reduces stress and helps individuals come to terms with their behavior. It is not coincidental that some of the most powerful people or institutions in many cultures encourage people to confess their transgressions. And there is very strong evidence that writing about upsetting experiences or dark secrets can benefit your mental and physical well-being.

Similar to religious confession, expressive writing encourages individuals to explore their deepest thoughts and feelings about upsetting experiences. For such emotional purges to work, people must be completely honest with themselves. Across hundreds of studies, we are now beginning to appreciate just how expressive writing works.

First, simply putting emotional turmoil into words changes how we think about it. Giving concrete form to secret experiences can help categorize them in new ways. For instance, when we translate emotional experiences into words and stories, we start to think about them in a simpler, less menacing context. There is no solid evidence to explain this phenomenon, but it most likely occurs because talking or writing about a disturbing event helps us understand it better. And things we do not understand cause greater anxiety.

Another possible explanation is that once we write about our upheavals, we tend to ruminate about them less, free-

ing us up to focus on other things. My colleagues and I have shown that people become more socially engaged in the weeks immediately following expressive writing exercises.

Dozens of studies have also shown that expressive writing is linked to less stress and improved sleep and cardiovascular function. We know that better sleep is associated with enhanced immune function and better general health—which correlate with better mental health, too.

Expressive writing and religious confession are not panaceas, but these forms of release can help us get through difficult times. The beauty is that you do not have to be religious to benefit from confession. The underlying mechanisms are available to anyone for the price of a pencil and paper.

## As a teacher, how can I help my students to develop their brains?

—Lola Irele London



**Daniel Willingham,** a professor of psychology at the University of Virginia and author of *Raising Kids Who Read: What Parents and Teachers Can Do*, responds:

I suggest that we not talk about the brains of our students but rather their behavior. After all, if we figured out some way to improve their brains—increase the volume of specific regions, say, or the number of interconnections—but we saw no change in their ability to succeed at their actual schoolwork, we would not be satisfied.

This distinction may sound like a matter of semantics, but there is an important practical implication. Focusing on the brain implies that once a

brain is in good shape, it will be better equipped to take on any task that comes along. There is probably some truth in that statement—some thinking skills are quite general. But in practice, enhancing them has proved difficult.

In the past decade or so researchers have experimented with various exercises meant to increase one such skill, namely the capacity of working memory. Working memory is the mental space you use to keep several things in mind at once—say, numbers such as 38 and 16—and to manipulate them, perhaps by multiplying them together. As you might guess, people who can keep more things in working memory and who are more efficient at manipulating them tend to be better at reasoning.

But the effectiveness of working memory training is controversial. Everyone agrees that people get better at the specific tasks they practice, but it is less clear whether that skill transfers to other, unpracticed tasks. Learning how to calculate least common multiples, for example, does not make you better at math in general.

This specificity is especially pronounced early in training. When someone spends years working at certain types of problems, they do develop thinking skills that can be more flexibly deployed. For example, a professional historian who specializes in the Italian Renaissance can do a creditable job analyzing documents from the American Civil War. But even so, experience matters. Our historian's training has made the person good at thinking like a historian, not good at thinking generally. Or to put it another way, Stephen Hawking may be a very smart guy, but I would not suggest he coach the Chicago White Sox.

Rather than thinking about developing our students' brains, I suggest focusing on specific thinking skills. What is a good writer able to do? What are our expectations for mathematical thinking? We must define the abilities that go into our definition of competence in each domain and give students ample practice in honing them. **M**



# 50 • 100 • 150 YEARS AGO



1965

1915

1865

DIGITAL  
ARCHIVE BUNDLE  
**\$9.99**  
Save 58% off the  
individual price

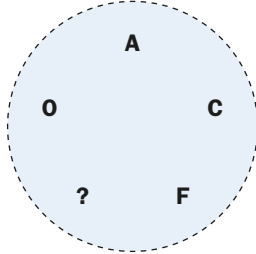
## A new treasure hunt every month at [scientificamerican.com/years](http://scientificamerican.com/years)

Travel back in time as chronicled in *Scientific American* 50, 100, and 150 years ago. Each month, our Senior Editors dust off a new collection of three vintage issues filled with fascinating science history frozen in time. View this month's treasures at [www.scientificamerican.com/years](http://www.scientificamerican.com/years)

### SCIENTIFIC AMERICAN™

**1** PATTERN WATCH

Starting with the letter "A," move clockwise around the circle, spot the pattern and fill in the missing letter.

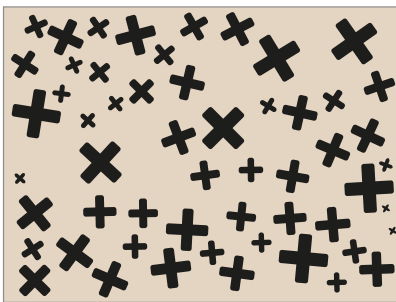


**2** SCORECARD

The math teacher posted the latest test scores. Xenia's score was not the lowest. Neil's was neither the best nor the worst. Neil beat Robin. Xenia beat Vera. Vera scored better than Robin and Neil. Will beat Vera but not Xenia. Who scored the highest?

**3** DIVIDING LINES

In the diagram below, use six straight lines to divide the rectangle into 10 sections. Each section must contain a different number of plus signs such that there are sections with one, two, three, four, five, six, seven, eight, nine and 10 of them.



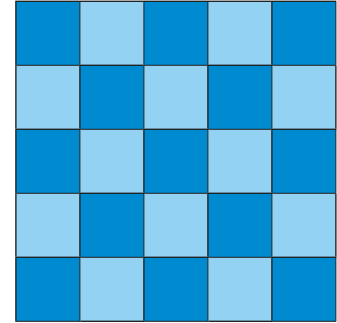
**4** CITY SCRAMBLER

Can you spell out the three 11-letter city names hidden in the string below?

**NMIGEWNNREYAANOPODRRLKCAPIIIDSSTY**

**5** SIMPLE SUDOKU

Arrange the digits 1 to 5 in a five-by-five grid so that each digit appears in every row, column and main diagonal only once. The same digit should never be next to itself in any direction.



**6** NUMBER HUNT

Each letter represents a number. The sums of the rows and columns are given. Find the missing total.

A	B	C	D	10
A	C	D	A	9
A	C	C	B	9
B	C	D	B	11
5	11	14	?	

**7** PLUS ONE

The terms below are missing their consonants. Each has something to do with having one extra. Can you figure them out?

\_ E A \_    \_ E A \_  
 \_ A \_ E ' \_    \_ O \_ E \_  
 \_ \_ U E    \_ O O \_

**8** MYSTERY MULTIPLIERS

The following multiplication problem uses every digit from 0 to 9 once and only once (except in the intermediate steps). Several of the digits are filled in to give you a head start.

$$\begin{array}{r} \quad \quad \quad ??? \\ \times \quad ?3 \\ \hline 5?,?01 \end{array}$$

**9** WORD TRAIL

A familiar statement is coiled in the grid below. To spell it out, start with one letter and move to an adjacent letter in any direction. (Hint: Start with an H.)



© 2016 AMERICAN MENSA, LTD., LEARN MORE AT HTTP://AMERICANMENSA.ORG/JOIN

Answers

6. 9. A = 1, B = 2, C = 3, D = 4.  
 7. LEAP YEAR, BAKER'S  
 DOZEN, BLUE MOON.  
 8. 927  
 58,401  
 × 63  
 -----  
 9. HE WHO HESITATES IS LOST.

4. NEW YORK CITY, GRAND RAPIDS, MINNEAPOLIS.  
 5.  

3	5	4	2	1
2	1	3	5	4
5	4	2	1	3
1	3	5	4	2
4	2	1	3	5



3.  
 1. J. Skip one letter, then two, then three and then four.  
 2. Xenia scored highest. Will scored second-highest, then Vera, then Neil and then Robin.



SCIENTIFIC  
AMERICAN™

Travel

BRIGHT  
HORIZONS™ 30

WEST COAST & MEXICO • OCTOBER 18TH – 29TH, 2016



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

Take a contrarian viewpoint and see North America's West Coast from offshore with Scientific American Bright Horizons 30. Encounter the scenic riches of a region where mountain, sea, and sky juxtapose in many beautiful variations. From the temperate rainforests and urban pleasures of Vancouver to Santa Barbara's wine country and Mexico's marine sanctuaries and endless sunny beaches, refresh your senses on a coastal cruise on Holland America's ms Westerdam.

While at sea hear the latest in science and gain an understanding of the questions (and answers) that inspire scientists today. Lively discussions extend the learning fun, and well informed dinner table conversations are a pleasant evening option.

Experience quintessential coastal California, Mexico's cultures and bountiful hospitality, and great contemporary science from the experts. Enjoy quiet moments, diverse cuisines, and outdoor adventure with a friend. Let us take care of the details so you can unwind. Please join us!

Cruise prices vary from \$1,129 for an Interior State-room to \$5,799 for a Pinnacle Suite, per person (pp). For those attending our SEMINARS, there is a \$1,575 fee. Add'l pp fees: gov't taxes and fees (\$209), Non-refundable Booking Service Fee (\$150), tour leader gratuities (\$120), and onboard gratuities (for your cabin steward and dining room staff, approx \$11.50 per day). The Program, cruise pricing, and options are subject to change. For more information email us at [Info@InsightCruises.com](mailto:Info@InsightCruises.com).



### Cyberspace

Speaker: Paul Rosenzweig, Esq.

#### Introduction to the Cyber Domain

Virtually every aspect of global civilization now depends on cyberspace—telecommunications, commercial and financial systems, government operations, food production. This ubiquity makes keeping these systems safe from threat one of the most pressing problems we face. We'll examine how cyberspace works and what makes the Internet so vulnerable.

#### Big Data— "They" Know Everything About You

In the new age of "Big Data" your Internet searches can be tracked, your cellphone can broadcast your geographical location instantly, and your online purchases can be catalogued. We'll ponder the consequences of these developments in this discussion of personal data tracking and privacy.



### Government Regulation of Cyberspace

Join the debate about government regulation of cyberspace in this discussion of both sides of the issue. By looking at the debate over government oversight of cybersecurity and whether we need it, you'll be better informed about a topic that has serious ramifications for how you use the Internet.

#### Listening In and Going Dark: The Encryption Debate

Learn how encryption and wiretapping work in cyberspace, and how both methods are becoming increasingly frustrating for law enforcement and national security officials. This "going dark" phenomenon, as you'll find in this discussion, brings benefits and causes problems—and the solutions seem to spur issues of their own.



### Physics

Speaker: Pauline Gagnon, Ph.D.

#### The Incredible Higgs Boson

Much has been said about the Higgs boson, but why is it so important? We'll demystify this little particle. Learn how the theory called the Standard Model describes the basic constituents of the universe and how these particles interact to form all visible matter around us.

#### The Dark Side of the Universe

Everything on Earth and in all stars and galaxies accounts for only five percent of the universe. The rest, called dark matter and



dark energy, remains completely mysterious. We'll discuss this great challenge and the various efforts on Earth and in space to understand this dark side of the cosmos.

### Gigantic Tools to Explore the Smallest Particles

The Large Hadron Collider (LHC) is 27 kilometers long and has four huge detectors weighing up to 14,000 tons each. Why is everything so big? Learn how the LHC team designed and built such behemoths and what hopes they have for new discoveries with the recent restart of the collider.

### The Tragic Destiny of Mileva Marić Einstein

How did Albert Einstein's first wife aid his extraordinary productivity in the first years of his career? The story of Mileva Marić has been largely unknown, but recent sources have shed more light on her life, allowing us to finally get a better idea of her contributions.

## Physics (cont.)

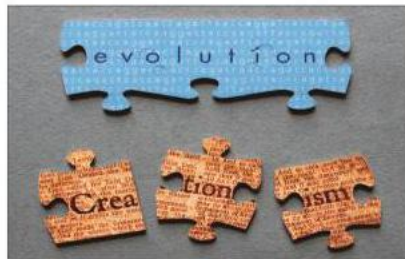
Speaker: Clara Moskowitz

### Hubble's Universe

We'll examine some of the most famous photographs from the Hubble Space Telescope. Learn how these images were created and how scientists turned the raw data into the colorful works of art we see. Finally, we'll discuss the future outlook for Hubble and its successor, the James Webb Space Telescope.

### The Particle Zoo

We'll take a tour through nature's fundamental particles, from the familiar ingredients of the atoms that make up you and me, to the more exotic species such as neutrinos. Hear the story of how we discovered some of these particles and the outlook for finding new species.



## Behind the Scenes

### The Evolution of Antievolution

Speaker: Steve Mirsky, M.Sc.

Evolution has been a subject of waxing and waning controversy since the day that Darwin published *The Origin of Species*. We'll look at some of the history of the anti-evolution movement, with special attention to the "creationist science" and "intelligent design" efforts of the past three decades, as well as famous court trials.



### What Do Scientific American Editors Read?

Speakers: Steve Mirsky, M.Sc. and Robin Lloyd, Ph.D.

Which newspapers, journals, feeds, and websites do *Scientific American* editors read? How do we filter the fire hose of news and information every day to get the most valuable drops on the latest breakthroughs and innovations? We'll discuss a recent survey of our staff on cutting-edge sources of information.

### How the Science Sausage Gets Made

Speakers: Steve Mirsky, M.Sc. and Robin Lloyd, Ph.D.

What's it like to be a science journalist? Hear the inside story from writers Steve Mirsky and Robin Lloyd, who have been at *Scientific American* for 11 and four years, respectively. They'll talk about how science gets turned into articles and some of the more amazing moments that have occurred during that process.





# Mental Compass

BY DWAYNE GODWIN  
& JORGE CHAM

THERE ARE FIVE COMMON BASIC SENSES:



BUT DID YOU KNOW THAT SOME BRAINS CAN SENSE MAGNETIC FIELDS, LIKE A COMPASS?



A VARIETY OF ANIMALS ARE ABLE TO NAVIGATE THE EARTH'S MAGNETIC FIELD TO AID THEM IN THEIR MIGRATION.



SOMEHOW THEIR BRAINS CAN DETECT THE SUBTLE MAGNETIC FIELD LINES CAUSED BY THE MOTION OF IRON IN THE EARTH'S MOLTEN OUTER CORE.

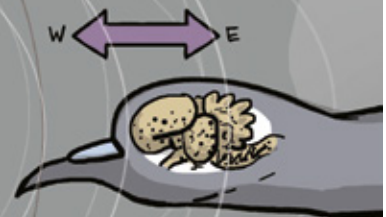


SCIENTISTS AREN'T SURE HOW THEY DO THIS, BUT THERE ARE SOME HYPOTHESES.

THE EARTH'S MAGNETIC NORTH POLE IS ACTUALLY A MAGNETIC SOUTH POLE.



ONE HYPOTHESIS IS THAT THESE ANIMALS HAVE SPECIAL DEPOSITS OF LODESTONE, A MAGNETIZED OXIDE OF IRON, IN THEIR BODIES.



SPECIAL RECEPTORS IN THEIR NERVOUS SYSTEM THEN SENSE HOW THESE DEPOSITS REACT TO AN OUTSIDE MAGNETIC FIELD.

IN ONE ANIMAL, IT HAS BEEN HYPOTHESIZED THAT QUANTUM ENTANGLEMENT PLAYS A KEY ROLE.



A PROTEIN CALLED CRYPTOCHROME IN THE EYE'S PHOTORECEPTORS GENERATES TWO COUPLED ELECTRONS WHEN LIGHT STRIKES IT.



THE ENTANGLED ELECTRONS' SPIN IS AFFECTED BY WEAK MAGNETIC FIELDS, WHICH MAY ALLOW THE ROBIN TO "SEE" THE SURROUNDING MAGNETIC FIELD LINES.

SO YOU COULD SAY THESE ANIMALS HAVE A GOOD HEAD FOR DIRECTIONS ...



... OR THAT THEY'RE LOADED WITH ANIMAL MAGNETISM.

● 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](http://www.phdcomics.com)



# Help your brain keep up

Modern life is complicated. Between work, kids, aging parents and home repairs, your brain's energy stores are constantly drained. Re-energize it with Cognizin® Citicoline. Backed by years of clinical trials, Cognizin increases ATP energy in brain cells and helps protect aging neurons from free radical damage.\* You ask a lot of your brain. Give it the energy, nourishment and protection it needs with Cognizin.\*

## Cognizin®

For the evolution of your mind®

Train-your-brain games at  
[www.cognizin.com](http://www.cognizin.com)



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

Cognizin® is a registered trademark of KYOWA HAKKO BIO CO., LTD. Copyright ©2016 KYOWA HAKKO U.S.A., INC. All Rights Reserved.

Look for Cognizin® Citicoline in these fine brands.





**THE ARCHIVES**

Explore over 170 years of science history. Search any issue from 1845–present.



# Enjoy All-Access!

Read any issue, any year, on any device.

Receive 12 new issues (one year) of *Scientific American* in both print and digital.

Plus, get full access to our award winning Archives, where you can explore any issue in our long history, 1845–present. Subscribe now. Go to:

[scientificamerican.com/all-access](http://scientificamerican.com/all-access)

**PRINT**

12 issues filled with the latest advances in science.



**DIGITAL**

Online access to your subscription using any computer, tablet or smartphone.

