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Changing Face

Many people assume facial movements broadcast emotions to other people. But the question is under contentious debate

INCLUDING

Brain-reading devices

The dark side of collaboration

Do Zoom meetings squash creativity?

WITH COVERAGE FROM nature

FROM THE EDITOR

Liz Tormes

Behind Every Smile

A fascinating study was published in 2015 showing that in cultures with higher rates of immigration, its citizens tended to smile more. Presumably among people who speak an array of languages, nonverbal communication is more crucial for everyone to understand one another and get along. The U.S., with 83 "source countries" populating its communities, scored far higher on this scale of emotional expressiveness than, for example, China, whose population is more homogeneous. Of course, many social factors play into how humans show their emotions through their facial gestures, as psychology professor Lisa Feldman Barrett writes in this issue (see "Darwin Was Wrong: Your Facial Expressions Do Not Reveal Your Emotions"). Perhaps as an American, I'm biased toward smiling faces, but it makes me grin to think about this happy by-product of our country's diversity.

Elsewhere in this edition, writer Lydia Denworth reports on a new study from the *Journal of Beatles Studies* (yes, one exists) that explores the role of luck in finding fame and success (see "Can't Buy Me Luck: The Role of Serendipity in the Beatles' Success"). As the study author tells Denworth, when it comes to achieving greatness for any of us, "something like lightning might strike, which can bring a smile to the face on a tough morning."

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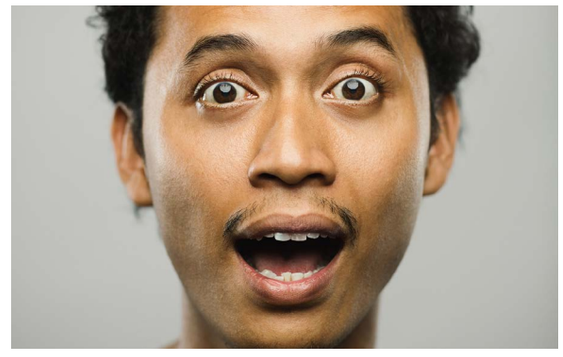

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On the Cover

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WHAT'S INSIDE

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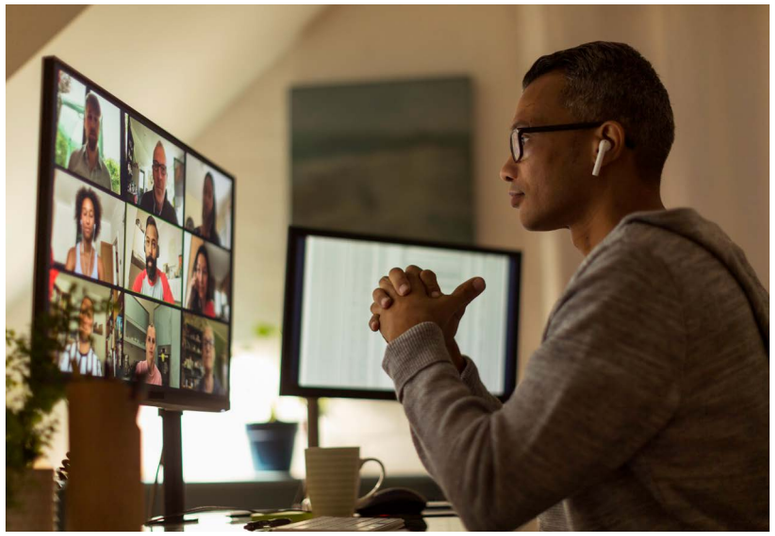

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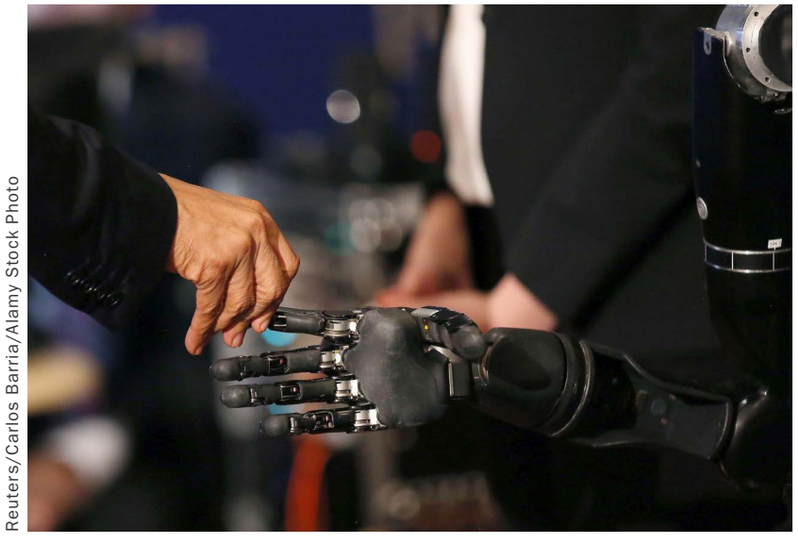

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NEWS

Spinal Stimulation Helps People with Paralysis Walk, Canoe and Stand at a Bar

A new system that targets specific spinal nerves restored motor function quickly in three patients unable to move their legs or trunk

For decades doctors and researchers have dabbled with using electrical stimulation of the spinal cord to help restore movement in people with paralysis. The technique, when combined with physical therapy, has even allowed some patients with complete paralysis to walk again.

Yet it has not worked for all paralyzed people. And researchers still have had trouble with improving complex movements in such patients, not just the capacity to take simple steps. Another goal is to make the treatment more accessible to the millions of people worldwide who suffer from paralysis.

Patient with complete spinal cord injury canoes after five months of rehabilitation.

Jimmy Ravier/NeuroRestore

Now a team of researchers has designed a new type of electrode system that successfully restored movement abilities in three patients with complete paralysis of muscles in the legs and trunk. What is more, improvement was seen within just one day of treatment—faster than most previously studied techniques—and it continued in the days and months to follow. The findings were published on February 7 in *Nature Medicine*.

Many of the stimulation technologies developed over the years were originally designed for treating pain and later repurposed for restoring movement. The downside to this approach is that these technologies failed to stimulate the specific nerves in the spinal cord that control movement in the legs and trunk.

Moreover, the new approach allows treatment to be personalized to each individual patient by zeroing in on particular dorsal roots. "This is the most precise stimulation of the spinal cord to date and associated recovery of movement in people with complete spinal cord injury," says Grégoire Courtine, co-senior author of the new paper and a neuroscientist at the Swiss Federal Institute of Technology Lausanne.

"This is the most precise stimulation of the spinal cord to date and associated recovery of movement in people with complete spinal cord injury."
—Grégoire Courtine

The new device actually targets "dorsal nerve roots," a bundle of nerve fibers that deliver sensory information to the spine. But this sensory input triggers other nerves responsible for moving the trunk and limbs. As the paper's other co-senior author Jocelyne Bloch puts it, "The pain electrode arrays are shorter and narrower; they were not designed to specifically target each individual nerve root to activate precisely and specifically the trunk and leg muscles." Bloch is a neurosurgeon at Lausanne University Hospital in Switzerland.

Courtine explains that while the treatment effects of his group's device are immediate, at first the patients did require additional body weight support, which consisted of either two parallel bars on the ground or on a treadmill. After one to three more days, however, they were actually able to walk, again using a support aid. And after a few months, they improved at performing other motor activities, including cycling, canoeing, and even standing up and having a drink at a bar.

The authors believe their device works because only a small number of nerve fibers can survive an accident, but they end up going dormant as a result of receiving no stimulation from nerves beyond the injury site. Spinal stimulation only needs to reach these few nerve fibers to bring them back to life.

There is a caveat, though: Long-term improvements occurred only while the patients had their stimulation device switched on. People with complete paralysis will need a permanent spinal implant for the treatment to work. But Courtine sees that as a small price to pay to regain some degree of movement.

"The [new] evidence is consistent with the possibility that the fine adjustments in the placement of electrodes, relative to the positions of the dorsal roots, could be a factor in resulting in relatively rapid recovery of motor functions," says V. Reggie Edgerton, a professor of physiology at the University of California, Los Angeles, who is conducting similar research with external stimulation techniques that do not require surgery.

Edgerton calls the new study an important advance in the field. Yet he asks to what degree the "preciseness" emphasized by the researchers is responsible for the outcomes reflected in motor behaviors, given that that patients still had to undergo extensive physical therapy.

Next for Bloch and Courtine is expanding access to spinal stimulation and movement recovery. Their group is collaborating with ONWARD, a collective of scientists, engineers and physicians aiming to develop therapies for spinal cord injuries. (Courtine is ONWARD's chief scientific officer.) The plan is to create a commercial version of their technology and validate it with a clinical study next year. He is uncertain of how much it will cost just yet but says the pricing will be similar to other nervous system stimulation technologies, such as deep-brain stimulation for Parkinson's disease.

As Courtine puts it, "[The idea] is to make this available to everyone."

—Bret Stetka

Can't Buy Me Luck: The Role of Serendipity in the Beatles' Success

The right combination of variables is needed to achieve a blazing success—one explanation for why there was never a "Kinksmania"

The Beatles at Television House, Kingsway, for an appearance on the television show *Ready Steady Go!*, March 1964.

Mirrorpix via Getty Images

Imagine there were no Beatles—or that there was no Beatlemania anyway and that the lads from Liverpool were just another band that never got a record deal or that split up before they hit it big. That is the premise Harvard University professor Cass R. Sunstein ponders in an entertaining and thought-provoking essay to be published in September in the first issue of the *Journal of Beatles Studies*. (A preliminary draft was posted online early this year.)

The fact that there could be an academic journal devoted just to John, Paul, George and Ringo is emblematic of how popular and influential the Beatles are. Many assume they were destined for greatness. "It was just a matter of time," said John Lennon in a 1980 interview. But maybe not. Early on, record executives were unimpressed ("The boys won't go," they told manager Brian Epstein). And the group did almost split up. Its members were carried along their winding road by an unusually enthusiastic manager (Epstein), a risk-taking producer (George Martin), a big local fan base, and more. "They were, at the crucial time, better than excellent," says Sunstein, who is a fan as well as a

The Kinks, another large talent that emerged in the early 1960s, never achieved the wild success of the Fab Four.

Interfoto/Alamy Stock Photo

legal and policy scholar at Harvard Law School. Nevertheless, it is quite possible that "if seven or 17 things had gone differently, the Beatles wouldn't have made it."

Because history is only run once, Sunstein cannot prove the theory that the Beatles got by with a little help from their friends. But that is not really the point. He uses the entertaining example of Beatlemania to explore the effects of early social influence in other realms. A lot of success in business, politics, academia and most other professions owes much to early opportunities that enable subsequent success. "Serendipity is a little bit of a black box," Sunstein says. "You have to unpack the ingredients."

Duncan Watts, a computational social scientist at the University of Pennsylvania and author of the book *Everything Is Obvious: *Once You Know the Answer*, is a fan of Sunstein's essay. "If you can accept the idea that the Beatles might be a product of luck and cumulative advantage, other things become conceivable," Watts says. "It's good to challenge people's intuition about the inevitability of the things that we know about. There's a lot of very talented people out there, and there's some process that selects a very small number to be superfamous."

That process, as sketched out by Sunstein, includes "informational cascades" (the statements and actions of some affect the statements and actions of others), "reputational cascades" (going along with the crowd to be liked), "network effects" (the value of a good increases as more people use it) and "group polarization" (groups make more extreme decisions than individuals do).

In one of the few experimental examples of such processes, Watts and his colleagues showed the power of early popularity. In a 2006 experiment, they presented more than 14,000 listeners with 48 unknown songs by unknown bands. In one condition, viewers independently decided which to download. In other conditions, they could see how many others had already downloaded each song. The best songs rarely did poorly, and the worst rarely did well.

But otherwise the results varied widely, and "to a significant degree, everything turned on initial popularity," Sunstein writes. A similar study replicated those results for political issues: a Republican issue could flip to become an issue for Democrats if they saw other Democrats cared about it, and vice versa.

Literary fame turns out to be equally fickle. Novelists and poets we now consider iconic, such as Jane Austen and John Keats, were not so highly regarded in their lifetime. Austen made a little money from her novels, but a similar author, Mary Brunton, was far more successful. Keats died young and mostly unheralded. Then Austen was propelled to enduring fame by a biography. And Brunton is now mostly forgotten. As for Keats, "somebody rolled out a really good edition with [Keats's] letters, and his letters are so lovely," says Heather Jackson, a retired professor of English at the University of Toronto, who studied lasting literary fame. "His fate fitted in with the myth of neglected genius." It also helped that he wrote about things that made for pretty illustrations. Entry into the literary pantheon, Jackson says, requires meeting thresholds for quality and quantity, but after that, "adventitious circumstances take over."

At a minimum, everyone needs a champion. Unfortunately, many talented people never find one, Sunstein says. He cites important work led by Harvard economist Raj Chetty that introduced the idea of "lost Einsteins," an unknown number of people who could have been innovative geniuses but were born and raised in communities where innovation was not cultivated. For them, circumstance—being born to a lower-income or minority family, for instance, or attending underperforming schools—too often determines success or failure.

Accepting that fact might lead us to throw open the doors of opportunity more widely. It might also make us more optimistic about our own chances in life. "To think that, for each of us, the path to some kind of success or failure is going to turn on little things that maybe can be moved a bit once we're alert to them, that's fun and an opportunity," Sunstein says. "Something like lightning might strike, which can bring a smile to the face on a tough morning." —*Lydia Denworth*

Brainstorming on Zoom Hampers Creativity

Turning off the camera when trying to hash out new ideas might help

For many of us, the COVID-19 pandemic has meant no more commutes, no more showering, no more putting on pants—just virtual meeting after virtual meeting. Some research shows this adjustment might not impact workplace productivity to any great degree. A new study, though, suggests otherwise.

The research, published in *Nature,* found that video calls, as opposed to in-person meetings, reduce creative collaboration and the generation of novel ideas. The results indicate that while the mental cogs keep running more or less smoothly when working remotely, group innovation might be hindered. The findings could stiffen employers' resolve to urge or require their employees to trek back to the office.

In the new study, the authors first recruited 602 participants, who were randomly paired and asked to come up with creative uses for a product. They were also randomly selected to work together either in person or virtually. The pairs were then ranked by assessing their gross number of ideas, as well as those concepts' degree of novelty, and asked to submit their best idea.

Among the groups, virtual pairs came up with significantly fewer ideas, suggesting that something about face-to-face interaction generates a prolific creative spark. Yet the virtual pairs scored better when selecting their highest-quality concept.

By analyzing a subset of study participants, the authors found that higher levels of in-person creativity might relate to a narrowing of cognitive focus during virtual communication. When random objects were placed in both the virtual and physical rooms, the virtual pairs of participants spent more time looking directly at each other rather than letting their gaze wander about the room and taking in the entire scene. Eyeing one's whole environment and noticing the random objects were associated with increased idea generation.

The study also included a real-world "field experiment" in which

Alistair Berg/Getty Images

virtual versus face-to-face creativity was assessed in nearly 1,500 telecommunications engineers from five different countries. Randomized participant pairs were asked to generate new ideas and decide on one to submit for future product development. Again, in-person encounters resulted in more creative concepts. Yet the quality of their final idea did not differ from that of pairs in the virtual group.

"We ran this experiment based on feedback from companies that it was harder to innovate with remote workers, and I'll admit I was skeptical," says Melanie Brucks, lead author of the new paper and an assistant professor of marketing at Columbia Business School. "Unlike other forms of virtual communication, like phone calls or e-mail, videoconferencing mimics the in-person experience quite well, so I was surprised when we found meaningful differences between in-person and video interaction for idea generation."

Yet Brucks emphasizes that something about virtual communications enables a group to select its best idea with equal or even better reliability.

"The findings show that face-to-face teams ideate better than virtual teams but that face-to-face teams and virtual teams are equally good at choosing the top solution or idea from a list of possible options," comments Brian Uzzi, a professor of leadership at the Kellogg School of Management, who reviewed the new study but was not directly involved in the research. Uzzi also co-authored a News & Views piece accompanying the paper in *Nature*.

"This study does a very nice job of highlighting the importance of attention in the process of creativity," comments Georgetown University neuroscientist Adam Green, who specializes in creativity research but was not involved in the new research. "A fundamental element of the process of generating creative ideas is that you have to point your attention inward. When something external draws a lot of your attention, there isn't as much attention available to support creative ideation."

The new work suggests that daydreaming and gazing around a conference room might enhance thinking during creative pursuits. On platforms such as Zoom, the screen monopolizes our interactions. Our

gaze wavers less. Looking away might come across as rude, Brucks speculates. "I think we feel compelled to look at the screen because that is the defined context of the interaction," she says, "the same way we wouldn't walk to another room while talking to someone in person."

Like most educators, Brucks primarily taught virtually throughout the pandemic, and she did notice some benefits of the approach as well. Her students were more likely to take turns speaking and less likely to talk over one another, as they tend to do in an in-person class. She also noticed that teaching remotely allowed her shyer students to speak up more often, rid of the anxiety that comes from addressing a large classroom.

Brucks adds that one solution to improving virtual idea generation might be to simply turn off our camera. She notes anecdotally that her students felt "freer" and more creative when asked to do so. "They were untethered to their screens while generating ideas," Brucks recalls.

This may be sound advice given that the American workplace has evolved, perhaps for good. A recent survey conducted by *Harvard Business Review* found that Americans would prefer to work remotely on an average of 2.5 days per week. Other research suggests that in the future, up to 20 percent of U.S. workdays will occur at home, even if the severity of the pandemic continues to lessen. Many major companies—Google, Microsoft, JPMorgan Chase and Amazon included—are adopting increasingly lenient work-from-home policies.

But Brucks's findings suggest that stepping foot in a physical office may have some advantages. And some corporations, such as Goldman Sachs, have demanded their employees return to full-time in-person work. (In Goldman's case, only half had done so as of February.)

Perhaps the American workplace will find a compromise—a sweet spot in the middle that balances working from both home and office.

"The office is not dead," Uzzi says. "Virtual teamwork can't replace face-to-face teamwork. Idea selection proficiency is only valuable if you have strong options to select from, and face-to-face teams are the best means to generate winning options."

—Bret Stetka

People Think Minority Groups Are Bigger Than They Really Are

Overestimating minority populations can lead to reduced support for diversity and inclusion programs

Our brain is attuned to noticing new things in the busy environment around us. This alertness to novelty means we are apt to overemphasize what holds our attention. When people stand out as different, they stick in our mind because of how much we initially notice their presence—and by how vividly we later recall them.

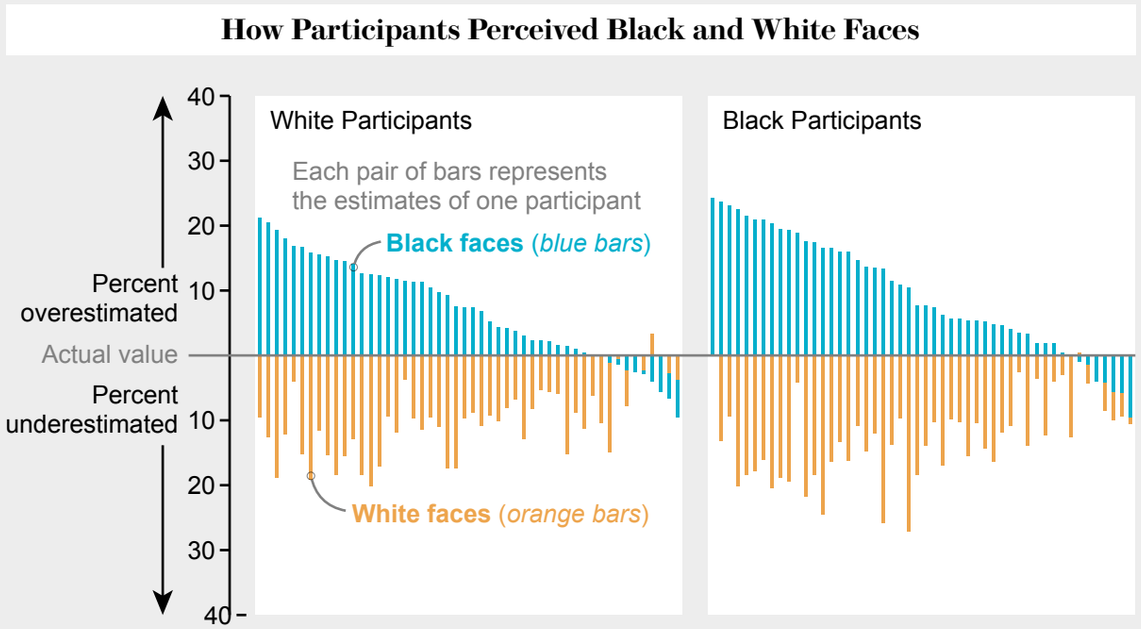
Our recollection of the unusual carries over into how we think about social groups. A recent survey by YouGov America illustrates the real-life tendency to overrepresent the size of minority populations. Residents of New York City, for example, are a tiny minority of Americans, only 3 percent of the population. But adult respondents to this nationwide survey thought that a whopping 30 percent of Americans live in the Big Apple. The survey also found a consistent overestimation of the size of ethnic and racial minority groups. Respondents on average figured that 41 percent of Americans are Black when the actual proportion is 12 percent.

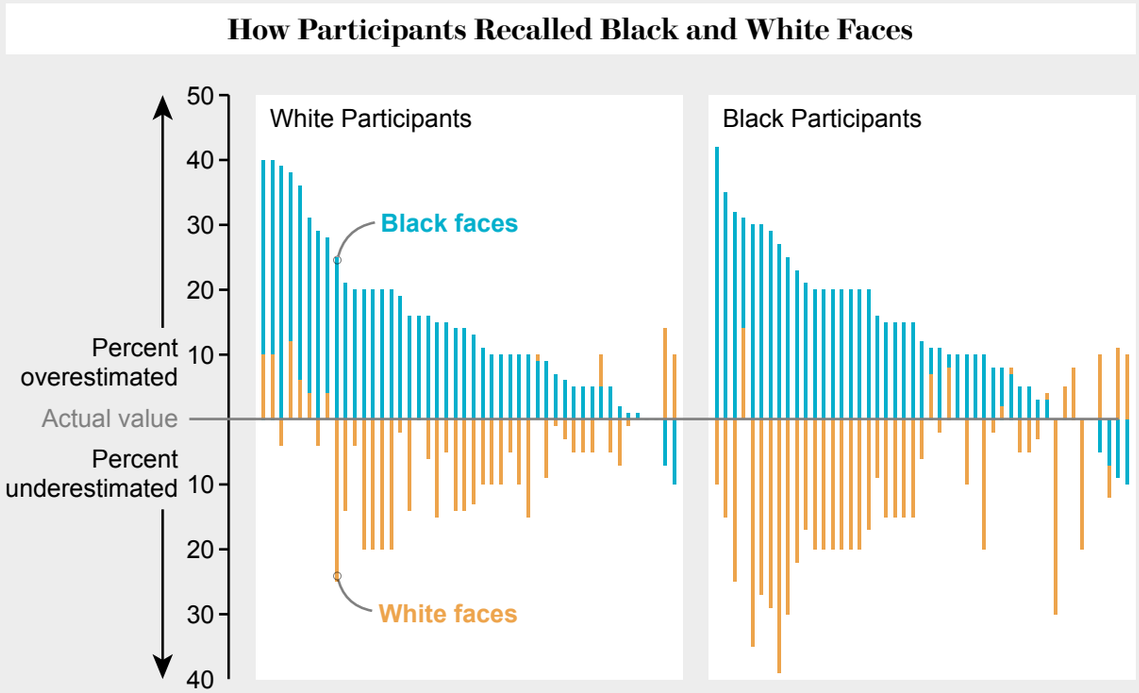
A study published recently in the *Proceedings of the National Academy of Sciences USA* demonstrates that extra attention to the uncommon around us may partly explain the bad mental math that contributes to misperceptions about other groups. When people make these overestimates, the study authors found, the result can be an "illusion of diversity" about the presence of minority groups in our social environment. That faulty perception, in turn, can have the paradoxical effect of decreasing support for measures to increase diversity.

Previous research has suggested that negative attitudes toward diversity and inclusion efforts are motivated when a majority group perceives a threat by overestimating minority group size, says Maureen Craig, a social psychologist and an assistant professor at New York University, who was not involved in

The Eyes Deceive, as Do Our Memories

A set of studies looked at how accurately we perceive and remember members of a minority group. In one set of experiments, study participants—50 Black people and 50 white people—estimated the percentage of those belonging to each racial group in an image showing a grid of faces they had looked at for two seconds. After observing 100 such grids, they also tried to guess an overall percentage for the whole set to test what they remembered. Overall, in both perception and memory, both Black and white participants overestimated the percentage of Black people and underestimated the proportion of white people.





Estimates that differed from the average of all responses by more than two standard deviations are not included.

Amanda Montañez; Source: "Minority Salience and the Overestimation of Individuals from Minority Groups in Perception and Memory," by Rasha Kardosh et al., in *Proceedings of the National Academy of Sciences USA*, Vol. 119, No. 12. Published online March 14, 2022

the new study. Its findings, she says, highlight a cognitive response that comes before the overestimation. People latch onto the unusual before making other judgments about it, such as the size of purportedly "competing" groups. Taking notice of what is uncommon to someone is "a basic cognitive phenomenon in which rare things stand out," Craig says.

The study's first author, Rasha Kardosh, a social psychologist at the Hebrew University of Jerusalem, and her team ran 12 experiments with 942 participants in both the U.S. and Israel. Across all these studies, 82.6 percent of participants overestimated the proportion of minority group members.

Some experiments took place at the Hebrew University, where most students speak Hebrew, a minority speak Arabic and culturally based visual signals can sometimes distinguish group members. Student

participants were asked to estimate the percentage of Arab students they thought were on campus. At the Hebrew University, 9.28 percent of students were Palestinian Israeli at the time of the study, but the Jewish Israeli students gave their estimate for the group as 31.56 percent, and the Palestinian Israeli students gave an estimate of 35.81 percent. Other students were tested for how quickly they detected images of women wearing either a Muslim or Jewish religious headscarf. They did so more quickly for images of women wearing scarves in the Muslim style.

In the U.S., the researchers had participants look at a screen showing a grid of 100 photographs with faces of Black people and white people in different proportions. Viewers had to estimate the overall percentages of Black and white people present after seeing a set of 20 such grids, each viewed for two seconds.

When 25 percent of the images in the grids were of Black people, white participants estimated the proportion of Black faces to be 43.22 percent, and Black participants put it at 43.36 percent. When 45 percent of the images were of Black faces, white participants estimated the proportion of Black people at 58.85 percent, and Black participants thought it was 56.18 percent.

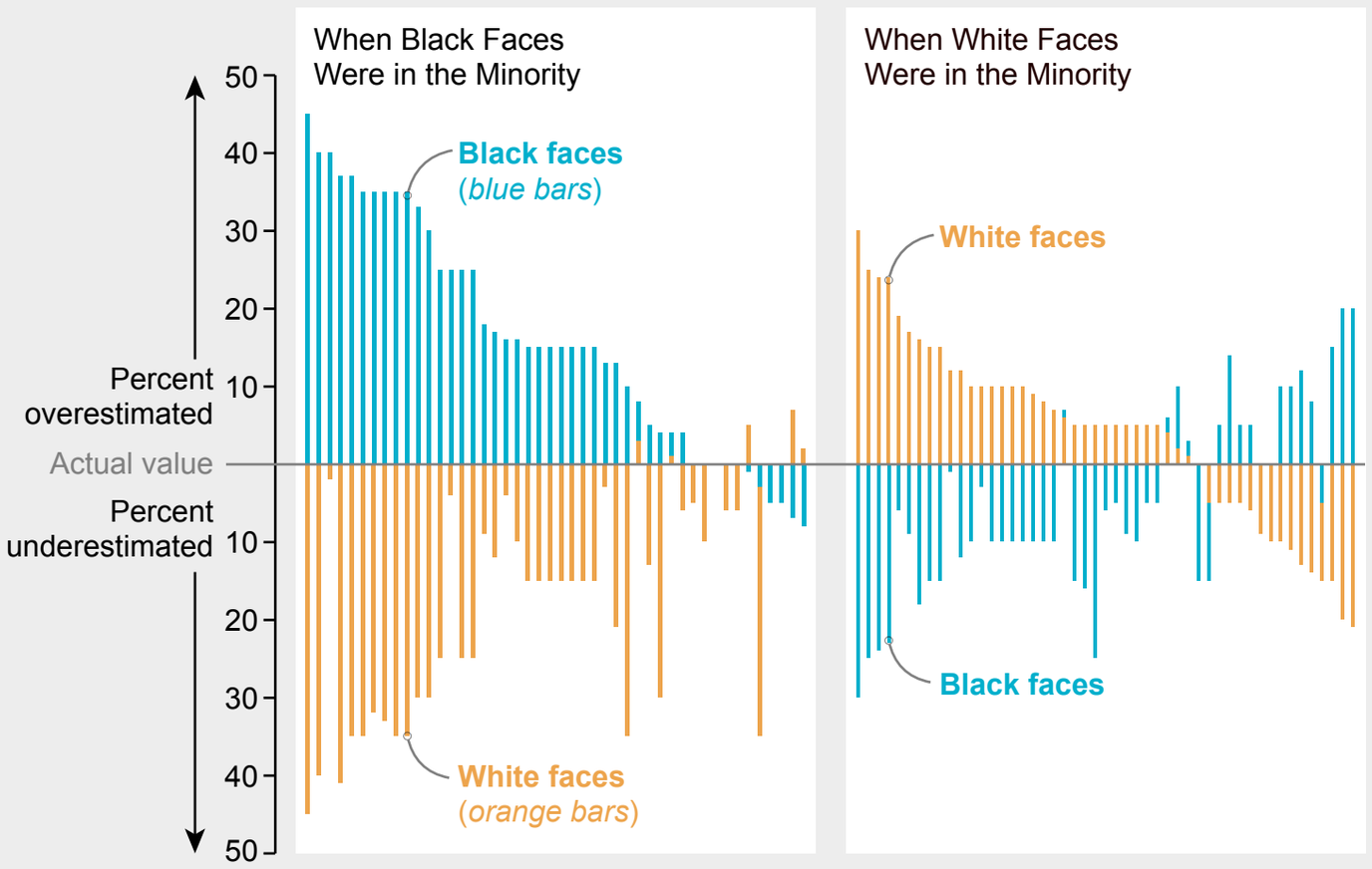
In other experiments, participants were asked to estimate the proportions of Black and white faces directly after seeing each of a series of grids and to then make the same calculation after having gone through the entire set of 20 grids. In both cases, they overestimated the proportion of Black faces and underestimated the percentage of white faces.

The researchers also wanted to know whether

A Critical Role for Social Expectations

In one experiment, 100 white participants overestimated the proportion of people whose racial group was in the minority in grids containing Black and white faces. They made a smaller misjudgment when white people were in the minority, possibly because of social expectations about which group should be identified as holding that status.

How the Effect Varied Based on Who Was in the Minority



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preexisting expectations about which group should be in the minority would affect the outcome. They showed 100 white participants grids in which 25 percent of the photographed faces were white, making them the minority, and another set in which 25 percent were Black. In both cases, the presence of faces from less common groups was judged to be higher than it really was. Overestimates were higher, though, when images of Black people were in the minority, illustrating the impact of social expectations.

"That was a really nice demonstration that you can flip it," says Craig, referring to the overestimation when white faces were in the minority. That overestimation "is a lot smaller effect, but it is new—I've not seen that before." This finding suggests that everyone has some cognitive bias that leads to overestimations of a numerical minority, she says, going beyond earlier work focused largely on how perceived growth of minority groups affects racial attitudes.

Charts of how the extent of overestimates and underestimates varied when white faces versus Black faces were in the minority.

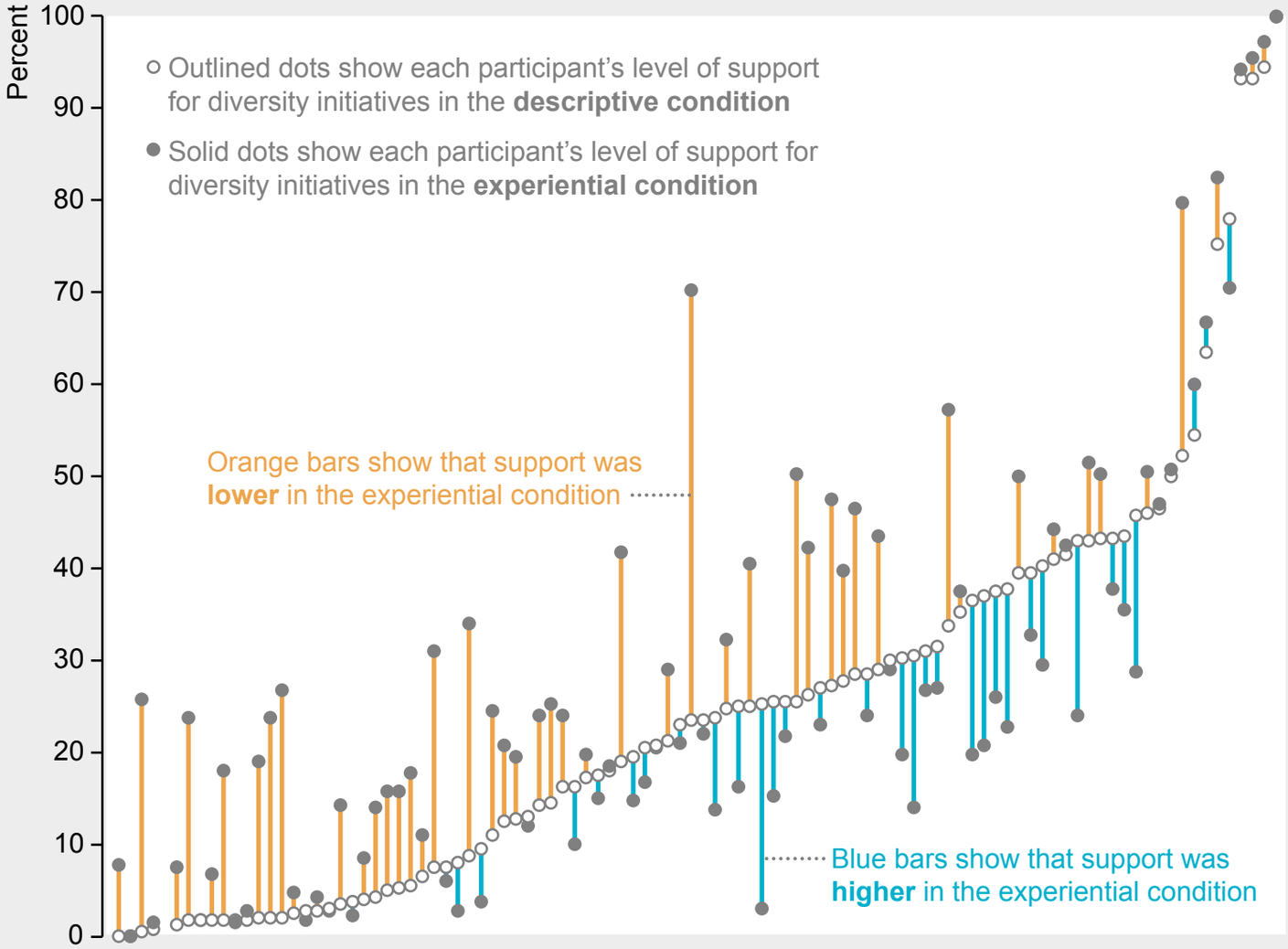
A final set of experiments examined how psychological bias affects support for academic diversity efforts. Participants were shown information about two college programs. In what the researchers called the "experiential" condition, participants viewed 20 grids of 100 photographs, with Black faces making up 5 percent. In what they called the "descriptive" condition, the group simply watched a video that informed viewers that 5 percent of a different

Misperceptions Undercut Support for Diversity

The psychological bias that leads us to see and remember more diversity than actually exists in a group diminishes backing for measures that can make society more equitable.

In the **descriptive condition** of this experiment, study participants saw a vignette about a college program whose population of 2,000 students was described as 5 percent Black and 95 percent white.

In the **experiential condition**, study participants saw 20 grids of 100 faces each that were meant to represent a population of 2,000 students at a different college program. Five percent of the faces were Black, and 95 percent of them were white. But participants were not told this. Instead they were asked to estimate percentages of Black and white students.



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college program's students were Black. After both exercises, participants were asked whether more should be done to increase diversity, rating their opinion on a scale from 0 (for "not at all") to 100 ("a great extent").

After viewing the photographic grids in the experiential condition, participants estimated the proportion of Black faces to be 14.75 percent, not 5 percent, while simultaneously underestimating the proportion of white faces as 83.26 percent, not 95 percent. Support for a diversity-improvement program was lower in the experiential condition, with an average score of 71.07, compared with 74.5 in the descriptive condition.

The researchers also assessed whether existing attitudes among the participants affected their estimates and found no such associations.

If people go with what their intuition tells them about minority representation rather than using actual numbers, doing so could be costly, says Ran Hassin, a cognitive scientist at the Hebrew University and senior author of the study. Relying on impressions instead of evidence, he says, might lead people to be less supportive of policies to enhance minority presence on a campus or in a workplace. The results show that "this is something we all share," Kardosh adds. "If you think you're immune, you're probably not."

People talk about "being sensitive to the optics" when it comes to diversity efforts in workplaces, says Susan Fiske, a professor of psychology and public affairs at Princeton University, who was not involved in the study but edited it for *PNAS*. This focus on awareness of optics is "saying that optics are really important," she says, which is why these results showing that the "optics can be wrong" deserve our attention.

—Emily Willingham

Your Brain Expands and Shrinks over Time: These Charts Show How

Researchers hope they could one day be used as a routine clinical tool by physicians

When neuroscientist Jakob Seidlitz took his 15-month-old son to the pediatrician for a checkup in March, he left feeling unsatisfied. There wasn't anything wrong with his son—the youngster seemed to be developing at a typical pace, according to the height and weight charts the physician used. What Seidlitz felt was missing was an equivalent metric to gauge how his son's brain was growing. "It is shocking how little biological information doctors have about this critical organ," says Seidlitz, who is based at the University of Pennsylvania.

Soon, he might be able to change that. Working with colleagues, Seidlitz has amassed more than 120,000 brain scans—the largest collection of its kind—to create the first comprehensive growth charts for brain development. The charts show visually how human brains expand quickly early in life and then shrink slowly with age. The sheer magnitude of the study, published in *Nature* on April 6, has stunned neuroscientists, who have long had to contend with reproducibility issues in their research, in part because of small sample sizes. Magnetic resonance imaging (MRI) is expensive, meaning that scientists are often limited in the number of participants they can enroll in experiments.

"The massive data set they assembled is extremely impressive and really sets a new standard for the field," says Angela Laird, a cognitive neuroscientist at Florida International University in Miami.

Even so, the authors caution that their database isn't completely inclusive—they struggled to gather brain scans from all regions of the globe. The resulting charts, they say, are therefore just a first draft, and further tweaks would be needed to deploy them in clinical settings.

If the charts are eventually rolled out to pediatricians, great care will be needed to ensure that they are not misinterpreted, says Hannah Tully, a pediatric neurologist at the University

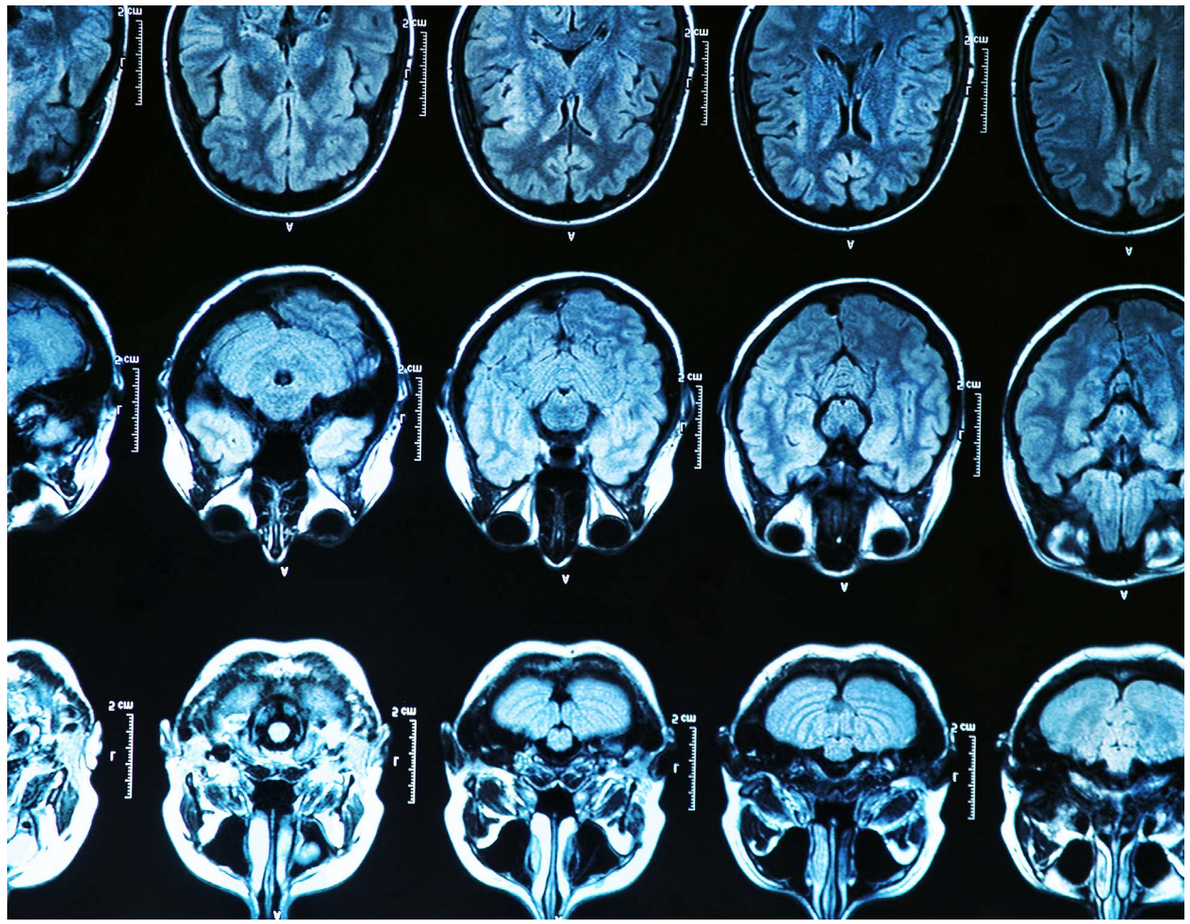
of Washington. “A big brain is not necessarily a well-functioning brain,” she says.

NO EASY TASK

Because brain structure varies significantly from person to person, the researchers had to aggregate a huge number of scans to create an authoritative set of growth charts with statistical significance. That’s no easy task, says Richard Bethlehem, a neuroscientist at the University of Cambridge and a co-author of the study. Instead of running thousands of scans themselves, which would take decades and be prohibitively costly, the researchers turned to already completed neuroimaging studies.

Bethlehem and Seidlitz sent e-mails to researchers all over the world asking if they would share their neuroimaging data for the project. The duo was amazed by the number of replies, which they attribute to the COVID-19 pandemic giving researchers less time in their laboratories and more time than usual with their e-mail inboxes.

In total, the team aggregated 123,894 MRI scans from 101,457 people, who ran the gamut from



fetuses 16 weeks after conception to 100-year-old adults. The scans included brains from neurotypical people, as well as people with a variety of medical conditions, such as Alzheimer’s disease, and neurocognitive differences, including autism spectrum disorder. The researchers used statistical models to extract information from the images and ensure that the scans were directly comparable, no matter what type of MRI machine had been used.

The end result is a set of charts plotting several key brain metrics by age. Some metrics, such as gray matter volume and mean cortical thickness (the width of the gray matter), peak early in a person’s development, whereas the volume of white matter (found deeper in the brain) tends to peak by around age 30. The data on ventricular volume (the amount of cerebrospinal fluid in the brain), in particular, surprised Bethlehem. Scientists knew that this volume increases with age because it is typically associated with brain atrophy, but Bethlehem was shocked by how rapidly it tends to grow in late adulthood.

A FIRST DRAFT

The study comes on the heels of a bombshell paper published in *Nature* in March showing that most brain-imaging experiments contain too few scans to reliably detect links between brain function and behavior, meaning that their conclusions might be incorrect. Given this finding, Laird expects the field to move toward adopting a framework similar to the one used by Seidlitz and Bethlehem, to increase statistical power.

To amass so many data sets is akin to a “diplomatic masterpiece,” says Nico Dosenbach, a neuroscientist at Washington University in St. Louis, who co-authored the March study. He says this is the scale on which researchers should operate when aggregating brain images.

Despite the size of the data set, Seidlitz, Bethlehem and their colleagues acknowledge that their study suffers from a problem endemic to

Bunyos/Getty Images

neuroimaging studies—a remarkable lack of diversity. The brain scans they collected come mainly from North America and Europe and disproportionately reflect populations that are white, university-aged, urban and affluent. This limits the generalizability of the findings, says Sarah-Jayne Blakemore, a cognitive neuroscientist at the University of Cambridge. The study includes only three data sets from South America and one from Africa—accounting for around 1 percent of all the brain scans used in the study.

Billions of people worldwide lack access to MRI machines, making diverse brain-imaging data difficult to come by, Laird says. But the authors haven't stopped trying. They have launched a Web site where they intend to update their growth charts in real time as they receive more brain scans.

WITH BIG DATA SETS, BIG RESPONSIBILITY

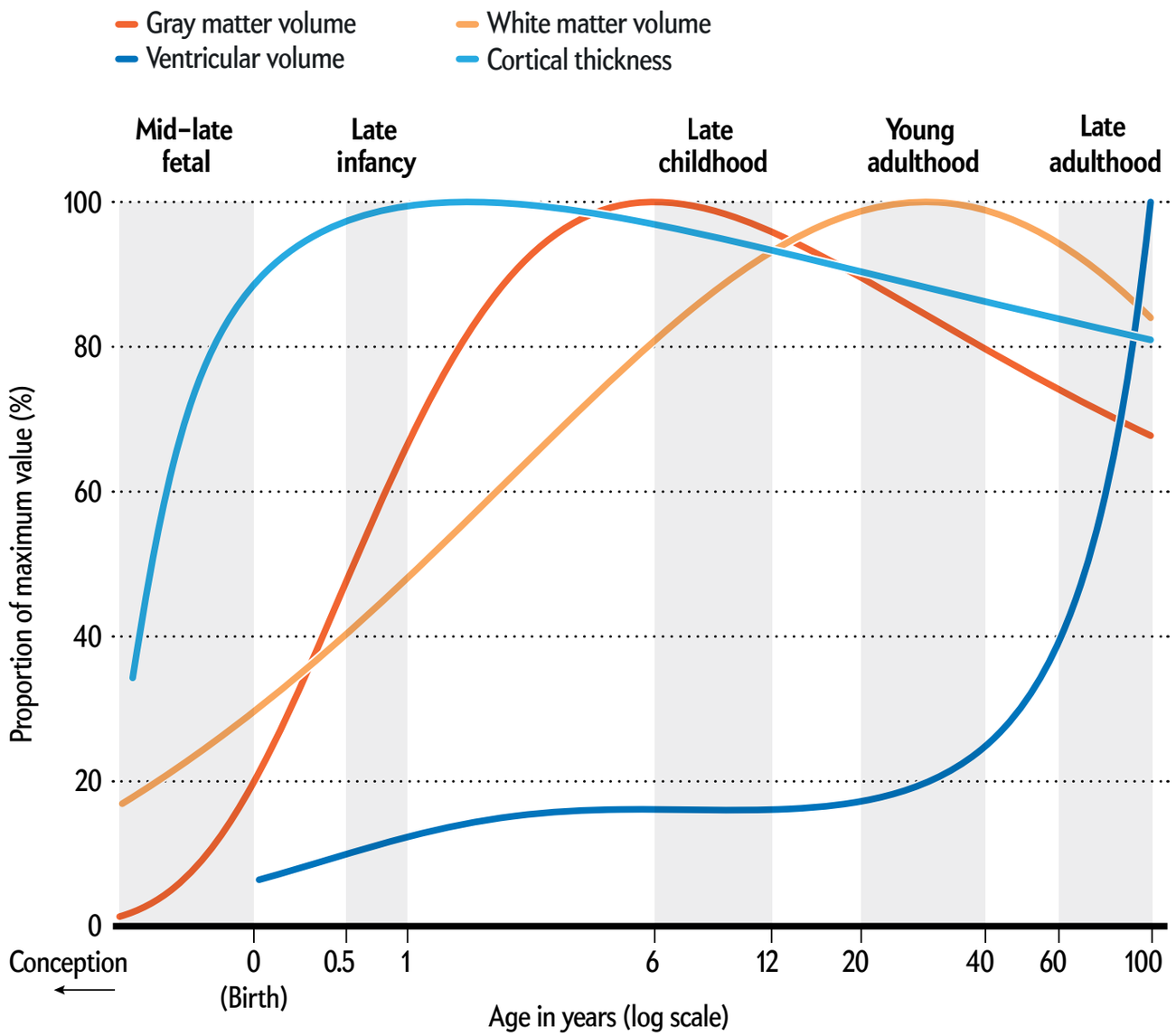
Another challenge was determining how to give proper credit to the owners of the brain scans used to construct the charts. Some of the scans came from open-access data sets, but others were closed to researchers. Most of the closed-data scans hadn't yet been processed in a way that would allow them to be incorporated into the growth charts, so their owners did extra work to share them. These scientists were then named as authors of the paper.

Meanwhile the owners of the open data sets received only a citation in the paper—which doesn't hold as much prestige for researchers seeking funding, collaborations and promotions. Seidlitz, Bethlehem and their colleagues processed these data. In most cases, Bethlehem says that there was essentially no direct contact with the owners of these data sets. The paper lists about 200 authors and cites the work of hundreds of others who contributed brain scans.

There are a number of reasons that data sets might be closed: for instance, to protect the privacy of health data or because researchers don't have the resources to make them public.

Brain Change

Researchers analyzed more than 120,000 brain scans to assemble the most comprehensive growth chart of the brain so far. White and gray matter volume and mean cortical thickness (the width of the gray matter) increase rapidly early in development, whereas ventricular volume (the amount of cerebrospinal fluid in the brain) increases rapidly later in life.



Data shown are median values.

"Your Brain Expands and Shrinks over Time: These Charts Show How," by Max Kozlov, in *Nature*, Vol. 604; April 2022

But this doesn't make it fair that the researchers who opened their data sets didn't get authorship, the authors say. In their paper's Supplementary Information, they argue that the situation "perversely disincentivises open science, since the people who do most to make their data openly available could be least likely to merit recognition." Bethlehem and Seidlitz contend that authorship guidelines from journals, including *Nature*—which say that each author is expected to have made "substantial contributions" to, for example, the analysis or interpretation of data—are an obstacle. (*Nature*'s news team is editorially independent of its publisher.)

A *Nature* spokesperson responds that the issue was "considered carefully by the editors and authors according to our authorship policies" and that "all data sets were appropriately credited per our data citation policy."

Ultimately these concerns can be traced back to how researchers are evaluated by the scientific enterprise, says Kaja LeWinn, a social epidemiologist at the University of California, San Francisco, who studies neurodevelopment. She says that it's incumbent on all the relevant stakeholders—including funders, journals and research institutions—to reevaluate how brain science can be properly recognized and rewarded, especially as these types of large-scale studies become more common.

—Max Kozlov

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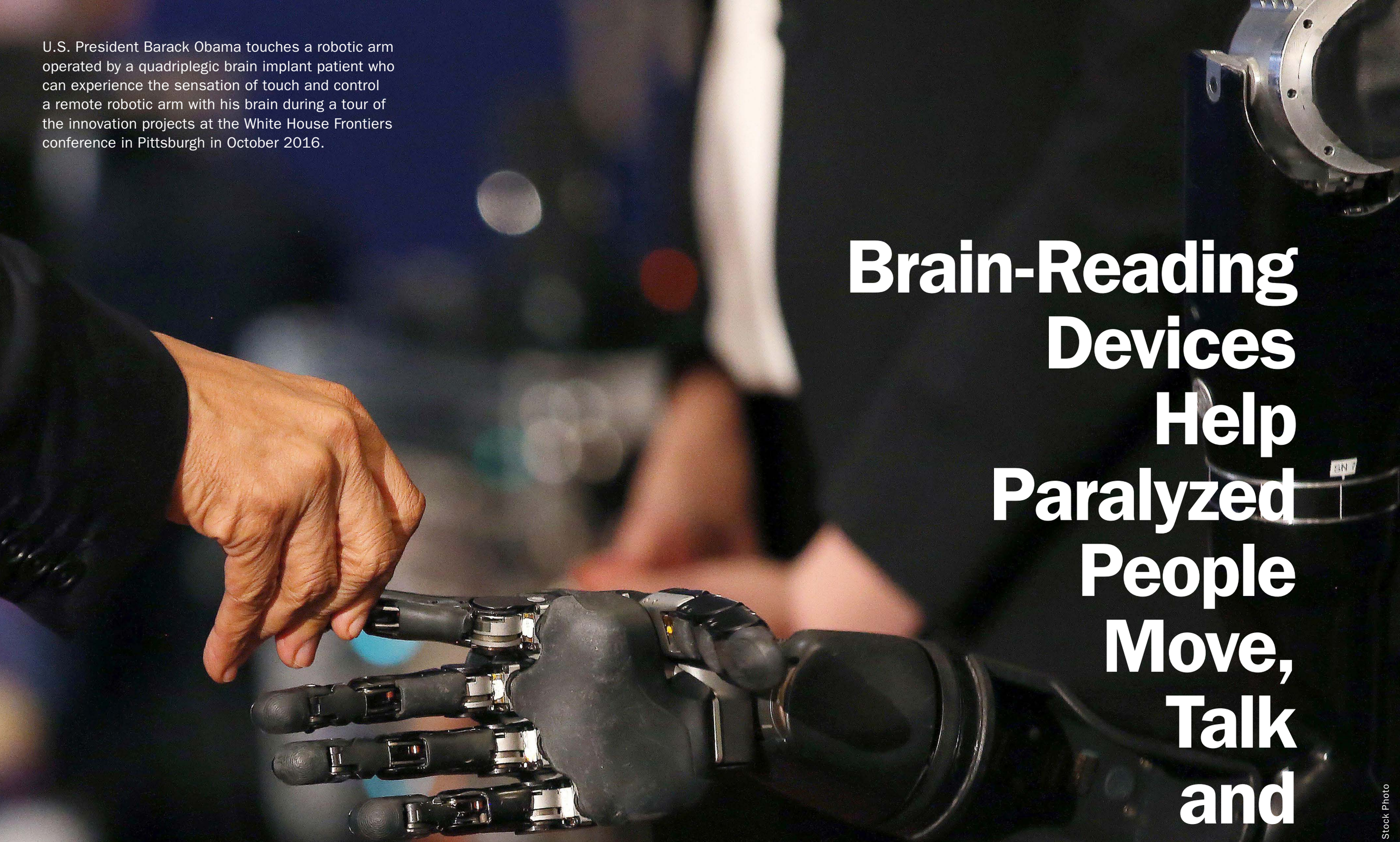

U.S. President Barack Obama touches a robotic arm operated by a quadriplegic brain implant patient who can experience the sensation of touch and control a remote robotic arm with his brain during a tour of the innovation projects at the White House Frontiers conference in Pittsburgh in October 2016.

Brain-Reading Devices Help Paralyzed People Move, Talk and Touch

Implants are becoming more sophisticated—and are attracting commercial interest

By Liam Drew

Reuters/Carlos Barria/Alamy Stock Photo

James Johnson hopes to drive a car again one day. If he does, he will do it using only his thoughts.

In March 2017 Johnson broke his neck in a go-carting accident, leaving him almost completely paralyzed below the shoulders. He understood his new reality better than most. For decades he had been a carer for people with paralysis. "There was a deep depression," he says. "I thought that when this happened to me there was nothing—nothing that I could do or give."

But then Johnson's rehabilitation team introduced him to researchers at the nearby California Institute of Technology, who invited him to join a clinical trial of a brain–computer interface (BCI). This would first entail neurosurgery to implant two grids of electrodes into his cortex. These electrodes would record neurons in his brain as they fired, and the researchers would use algorithms to decode his thoughts and intentions. The system would then use Johnson's brain activity to operate computer applications or to move a prosthetic device. All told, it would take years and require hundreds of intensive training sessions. "I really didn't hesitate," Johnson says.

The first time he used his BCI, implanted in November 2018, Johnson moved a cursor around a computer screen. "It felt like *The Matrix*," he says. "We hooked up to the computer, and lo and behold I was able to move the cursor just by thinking."

Johnson has since used the BCI to control a robotic arm, use Photoshop software, play "shoot-'em-up" video games, and now to drive a simulated car through a virtual environment, changing speed, steering and reacting to hazards. "I am always stunned at what we are able to do," he says, "and it's frigging awesome."

Johnson is one of an estimated 35 people who have had a BCI implanted long term in their brain. Only around a dozen laboratories conduct such research, but that number is growing. And in the past five years the range of skills these devices can restore has expanded enormously. Last year alone scientists described a study participant using a robotic arm that could send sensory feedback directly to his brain; a prosthetic speech device for someone left unable to speak by a stroke; and a person able to communicate at record speeds by imagining himself handwriting.

So far the vast majority of implants for recording long term from individual neurons have been made by a single company: Blackrock Neurotech, a medical device developer based in Salt Lake City. But in the past seven years commercial interest in BCIs has surged. Most notably, in 2016 entrepreneur Elon Musk launched Neuralink in San Francisco, with the goal of connecting humans and computers. The company has raised $363 million. Last year Blackrock Neurotech and several other newer BCI companies also attracted major financial backing.

Bringing a BCI to market will, however, entail transforming a bespoke technology, road-tested in only a small number of people, into a product that can be manufactured, implanted and used at scale. Large trials will need to show that BCIs can work in nonresearch settings and demonstrably improve the everyday lives of users—at prices that the market can support. The time line for achieving all this is uncertain, but the field is bullish. "For thousands of years we have been looking for some way to heal people who have paralysis," says Matt Angle, founding chief executive of Paradromics, a neurotechnology company in Austin, Tex. "Now we're actually on the cusp of having technologies that we can leverage for those things."

Liam Drew is a freelance science writer in London.

INTERFACE EVOLUTION

In June 2004 researchers pressed a grid of electrodes into the motor cortex of a man who had been paralyzed by a stabbing. He was the first person to receive a long-term BCI implant. Like most people who have received BCIs since, his cognition was intact. He could imagine moving, but he had lost the neural pathways between his motor cortex and his muscles. After decades of work in many labs in monkeys, researchers had learned to decode the animals' movements from real-time recordings of activity in the motor cortex. They now hoped to infer a person's imagined movements from brain activity in the same region.

In 2006 a landmark paper described how the man had learned to move a cursor around a computer screen, con-

trol a television, and use robotic arms and hands just by thinking. The study was co-led by Leigh Hochberg, a neuroscientist and critical-care neurologist at Brown University and at Massachusetts General Hospital. It was the first of a multicenter suite of trials called BrainGate, which continues today.

"It was a very simple, rudimentary demonstration," Hochberg says. "The movements were slow or imprecise—or both. But it demonstrated that it might be possible to record from the cortex of somebody who was unable to move and to allow that person to control an external device."

Today's BCI users have much finer control and access to a wider range of skills. In part, this is because researchers began to implant multiple BCIs in different brain areas of the user and devised new ways to identify useful signals. But Hochberg says the biggest boost has come from machine learning, which has improved the ability to decode neural activity. Rather than trying to understand what activity patterns mean, machine learning simply identifies and links patterns to a user's intention.

"We have neural information; we know what that person who is generating the neural data is attempting to do; and we're asking the algorithms to create a map between the two," Hochberg says. "That turns out to be a remarkably powerful technique."

MOTOR INDEPENDENCE

Asked what they want from assistive neurotechnology, people with paralysis most often answer "independence." For people who are unable to move their limbs, this typically means restoring movement.

One approach is to implant electrodes that directly stimulate the muscles of a person's own limbs and have the BCI directly control these. "If you can capture the native cortical signals related to controlling hand movements, you can essentially bypass the spinal cord injury to go directly from brain to periphery," says Bolu Ajiboye, a neuroscientist at Case Western Reserve University.

In 2017 Ajiboye and his colleagues described a participant who used this system to perform complex arm movements, including drinking a cup of coffee and feeding himself. "When he first started the study," Ajiboye says, "he had to think very hard about his arm moving from point A to point B. But as he gained more training, he could just think about moving his arm, and it would move." The participant also regained a sense of ownership of the arm.

Ajiboye is now expanding the repertoire of command signals his system can decode, such as those for grip force. He also wants to give BCI users a sense of touch, a goal being pursued by several labs.

In 2015 a team led by neuroscientist Robert Gaunt of the University of Pittsburgh reported implanting an electrode array in the hand region of a person's somatosensory cortex, where touch information is processed. When they used the electrodes to stimulate neurons, the person felt something akin to being touched.

Gaunt then joined forces with Pittsburgh colleague Jennifer Collinger, a neuroscientist advancing the control of robotic arms by BCIs. Together they fashioned a robotic arm with pressure sensors embedded in its fingertips, which fed into electrodes implanted in the somatosensory cortex to evoke a synthetic sense of touch. It was not an entirely natural feeling—sometimes it felt like pressure or being prodded; other times it was more like a buzzing, Gaunt explains. Nevertheless, tactile feedback made the prosthetic feel much more natural to use, and the time it took to pick up an object was halved, from roughly 20 seconds to 10.

Implanting arrays into brain regions that have different roles can add nuance to movement in other ways. Neuroscientist Richard Andersen—who is leading the trial at Caltech in which Johnson is participating—is trying to decode users' more abstract goals by tapping into the posterior parietal cortex (PPC), which forms the intention or plan to move. That is, it might encode the thought "I want a drink," whereas the motor cortex directs the hand to the coffee, then brings the coffee to the mouth.

Andersen's group is exploring how this dual input aids BCI performance, contrasting use of the two cortical regions alone or together. Unpublished results show that Johnson's intentions can be decoded more quickly in the PPC, "consistent with encoding the goal of the movement", says Tyson Aflalo, a senior researcher in Andersen's lab. Motor cortex activity, in contrast, lasts throughout the whole movement, he says, "making the trajectory less jittery."

This new type of neural input is helping Johnson and others to expand what they can do. Johnson uses the driving simulator, and another participant can play a virtual piano using her BCI.

MOVEMENT INTO MEANING

"One of the most devastating outcomes related to brain injuries is the loss of ability to communicate," says Edward Chang, a neurosurgeon and neuroscientist at the University of California, San Francisco. In early BCI work, participants could move a cursor around a computer screen by imagining their hand moving and then imagining grasping to "click" letters—offering a way to achieve communication. But more recently, Chang and others have made rapid progress by targeting movements that people naturally use to express themselves.

The benchmark for communication by cursor control—roughly 40 characters per minute—was set in 2017 by a team led by Krishna Shenoy, a neuroscientist at Stanford University.

Then, last year, this group reported an approach that enabled study participant Dennis Degray, who can speak

but is paralyzed from the neck down, to double the pace.

Shenoy's colleague Frank Willett suggested to Degray that he imagine handwriting while they recorded from his motor cortex. The system sometimes struggled to parse signals relating to letters that are handwritten in a similar way, such as r, n and h, but generally it could easily distinguish the letters. The decoding algorithms were 95 percent accurate at baseline, but when they were autocorrected using statistical language models that are similar to predictive text in smartphones, this jumped to 99 percent.

"You can decode really rapid, very fine movements," Shenoy says, "and you're able to do that at 90 characters per minute."

Degray has had a functional BCI in his brain for nearly six years and is a veteran of 18 studies by Shenoy's group. He says it's remarkable how effortless tasks become. He likens the process to learning to swim, saying, "You thrash around a lot at first, but all of a sudden, everything becomes understandable."

Chang's approach to restoring communication focuses on speaking rather than writing, albeit using a similar principle. Just as writing is formed of distinct letters, speech is formed of discrete units called phonemes, or individual sounds. There are around 50 phonemes in English, and each is created by a stereotyped movement of the vocal tract, tongue and lips.

Chang's group first worked on characterizing the part of the brain that generates phonemes and, thereby, speech—an ill-defined region called the dorsal laryngeal cortex. Next the researchers applied these insights to create a speech-decoding system that displayed the user's intended speech as text on a screen. Last year they reported that this device enabled a person left unable to talk by a brain stem stroke to communicate, using a preselected vocabulary of 50 words and at a rate of 15 words per minute. "The most important thing that we've learned," Chang says, "is that it's no longer a theoretical; it's truly possible to decode full words."

"Everybody looks at me in the chair and they always say, 'Oh, that poor guy, he can't play golf any more.' That's bad. But the real terror is in the middle of the night when a spider walks across your face. That's the bad stuff."

—Dennis Degray

Unlike other high-profile BCI breakthroughs, Chang didn't record from single neurons. Instead he used electrodes placed on the cortical surface that detect the averaged activity of neuronal populations. The signals are not as fine-grained as those from electrodes implanted in the cortex, but the approach is less invasive.

The most profound loss of communication occurs in people in a completely locked-in state, who remain conscious but are unable to speak or move. In March a team that included neuroscientist Ujwal Chaudhary and others at the University of Tübingen in Germany reported restarting communication with a man who has amyotrophic lateral sclerosis (ALS, or motor neuron disease). The man had previously relied on eye movements to communicate, but he gradually lost the ability to move his eyes.

The team of researchers gained consent from the man's family to implant a BCI and tried asking him to imagine movements to use his brain activity to choose letters on a screen. When this failed, they tried playing a sound that mimicked the man's brain activity—a higher tone for more activity, lower for less—and taught him to modulate his neural activity to heighten the pitch of a tone to signal yes and to lower it for no. That arrangement allowed him to pick out a letter every minute or so.

The method differs from that in a paper published in 2017, in which Chaudhary and others used a noninvasive technique to read brain activity. Questions were raised about the work, and the paper was retracted, but Chaudhary stands by it.

These case studies suggest that the field is maturing rapidly, says Amy Orsborn, who researches BCIs in nonhuman primates at the University of Washington. "There's been a noticeable uptick in both the number of clinical studies and of the leaps that they're making in the clinical space," she says. "What comes along with that is the industrial interest."

LAB TO MARKET

Although such achievements have attracted a flurry of attention from the media and investors, the field remains a long way from improving day-to-day life for people who've lost the ability to move or speak. Currently study participants operate BCIs in brief, intensive sessions; nearly all must be physically wired to a bank of computers and supervised by a team of scientists working constantly to hone and recalibrate the decoders and associated software. "What I want," says Hochberg, speaking as a critical-care neurologist, "is a device that is available, that can be prescribed, that is 'off the shelf' and can be used quickly." In addition, such devices would ideally last users a lifetime.

Many leading academics are now collaborating with companies to develop marketable devices. Chaudhary, in contrast, has co-founded a not-for-profit company, ALS Voice, in Tübingen, to develop neurotechnologies for people in a completely locked-in state.

Blackrock Neurotech's existing devices have been a mainstay of clinical research for 18 years, and it wants to

market a BCI system within a year, according to chair Florian Solzbacher. The company came a step closer last November, when the U.S. Food and Drug Administration, which regulates medical devices, put the company's products onto a fast-track review process to facilitate developing them commercially.

This possible first product would use four implanted arrays and connect through wires to a miniaturized device, which Solzbacher hopes will show how people's lives can be improved. "We're not talking about a 5, 10 or 30 percent improvement in efficacy," he says. "People can do something they just couldn't before."

Blackrock Neurotech is also developing a fully implantable wireless BCI intended to be easier to use and to remove the need to have a port in the user's cranium. Neuralink and Paradromics have aimed to have these features from the outset in the devices they are developing.

These two companies are also aiming to boost signal bandwidth, which should improve device performance, by increasing the number of recorded neurons. Paradromics's interface—currently being tested in sheep—has 1,600 channels, divided between four modules.

Neuralink's system uses very fine, flexible electrodes, called threads, that are designed to both bend with the brain and to reduce immune reactions, says Shenoy, who is a consultant and adviser to the company. The goal is to make the device more durable and recordings more stable. Neuralink has not published any peer-reviewed papers, but a 2021 blogpost reported the successful implantation of threads in a monkey's brain to record at 1,024 sites. Academics would like to see the technology published for full scrutiny, and Neuralink has so far trialed its system only in animals. But, Ajiboye says, "if what they're claiming is true, it's a game changer."

Just one other company besides Blackrock Neurotech has implanted a BCI long term in humans—and it might prove an easier sell than other arrays. Synchron in New York City has developed a "stentrode"—a set of 16 electrodes fashioned around a blood vessel stent. Fitted in a day in an outpatient setting, this device is threaded through the jugular vein to a vein on top of the motor cortex. First implanted in a person with ALS in August 2019, the technology was put on a fast-track review path by the FDA a year later.

Akin to the electrodes Chang uses, the stentrode lacks the resolution of other implants, so it can't be used to control complex prosthetics. But it allows people who cannot move or speak to control a cursor on a computer tablet and so to text, surf the Internet and control connected technologies.

Synchron's co-founder, neurologist Thomas Oxley, says the company is now submitting the results of a four-person feasibility trial for publication, in which participants used the wireless device at home whenever they chose. "There's nothing sticking out of the body. And it's always working," Oxley says. The next step before applying for FDA approval, he says, is a larger-scale trial to assess whether the device meaningfully improves functionality and quality of life.

CHALLENGES AHEAD

Most researchers working on BCIs are realistic about the challenges before them. "If you take a step back, it is really more complicated than any other neurological device ever built," Shenoy says. "There's probably going to be some hard growing years to mature the technology even more."

Orsborn stresses that commercial devices will have to work without expert oversight for months or years—and that they need to function equally well in every user. She anticipates that advances in machine learning will address the first issue by providing recalibration steps for users to implement. But achieving consistent performance across users might present a greater challenge.

"Variability from person to person is the one where I don't think we know what the scope of the problem is," Orsborn says. In nonhuman primates, even small variations in electrode positioning can affect which circuits are tapped. She suspects there are also important idiosyncrasies in exactly how different individuals think and learn—and the ways in which users' brains have been affected by their various conditions.

Finally, there is widespread acknowledgment that ethical oversight must keep pace with this rapidly evolving technology. BCIs present multiple concerns, from privacy to personal autonomy. Ethicists emphasize that users must retain full control of the devices' outputs. And although current technologies cannot decode people's private thoughts, developers will have records of users' every communication and crucial data about their brain health. Moreover, BCIs present a new type of cybersecurity risk.

There is also a risk to participants that their devices might not be supported forever or that the companies that manufacture them fold. There are already instances in which users were let down when their implanted devices were left unsupported.

Degray, however, is eager to see BCIs reach more people. What he would like most from assistive technology is to be able to scratch his eyebrow, he says. "Everybody looks at me in the chair and they always say, 'Oh, that poor guy, he can't play golf any more.' That's bad. But the real terror is in the middle of the night when a spider walks across your face. That's the bad stuff."

For Johnson, it's about human connection and tactile feedback—a hug from a loved one. "If we can map the neurons that are responsible for that and somehow filter it into a prosthetic device some day in the future, then I will feel well satisfied with my efforts in these studies." **M**

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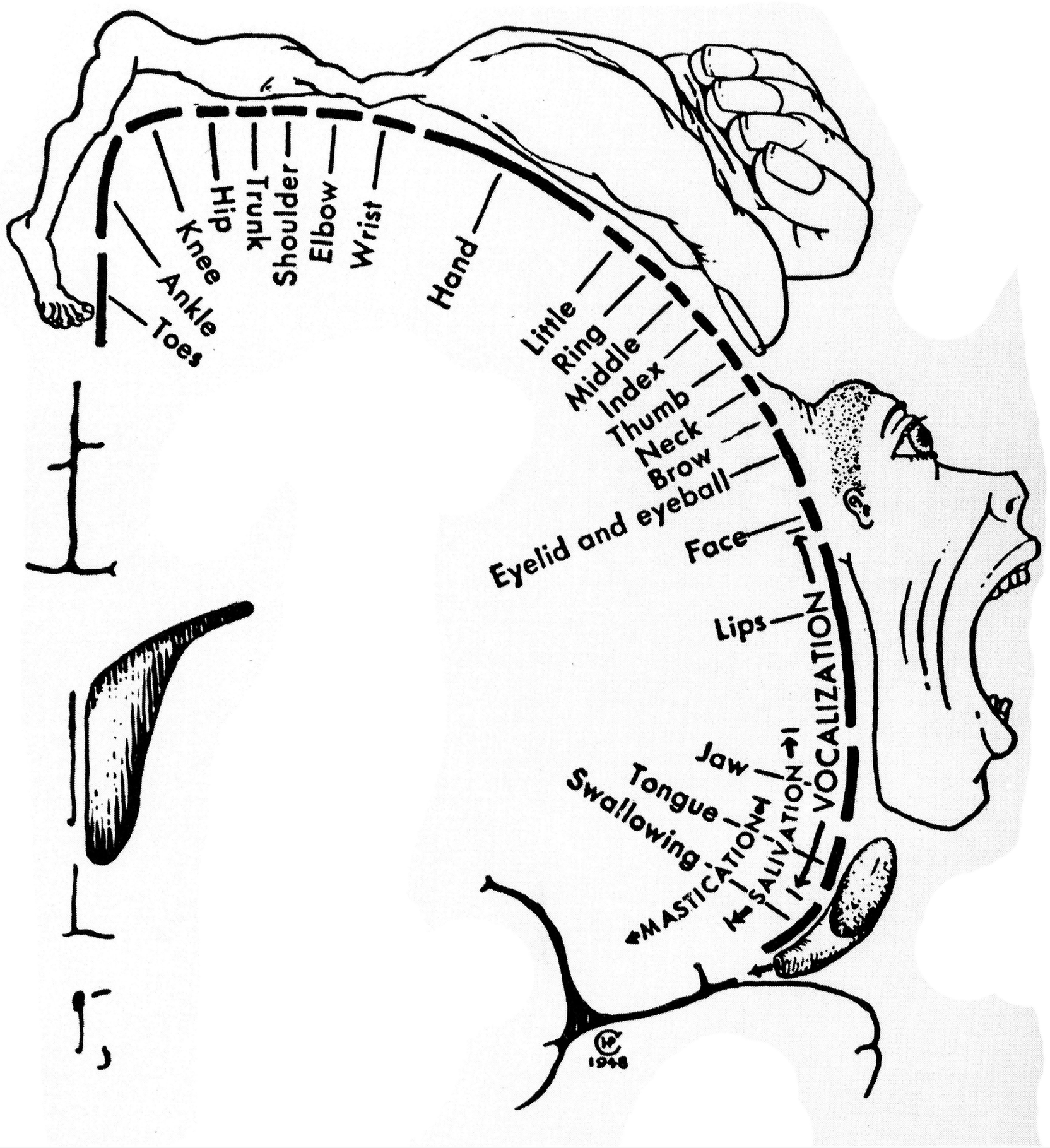
Where Are Genitals Represented in the Brain?

The homunculus of textbook fame still does not take into account the relevant locations in the cerebral cortex that process touch for the sex organs

By Dana G. Smith



Wilder Penfield's homunculus, published in 1950, shows areas of the cerebral cortex that process touch for different body parts. In some versions, the cortical area for the genitals is just below the one for the toes.

Interfoto/Alamy Stock Photo

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PARACELSUS, THE GERMAN-SWISS PHYSICIAN and alchemist, asserted in the 16th century that he knew how to create a "little man"—or homunculus—by placing human semen in a sealed vessel packed with horse manure that was then nurtured with blood to gestate. The recipe was no more useful than the ones for turning base metals into gold, but the term has survived through the centuries, making its way into literature (*Faust*), television (*Doctor Who*) and even video games (Castlevania: Dawn of Sorrow). Despite the stiff competition from popular culture, neuroscience textbooks have succeeded better than any other medium in defining the contemporary meaning of homunculus.

In 1950 neurosurgeon Wilder Penfield and a colleague published a depiction of a homunculus that wrapped around the somatosensory cortex and illustrated where the brain processed touch for specific body parts. The position of the head, shoulders, knees and toes in the cortex were laid out somatotopically, meaning they were presented in the same order in the brain as they appear on the body. Neurons for the face were positioned at the very outside edge of the postcentral gyrus—the ridge at the top of the brain where touch information is processed that runs from ear to ear like a set of headphones. The feet, meanwhile, were located at the midline, where the two hemispheres of the brain meet. (Sensory information from the left side of the body is processed in the right hemisphere, and vice versa.) The only exception in all this was the penis, which was buried underneath the toes, tucked on the inside wall of the gyrus. In terms of sex, the homunculus in this first rendition of a neural touch map was truly a "little man" because it ignored the physiological constituents for what can be labeled a "hermunculus."

The map's placement of the male genitals, shown as being literally underfoot, has puzzled neuroscientists for decades. With the advent of neuroimaging technology, several laboratories have used electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) to try to confirm—or refute—Penfield's map. But, somewhat amazingly, scientists are still without a firm answer as to how to draw a homunculus with the correct placement of male and female genitalia. Some relatively recent studies find the genitals in the same location Penfield did. Others pinpoint a different region, located higher up on the somatosensory cortex—a patch of cells that more appropriately lies between the areas designated for the hips and the knees.

"The Penfield location is a bit mysterious because it's a break in the continuum of the somatotopy of the body," says John-Dylan Haynes, director of the Berlin Center for Advanced Neuroimaging. "It's like a biological basic principle, and that is the exception. You look at the Penfield maps, and the penile representation is in the wrong place. Why is it there?"

The homunculus that we know today was developed based on electrical stimulation of different parts of the cortex in more than 400 people undergoing brain surgery for epilepsy or to remove a tumor. During surgery, for which people received just a local anesthetic, Penfield asked patients to describe the sensations they felt in their body in response to electrodes stimulating different parts of the brain. Based on these reports, Penfield employed medical artist Hortense Cantlie to draw a map of the somatosensory cortex with its corresponding body parts.

In contrast to Penfield's thoroughness with the rest of the body, only three patients described genital sensation with neural stimulation. In an article published in *Brain* in 1937 that first described the work that led to the development and refinement of the homunculus, Penfield wrote that the lack of responses from other patients may have been because of "a false sense of modesty."

Penfield also acknowledged that finding the penis underneath the foot in the somatosensory cortex was unusual, writing, "Presumably rectum and genitalia should be placed above feet..., but our evidence is not sufficient for conclusion and they seem to be somewhat posterior to feet."

Despite this mystery, Penfield's map of the somatosensory cortex was quickly adopted as the standard, so the genitals remained underneath the feet for decades. Studies conducted in the 1990s using EEG and the imaging technique magnetoencephalography (MEG) largely confirmed the positioning of the classic homunculus, placing the genitals on the inside wall of the postcentral gyrus. This time the scientists worked in the opposite direction, stimulating parts of the body to see what region of the brain lit up. The spatial resolution of the two encephalography technologies is notoriously imprecise, however, because the recordings are made through the scalp.

"EEG and MEG are not techniques that will tell you, 'Is it two centimeters higher or lower?' " Haynes says. "Ultimately we're talking about a few centimeters here, so they don't give you the spatial resolution."

It wasn't until 2005 that a study challenged Penfield's placement of the penis. Using fMRI to conduct the neuroimaging and a toothbrush to stimulate the penis, big toe and abdomen, the researchers found penile activity positioned in the cortex below the torso and above the foot. Since then, the handful of other fMRI studies that have been conducted have largely confirmed the new location.

Notably absent from this conversation were distinguishing features of female anatomy. Penfield's original homunculus did not include the vulva or breasts, and out of the more than 400 people involved, only nine of them were women.

"Penfield really didn't study very many women, and so the assumption has always been that what is the case for men will be the case for women," says Gillian Einstein, a psychology professor at the University of Toronto, who coined the term "hermunculus." "We really need to understand the somatosensory cortex of women in addition to all the men."

It wasn't until 1983 that scientists thought to look at vulval stimulation in the brain to see if it differed from the penis. Like the EEG studies in men, the genitals were estimated to be on the inside wall of the somatosensory cortex, underneath the feet. The first study using fMRI, however, found the region higher up, closer to the hips. The most recent paper, published earlier this year by Haynes and his colleagues in the *Journal of Neuroscience*, located the clitoris in the same area.

Thanks to this type of higher-resolution imaging technology, a consensus has started to form in the past decade that the male and female genitals are, in fact, located in the same relative area in the brain as they are in the body—between the torso and legs.

One dissent, though, comes from the work of psychologist Barry Komisaruk's lab at Rutgers University. In studies of women and of men—published in 2011 and 2020, respectively—Komisaruk saw activation both above and below the foot in the somatosensory cortex. His theory holds that the higher-up region represents the general area of the groin, whereas the genitals are tucked lower down. He thinks that the lack of specificity in the other studies is because of their use of either electric or vibratory stimulation of the genitals that could activate other sensory nerves in the area.

"I think the basis for the debate is not making a clear distinction between the stimulation that's applied and how specific it is to the genitals, as opposed to the rest of the pubic area," Komisaruk says. "Because the pubic area does indeed have a very different distribution on the surface of the cortex."

On the other side of the debate, Haynes says that the activation Komisaruk sees on the inside wall of the cortex is actually from the supplementary motor area (SMA), which is involved in planning movement. Participants in Komisaruk's two studies touched themselves instead of having a partner or automated device stimulate the region, as in the other research.

"I think the reason they see this … activity is simple: it's an artifact of people planning to move, planning their movements for the self-stimulation," Haynes says. "It's in exactly the spot where the SMA is."

Why do scientists care whether the genitals are located a few centimeters up or down? The answer is that the information could potentially be used therapeutically. In his latest paper, Haynes revealed that the thickness of the relevant area of the cortex correlated with how often the women in the study had sex in the past year, suggesting that neuroplasticity, a reorganization of neural connections, may occur in the area in response to experience. It is possible that harnessing that plasticity could be helpful in the healing of abused women. In future work, Haynes plans to investigate whether the representation of the vulva in the somatosensory cortex differs in women who have experienced sexual trauma.

To obtain that needed level of specificity, instead of assuming where the vulva is generally located in the cortex, researchers need to map each woman's brain individually because the precise location varies from person to person. That important detail, Einstein says, could explain the divergence between studies. "There are huge individual differences, depending on experience and exposure to different types of stimuli," she says. "I wouldn't rule out a slightly different region of localization in the brain for different people. I think the more people we study, the more variation we're going to find."

In other words, Penfield's original map may have been accurate for the three men he looked at who reported genital sensation. Or his methods might have led him down the wrong path. Recent studies using fMRI, MEG and even cortical electrostimulation (like Penfield's work) found variations in the somatosensory representations of other body parts, including the head and legs.

The key to finally pinning down the location of the genitals, as with everything in science, will be large sample sizes and repeated experiments with consistent methods. In the past 40 years, 17 studies using several different imaging and stimulation techniques have mapped the genitals of 264 people—an average of just 15 people per study. Small wonder that they disagree.

To settle the debate once and for all, researchers need to conduct a large, comprehensive investigation of people of different ages, sexes and sexual experiences that will compare activation in response to genital self-stimulation and stimulation by another person or device. Until that happens, the textbook homunculus—and the missing details for a hermunculus—will likely remain unchanged. **M**

Trial coordinator Eric McDade assesses participant Marty Reiswig for cognitive ability.

Matt Miller/Washington University School of Medicine

Treating Alzheimer's before It Takes Hold

Researchers are giving drugs to healthy people in hope of clearing away toxic proteins in the brain and preventing neurodegeneration

By Alison Abbott

Alison Abbott works for *Nature* magazine.

Every two weeks a nurse visits 43-year-old Marty Reiswig in Denver, Colo., and injects him with an experimental drug called gantenerumab. Every month Reiswig drives into town for a brain scan to make sure the drug has not caused any bleeds. And every year he flies to St. Louis, Mo., for four days of brain scans, spinal taps, blood analyses, and exhaustive tests of his memory and reasoning capacity.

Reiswig is fit and healthy and runs two local businesses. He goes through all of this because he has a rare genetic mutation that almost guarantees he will develop early-onset Alzheimer's disease. He hopes that the international clinical trial he has been part of for nine years might prevent, or at least delay, the onset of symptoms that will otherwise arise in just a few years' time.

"I always do my best to give the researchers as much as I can—even if it turns out not to help me, it might help my children," he says.

The trial is one of several trying to understand whether treating the root cause of Alzheimer's before symptoms start might be the best way to handle a disease that exacts such a large toll. The drugs under scrutiny are all antibodies that have been developed to target and clear amyloid-β proteins in the brain, which clog together into toxic masses called plaque. These drugs are of the same type as aducanumab, made by Biogen in Cambridge, Mass., which was provisionally approved last year by the U.S. Food and Drug Administration for the treatment of mild Alzheimer's, in large part because of its ability to remove amyloid-β.

And because such toxic proteins are a feature of several types of dementia, these antibody studies might also offer hints for how to treat the 55 million people around the world who have these conditions, says neurologist Paul Aisen of the University of Southern California, who is a leader of the U.S. Alzheimer's Clinical Trials Consortium. Most dementias hit after 65 years of age; all have proved to be stubbornly incurable. Of more than 100 trials around the world, most are aiming to treat symptoms of the disease rather than its root cause.

But Aisen foresees a future—maybe just a decade or so down the line—in which much of the burden of Alzheimer's might actually be prevented. "We're heading toward screening people from middle age on with blood tests and treating those who show amyloid abnormalities with drugs that reduce the generation of amyloid plaques," he says. "I am optimistic."

A lot needs to go right for this hopeful view to become reality. Large clinical trials will have to show that these therapies work, and amyloid-clearing drugs will have to be proven to be safe and affordable. After decades of setbacks and failed clinical trials, some dementia researchers prefer to express caution. "The field is taking tremendous risks by engaging in studies that can cost billions of dollars," says neurologist David Knopman of the Mayo Clinic in Rochester, Minn.

It will take a while for answers to emerge. Some trials of Alzheimer's disease prevention are just getting started, and some ongoing ones could stretch into the next decade.

GETTING IN EARLY

It was 1986 when Carol Jennings in Nottingham, England, wrote a letter to geneticist John Hardy asking whether she could be of use in his research. Just like Reiswig, Jennings had many relatives who succumbed to early-onset dementia. Hardy's team, now at University College London, was interested in the genetics of Alzheimer's and invited the Jennings family to donate blood to its project.

A few years later the team identified a mutation shared by the affected family members. It was in a gene that codes for a large protein that sits in the membranes of neurons, the amyloid precursor protein (APP).

APP in the brain is chopped into amyloid-β and other short chains of amyloid protein by a suite of enzymes. In healthy brains, these amyloid peptides might serve useful functions, but over time they can accumulate—perhaps because the brain's molecular system for clearing them loses efficiency—and clump together into plaques.

In someone with a mutation in the gene that codes for APP, the amyloid-β proteins are stickier or more profuse, and the disease manifests earlier than in people who do not have the mutation.

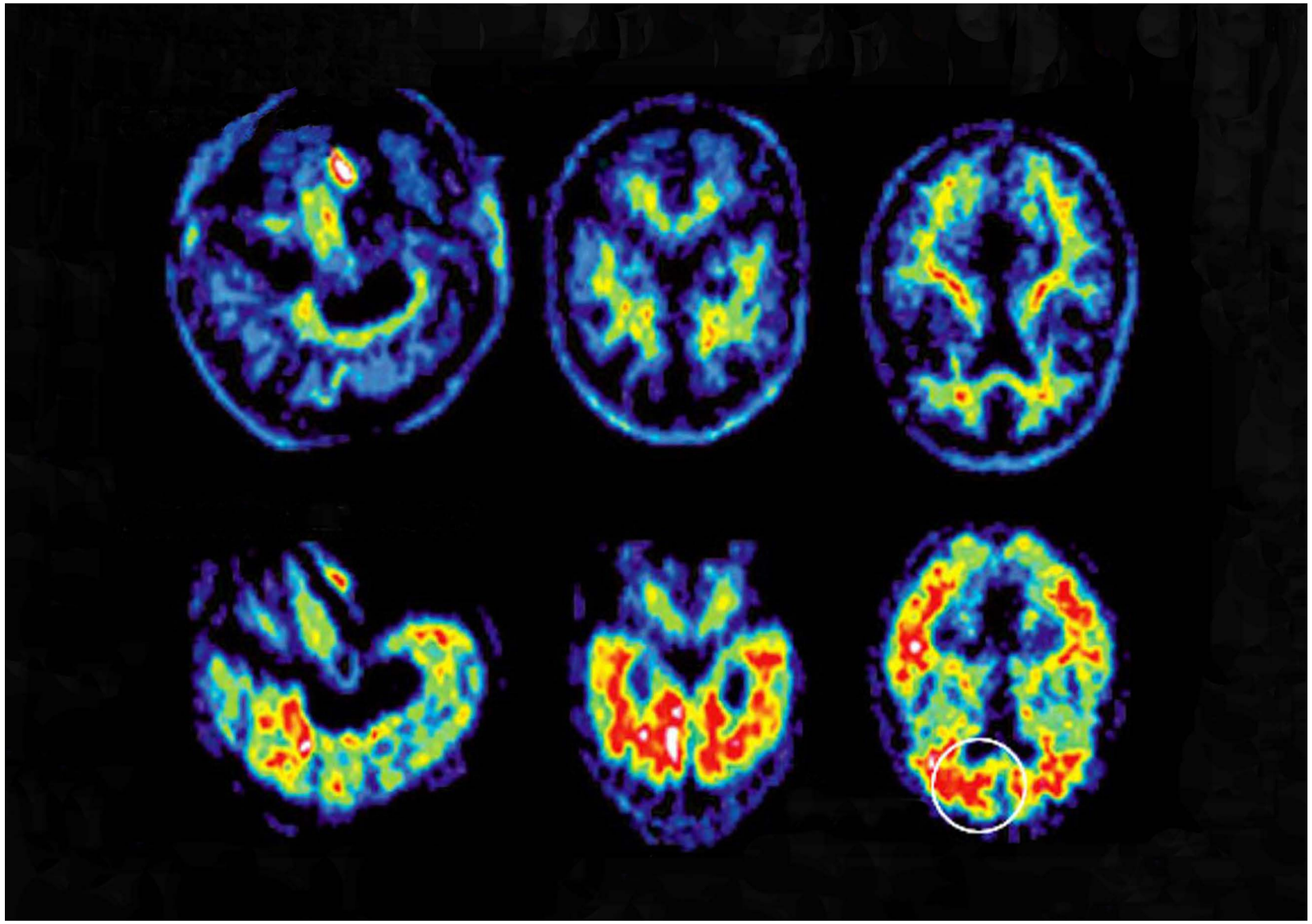
This is the basis of the amyloid hypothesis of Alzheimer's, first formulated by Hardy and his colleagues after their discovery of a disease-causing *APP* mutation. According to that theory, preventing the triggering event of amyloid-β accumulation might slow the disease process—or even stop it happening in the first place.

Pharmaceutical and biotechnology companies set about targeting the amyloid system, developing drugs to block the enzymes that cleave APP or creating antibodies to the amyloid-β peptides. But their drugs continuously bombed in clinical trials. Five phase III clinical trials of a drug that blocks an amyloid-chopping enzyme, β-secretase, were discontinued because of side effects that made cognition temporarily worse. Blockers of another enzyme, γ-secretase, went the same way. Time and time again, trials of antibodies designed to latch onto and bind to amyloid-β failed to improve people's clinical symptoms. At least one major pharmaceutical company, Pfizer, left the Alzheimer's field, in 2018.

The serial failures divided the research community into camps. One camp argued that if targeting amyloid hadn't worked, then the amyloid hypothesis must be wrong. Knopman accepts that APP processing is part of the disease initiation process but says that the role of amyloid-β has not been proved. "It's plausible, for example, that other APP cleavage products are more important to the disease process," he says.

The other camp argued that the trials had been poorly designed, in particular because they recruited people who had already begun to show early signs of Alzheimer's disease.

"The fact is that to optimize the potential impact of removing amyloid, you need to do so as early as possible," Aisen says. Amyloid-β accumulation begins its slow and silent campaign of destruction in the brain many years before its damage is extensive enough to cause symptoms, he says. "The total duration of Alzheimer's is over 25 years, and the trials were only engaging in the final decade when there is constant worsening of neurodegeneration."



PET (positron emission tomography) scans of the brain of a person with Alzheimer's show the buildup of amyloid plaques (*circled*) not present in healthy brains.

Science History Images/Alamy Stock Photo

Animal studies back up this insight. In mice that were genetically altered to overexpress *APP,* treating young animals with aducanumab before amyloid-β deposits were detectable resulted in significant reductions in deposits and fewer signs of disease in the brain six months later.

When the FDA made the controversial decision to approve Biogen's aducanumab in June last year, it was recognizing this long-term picture: that the drug's ability to remove amyloid-β made it likely that it could reduce Alzheimer's symptoms down the line. Biogen's large, placebo-controlled trials of aducanumab in people with mild Alzheimer's had not unambiguously improved their clin-

ical symptoms, but the drug did a good job of clearing amyloid plaques from their brains. The agency declared that aducanumab was the first treatment to affect the biological cause of the disease.

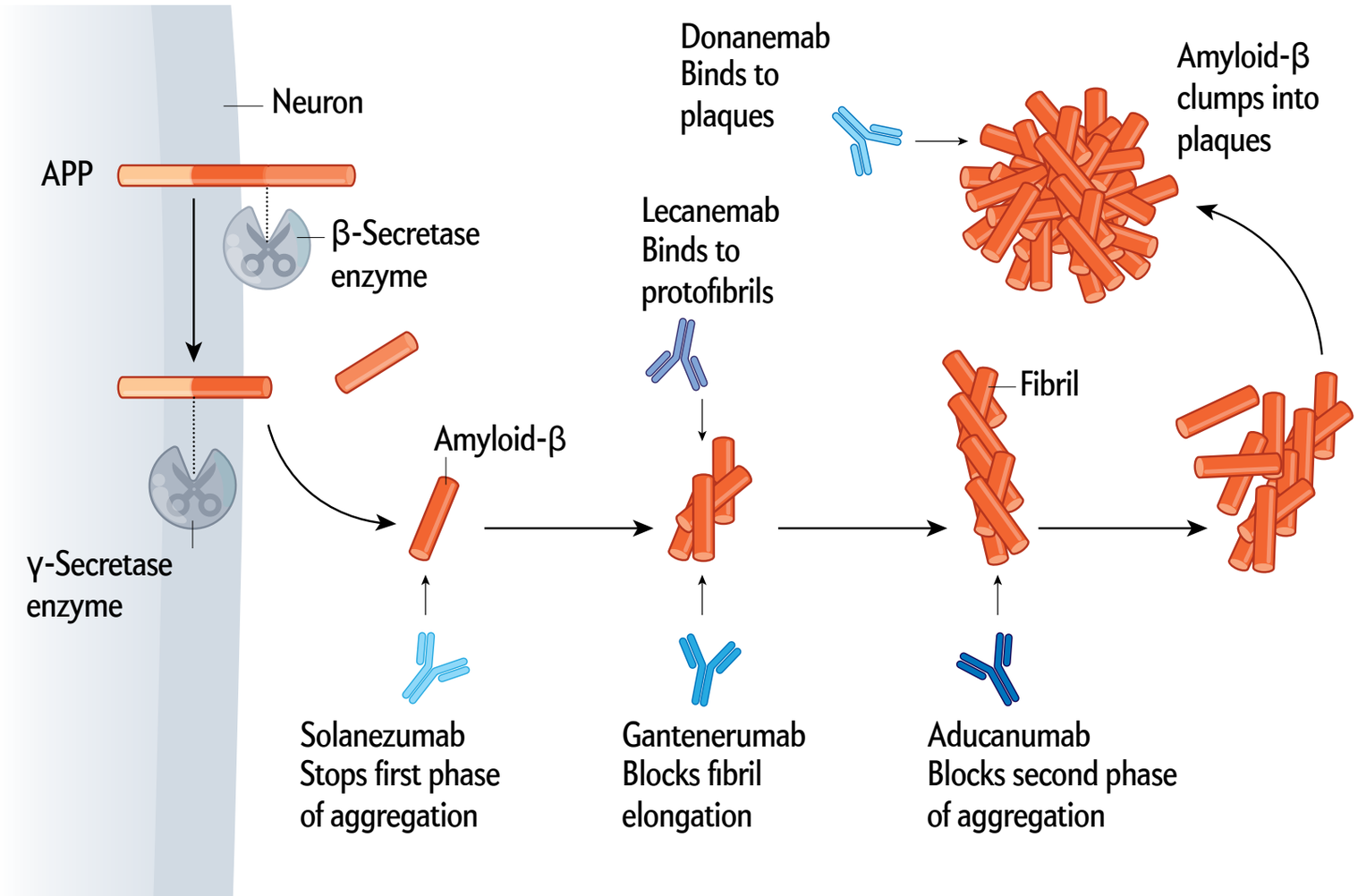
The decision enraged many researchers who claimed that the FDA had lowered its standards. (Knopman resigned from the FDA's advisory committee over this issue.) But in the following months, more data emerged from other trials of different drugs, showing trends toward a modest slowing of cognitive decline as amyloid-β was cleared, as well as reductions in other biomarkers of Alzheimer's progression, such as the buildup of a protein called tau. Later that year the agency put three further antibodies onto a fast-track review process: Genentech-Roche's gantenerumab, Biogen-Eisai's lecanemab and Eli Lilly's donanemab. Similarly to aducanumab, all three have been shown in early trials to clear plaques.

"These drugs are big, big game changers," says neuroscientist Bart de Strooper, director of the U.K. Dementia Research Institute at University College London. "They will allow the amyloid hypothesis to be tested definitively."

Many researchers agree that the best test of the hypothesis—and the best way to stop the disease in its tracks—is to give people these drugs early, without waiting for Alzheimer's symptoms to set in first.

Antibodies against Amyloid

Several clinical trials are testing whether drugs called monoclonal antibodies can stem the symptoms of Alzheimer's by preventing the toxic clumping of amyloid-β proteins. This process starts when enzymes cleave the amyloid precursor protein (APP). Amyloid-β proteins elongate into fibrils and then nucleate into plaques. All of the drugs bind to amyloid-β, but their primary targets in the process are different.

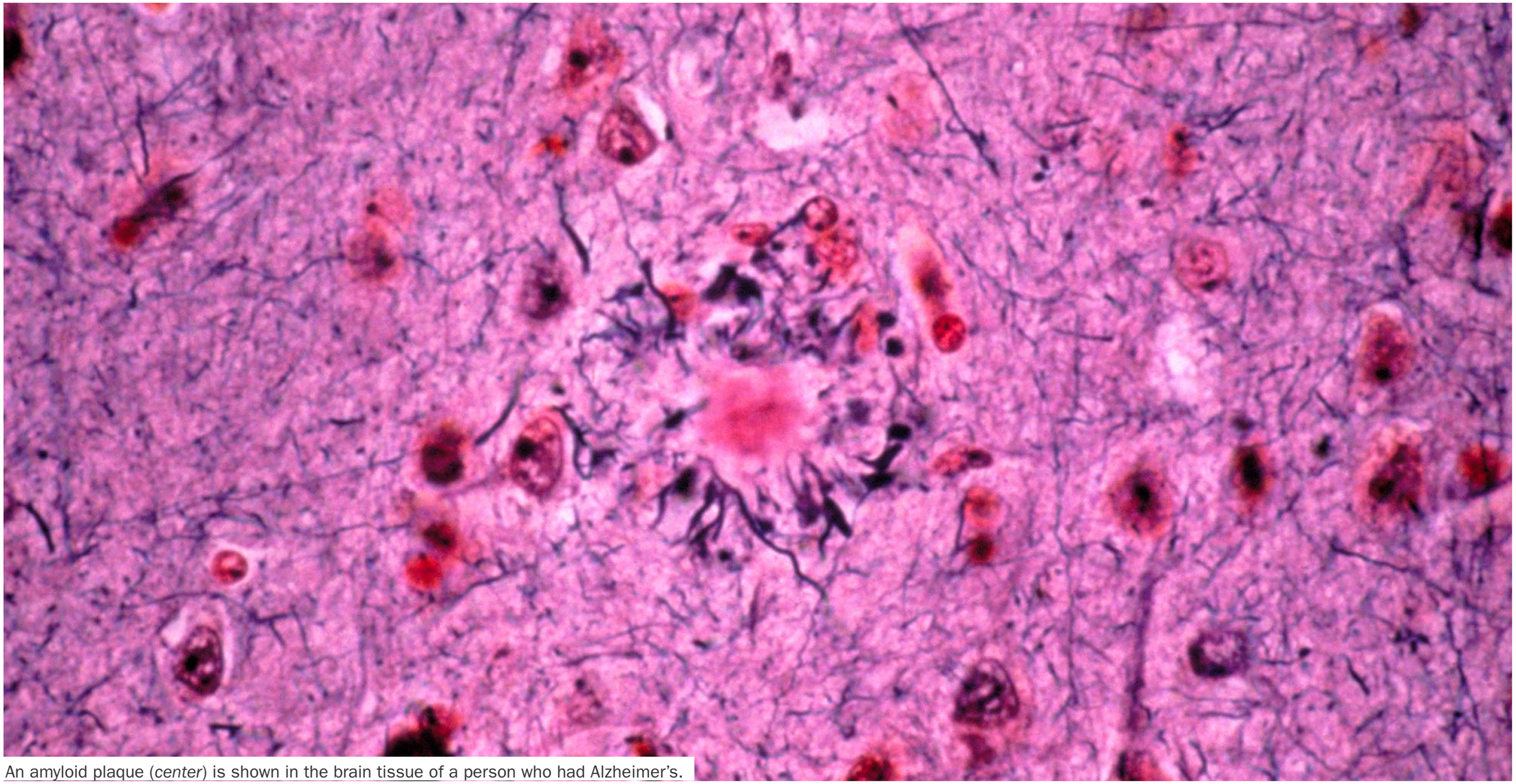


Nik Spencer/Nature

TIMING IS EVERYTHING

According to Hardy, designers of even the earliest trials might have realized that they were recruiting too late in the disease. "Through the retrospectoscope, it was clear—the data were already there," he says. In the 1980s pathologist George Glenner of the University of California, San Diego, and his colleagues discovered that individuals with Down syndrome developed dementia relatively young. They suggested that this was because people with Down syndrome have an extra chromosome 21 (where the *APP* gene sits). Their postmortem studies showed that plaques developed many years before cognitive symptoms did.

The field is not ignoring the importance of finding treatments for symptomatic Alzheimer's, Aisen says. But clinical researchers are now turning more attention to drug trials for the treatment of presymptomatic Alzheimer's. It is not easy to find participants for such trials, however. People need to be symptomless but highly likely to begin developing symptoms on a measurable timescale. There are two approaches to identifying these individuals: find people like Reiswig with a rare genetic predisposition or people in the general population with a



An amyloid plaque (*center*) is shown in the brain tissue of a person who had Alzheimer's.

high risk of developing Alzheimer's because of the presence of amyloid-β in their brains.

To identify the rare genetic cases, the U.S. National Institute on Aging (NIA) funded the launch of the Dominantly Inherited Alzheimer Network (DIAN) in 2008. It now includes more than 600 people from 20 countries, representing around 300 families who have mutations in one of the three genes associated with early-onset Alzheimer's. Each family member has a 50 percent chance of inheriting a mutation.

The network quickly gathered more funding and research partners and began enrolling families, including Reiswig's, into an observational program. The researchers conducted positron emission tomography (PET) scans of the brain to check for amyloid-β and other biomarkers of Alzheimer's at regular intervals and then compared family members who carried the gene with those who did not. They also noted when symptoms tended to begin in each family. The network's 2018 report confirmed that the first signs of amyloid abnormalities can occur up to 25 years before symptoms start.

The DIAN consortium began a seven-year trial of amyloid-binding antibodies in 2012. It aimed to delay the progress of disease in people who have no cognitive symptoms but who have started to develop the primary markers of Alzheimer's—amyloid plaques—in their brains. The trial recruited 194 participants at various stages of their condition and divided them into groups to receive either one of two antibodies, gantenerumab or solanezumab, or a placebo.

Martin M. Rotker/SPL

But the results of the trial, announced in 2020, were disappointing. The trial failed to prove that the drugs could slow cognitive decline—although there was little decline in treated presymptomatic participants, there was also little decline in the placebo group. "That meant that we were simply unable to say whether the drugs would eventually help an asymptomatic population or not," says Randall Bateman of the Washington University School of Medicine in St. Louis, who leads the DIAN Trials Unit that conducted the study.

Still, one of the antibodies, gantenerumab, had a notable impact on the biological markers of the disease. It not only reduced amyloid plaques but also reduced levels of tau protein and of another marker of neurodegeneration, a neuronal protein that shows up in the blood.

These results encouraged Bateman and the DIAN consortium to continue studying gantenerumab for a further three years, dropping the solanezumab and placebo arms but allowing participants in those groups to convert to gantenerumab and letting them know what drug they were taking.

That presented Reiswig with a dilemma. When he was originally tested for the gene mutation, he had chosen not to be informed of the result. But the extension of the study was only available to mutation carriers, so a request to participate would automatically reveal his genetic status. "I decided it was time for me to know, but I planned things carefully," he says. He retreated to a holiday rental in Colorado with his wife to receive the phone call from his genetic counselor. "I didn't want to find out in my own house—that was at least something I wanted to have control over." Reiswig wept when he learned that he carried the mutation and decided that his only chance was to continue with the trial.

Last year the consortium decided to try treating people with no cognitive symptoms and no plaques in their brains. "It's really going to be the ultimate trial of Alzheimer's prevention," Bateman says. In the next few months the team plans to begin recruiting 160 mutation carriers, some as young as 18, who are not expected to develop symptoms for another 11 to 25 years. The placebo-controlled trial will run for four years, monitoring people's amyloid status at regular intervals. Then it will move into an open-label study for a further few years: the placebo arm will be dropped, and all the participants will receive the trial drug. At that point, it will also measure other biomarkers of disease progression.

"We're heading toward screening people from middle age on with blood tests and treating those who show amyloid abnormalities with drugs that reduce the generation of amyloid plaques. I am optimistic."

—Paul Aisen

It would be impractical to run the trial for the decades it might take for participants to develop symptoms, says Eric McDade, the trial's principal investigator at Washington University in St. Louis. Instead the team will monitor changes in biomarkers, such as amyloid-β and tau, that are now known to predict symptom onset during the long silent period of the disease. "The more of these other biomarkers that we can alter, the higher the probability that we can offset or at least significantly delay onset." The researchers will continue to monitor as many participants as possible after the trial's second phase, he says.

Outside the DIAN consortium, other trials for early-onset Alzheimer's are underway, testing drugs in people who already have some amyloid buildup. Genentech-Roche is studying individuals from a large family in Colombia, half of whom carry a pathological mutation in a gene that encodes part of one of the amyloid-chopping secretase enzymes. Its trial of the drug crenezumab will finish this year. Studies are also gearing up to test Alzheimer's drugs in people with Down syndrome.

STOPPING SYMPTOMS

The second approach to preventive trials is to identify those in the general population who are at high risk of developing late-onset Alzheimer's. The international Alzheimer's Disease Neuroimaging Initiative, a public–private partnership headquartered at the University of California, San Francisco, tracks Alzheimer's biomarkers in many hundreds of people through normal aging and all stages of the disease. Its data show that around one third of cognitively normal people older than 65 have amyloid plaques in their brains and that more than 85 percent of them will go on to develop symptoms of Alzheimer's within 10 years.

On this basis, three large, placebo-controlled clinical trials are underway, each recruiting more than 1,000 people who are cognitively fit but have brain plaques, as seen by PET scanning. Each trial is testing a different antibody. All three will run for four years, by which time cognitive decline is usually measurable after plaques begin to accumulate.

Aisen's institute is coordinating the A4 trial—Anti-Amyloid treatment in Asymptomatic Alzheimer's—which is testing the Lilly drug solanezumab. Results are expected next year. Aisen also co-leads the AHEAD 3-45 trial, which began in 2020 and is testing lecanemab. That same

year Lilly started a trial called-Alz 2 with donanemab. And this year Roche is launching its own phase III trial with gantenerumab, which will run for six years.

The costs of such trials "is typically hundreds of millions of dollars," Aisen says. Just recruiting the 1,169 participants in the A4 trial required around 4,500 PET scans, each costing an average of $7,000. "But costs to society of this disease in terms of suffering, mortality and economic impact justify enormous investments in effective treatment," he says.

In recent years there has been substantial progress in developing simpler, blood-based biomarkers of Alzheimer's disease. Two of these prevention trials are using such biomarkers to help select people for PET screening, chipping away at the cost of PET scans and the inconvenience for participants. One biomarker measures the ratio of two slightly different forms of amyloid-β, and another measures a tau-related molecule.

So far the preventive trials all use antibodies against amyloid-β. These drugs have two disadvantages. They can have side effects: small brain bleeds or swellings, which are mostly harmless but which can be serious. And they are expensive. Biogen initially fixed its price of a year's treatment with aducanumab at $56,000, although it halved it in December 2021.

But the field is thinking about revisiting simpler, small-molecule drugs, which would be much cheaper to produce than antibody-based therapies. Some companies are starting to consider revisiting the secretase enzymes, Aisen says, perhaps tweaking the structure of the enzyme-blocking molecules that failed in early trials or finding better ways to administer them.

COMPLEX CAUSES

Researchers in the field are aware that addressing dementia also requires an effort beyond amyloid-β. "Alzheimer's disease is more complex," says neurobiologist Roger Nitsch, one of the original developers of aducanumab at the University of Zurich. "Amyloid is a very slow-burning neurotoxin that initiates the disease, but brain cells—including those connecting to blood vessels and cells of the immune system—fight back." There will be more ways to target established disease, he says. Also, only around two thirds of all dementias are of the Alzheimer's type, and postmortem studies show that half of these have mixed pathology—the brains contain other toxic proteins in addition to amyloid and tau or signs of blood vessel damage.

Prevention trials are important and promising, says NIA director Richard Hodes, "but we are not giving up on people who already have disease." Because there will probably be multiple contributors to dementia—even in the same individual—a range of treatments will be needed, he says. The NIA is funding 72 clinical trials for dementia, trialing drugs aimed at various targets. Some, for example, aim to lower blood pressure to reduce the risk of small blood vessels breaking in the brain; others target tau. Only 20 target amyloid. The NIA is also supporting at least 120 trials to study the impact of nonpharmacological interventions, such as cognitive training, exercise and diet.

Researchers estimate that in 2021 a total of at least 126 different agents—including those in NIA studies—were being investigated in clinical trials around the world.

As a volunteer, Reiswig has had to accept the special burden that his particular trial brings—not just the time commitment but also the constant reminders of the fate that awaits him if the trial drug doesn't work. It helps, he says, that the DIAN consortium brings participants from all over the world together once a year to share their experiences. "We've created a wonderful community, and we know we contribute strongly to science." **M**

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Darwin Was Wrong: Your Facial Expressions Do Not Reveal Your Emotions

The emotion AI industry, courts and child educators are unknowingly relying on a misunderstanding of Darwin's ideas

Cavan Images/Getty Images

Do your facial movements broadcast your emotions to other people? If you think the answer is yes, think again. This question is under contentious debate. Some experts maintain that people around the world make specific, recognizable faces that express certain emotions, such as smiling in happiness, scowling in anger and gasping with widened eyes in fear. They point to hundreds of studies that appear to demonstrate that smiles, frowns, and so on are universal facial expressions of emotion. They also often cite Charles Darwin's 1872 book *The Expression of the Emotions in Man and Animals* to support the claim that universal expressions evolved by natural selection.

Other scientists point to a mountain of counterevidence showing that facial movements during emotions vary too widely to be universal beacons of emotional meaning. People may smile in hatred when plotting their enemy's downfall and scowl in delight when they hear a bad pun. In Melanesian culture, a wide-eyed gasping face is a symbol of aggression, not fear. These experts say the alleged universal expressions just represent cultural stereotypes. To be clear, both sides in the debate acknowledge that facial movements vary for a given emotion; the disagreement is about whether there is enough uniformity to detect what someone is feeling.

This debate is not just academic; the outcome has serious consequences. Today you can be turned down for a job because a so-called emotion-reading system watching you on camera applied artificial intelligence to evaluate your facial movements unfavorably during an interview. In a U.S. court of law, a judge or jury may sometimes hand down a harsher sentence, even death, if they think a defendant's face showed a lack of remorse. Children in preschools across the country are taught to recognize smiles as happiness, scowls as anger and other expressive stereotypes from books, games and posters of disembodied faces. And for children on the autism spectrum, some of whom have difficulty perceiving emotion in others, these teachings do not translate to better communication.

So who is right? The answer involves an unwitting physician, a scientific error and a century-long misinterpretation of Darwin's writing. Ironically, his own observations offer a powerful resolution that is transforming the modern understanding of emotion.

The assumption of universal facial expressions can be traced back to several sources, most notably a set of photographs by 19th-century French physician Guillaume-Benjamin-Amand Duchenne. In the early days of photography, Duchenne electrically stimulated people's facial muscles and photographed the contractions.

His photographs inspired Darwin to propose in *Expression* that certain facial movements were universal signs of emotion. In happiness, Darwin wrote, people smile. In sadness, they frown. The way the story is usually told, Darwin discovered that emotions have innate, biologically based expressions that are made and recognized universally and shared with other animals. That story presents facial movements as a sort of signaling system in which you can look at a person's face, detect their emotional state and receive important information to keep you—and them—alive and healthy.

Or so it would seem. A preponderance of evidence shows that Darwin was wrong, and his mistake was a doozy. In real life, people express a given emotion with tremendous variability. In anger, for example, people in urban cultures scowl (or make some of the facial movements for a scowl) only about 35 percent of the time, according to meta-analyses of studies measuring facial movement during emotion. Scowls are also not specific to anger, because people scowl for other reasons, such as when they are concentrating or when they have gas. The same tremendous variation occurs for every emotion studied—and for every other measure that purportedly tells us about someone's emotional state, whether it's their physiology, voice or brain activity.

Emotion AI systems, therefore, do not detect emotions. They detect physical signals, such as facial muscle movements, not the psychological meaning of those signals. The conflation of movement and meaning is deeply embedded in Western culture and in science. An example is a recent high-profile study that applied machine learning to more than six million Internet videos of faces. The human raters, who trained the AI system, were asked to label facial movements in the videos, but the only labels they were given to use were emotion words, such as "angry," rather than physical descriptions, such as "scowling." Moreover, there was no objective way to confirm what, if anything, the anonymous people in the videos were feeling in those moments.

There's also considerable evidence that facial movements are just one signal of many in a much larger array of contextual information that our brain takes in. Show people a grimacing face in isolation, and they may perceive pain or frustration. But show the identical face on a runner crossing the finish line of a race, and the same grimace conveys triumph. The face is often a weaker signal of a person's internal state than other signals in the array.

Darwin's *Expression* suggests that instances of a particular emotion, such as anger, share a distinct, immutable, physical cause or state—an essence—that makes the instances similar even if they have superficial differences. Scientists have proposed a variety of essences, some of which are

easily seen, such as facial movements, and others, such as complex, intertwined patterns of heart rate, breathing and body temperature, that are observed only with specialized instruments. This belief in essences, called essentialism, is compellingly intuitive. It's also pernicious because it is virtually impossible to prove that an essence doesn't exist. People who believe in essences but fail to observe them despite repeated attempts often continue to believe in them anyway. Researchers, in particular, tend to justify their belief by suggesting that tools and methods are not yet sufficient to locate the essences they seek.

A solution to this conundrum can be found in Darwin's more famous book *On the Origin of Species,* written 13 years before *Expression*. Ironically, it is celebrated for helping biology "escape the paralyzing grip of essentialism," according to heralded biologist Ernst Mayr. Before *Origin* was published, scholars believed that each biological species had an ideal form, created by God, with defining properties—essences—that distinguished it from all other species. Think of this as the "dog show" version of biology. In a dog show, each competitor is judged against a hypothetical ideal dog. Deviation from the ideal is considered error. Darwin's *Origin* proposed, radically, that a species is a vast population of varied individuals with no essence at its core. The ideal dog doesn't exist—it is a statistical summary of many diverse dogs. Variation is not error; it is a necessary ingredient for natural selection by the environment. When it came to emotions, however, Darwin fell prey to essentialism, ignoring his most important discovery.

Darwin's *Expression* suggests that instances of a particular emotion, such as anger, share a distinct, immutable, physical cause or state—an essence—that makes the instances similar even if they have superficial differences.

The power of essentialism led Darwin to some beautifully ridiculous ideas about emotion, including that emotional imbalance can cause frizzy hair and that insects express fear and anger by frantically rubbing their body parts together.

Essentialism likewise appears to lure designers of emotion AI systems to follow Darwin down this comfortable path, with its assumption that emotions evolved via natural selection to serve important functions. But if you actually read *Expression*, you'll find that Darwin barely mentioned natural selection. He also did not write that facial expressions are functional products of evolution.

In fact, he wrote the opposite: that smiles, frowns, eye widening and other physical expressions were "purposeless"—vestigial movements that no longer serve a function. He made this statement more than 10 times in *Expression*. For Darwin, emotional expressions were compelling evidence that humans are animals and that we've evolved. By his logic, if we share expressions with other animals, but the expressions are functionally useless for us, they must have come from a long-gone, common ancestor for whom the expressions were useful.

Expression has been cited incorrectly for more than 100 years. How did this happen? I discovered the answer lurking in the work of an early-20th-century psychologist, Floyd Allport. In his 1924 book *Social Psychology*, Allport made a sweeping inference from Darwin's writing to say that expressions begin as vestigial in newborns but quickly assume useful social functions. He wrote, "Instead of the biologically useful reaction being present in the ancestor and the expressive vestige in the descendant, we regard both these functions as present in the descendant, the former serving as a basis from which the latter develops."

Allport's idea, though incorrect, was attributed back to Darwin and eagerly adopted by like-minded scientists. They could now write about facial expressions as universal and claim to be the heirs of the unassailable Charles Darwin. With a single sentence, Allport misdirected the Western understanding of emotions, not only in science but in law, medicine, the eyes of the public and now emotion AI systems.

Nevertheless, this scientific tale has a happy ending because there is a name for the kind of variation we observe in real-life instances of emotion. It's the same variation that Darwin himself observed in animal species. In *Origin,* Darwin described an animal species as a collection of varied individuals with no biological essence at its core. This key observation became known more

generally as population thinking, and it's supported by the modern study of genetics.

Population thinking has been revolutionizing biology for the past century, and it is now revolutionizing the science of emotion. Like a species, a given emotion such as fear, grief or elation is a vast population of varied instances. People may indeed widen their eyes and gasp in fear, but they may also scowl in fear, cry in fear, laugh in the face of fear and, in some cultures, even fall asleep in fear. There is no essence. Variation is the norm, and it is intimately linked to a person's physiology and situation, just as variation in a species is linked to the environment its members live in.

An increasing number of emotion researchers are taking population thinking more seriously and moving beyond the essentialist ideas of the past. It is time for emotion AI proponents and the companies that make and market these products to cut the hype and acknowledge that facial muscle movements do not map universally to specific emotions. The evidence is clear that the same emotion can accompany different facial movements and that the same facial movements can have different (or no) emotional meaning. Variety, not uniformity, is the rule.

Darwin's *Expression* is best viewed as a historical text, not a definitive scientific guide. That leads to a deeper lesson here: Science is not truth by authority. Science is the quantification of doubt by repeated observation in varied contexts. Even the most exceptional scientists can be wrong. Fortunately, mistakes are part of the scientific process. They are opportunities for discovery.

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The Dark Side of Collaboration

People working together often scheme to put profits ahead of telling the truth. New research points to ways to stop this behavior

H. Armstrong Roberts/Classic Stock/Getty Images

Between 2008 and 2015, groups of engineers at Volkswagen repeatedly faked car-engine emissions levels during laboratory tests. Engineers manipulated the vehicles to release pollutants at low levels in the lab so they could meet emissions standards in the U.S. and Europe. But when the cars hit the road, their emissions rates were much higher than allowable standards—up to 40 times higher in the U.S. The scam, dubbed "Dieselgate" in the press, had severe consequences. The additional pollution in the U.S. alone could contribute to dozens of premature deaths.

Dieselgate is just one example of what researchers call "collaborative dishonesty." Often discussion of collaboration emphasizes its many advantages; group work improves social bonds and helps people solve complex problems they could not address alone. But other situations exist in which group work can become fertile ground for dishonest behavior, as it did in the Volkswagen scandal.

My colleagues and I pooled together data from many past studies to understand the forces that shape and underlie group dishonesty. Our work uncovered that unethical behavior is common in collaboration, but there are limits to the amount of lying that occurs—a finding that may help teams avoid falling into problematic behavior in the future.

We analyzed 34 relevant research articles by psychologists, economists and management researchers that involved more than 10,000 participants altogether. In these experiments, scientists asked people to play economic games or carry out decision-making tasks while part of a team. The specific instructions varied from one study to the next, but across experiments, participants could gain money through honesty and teamwork. In addition, they had opportunities to earn some additional money as a group by lying. For example, in some tasks, teams might receive a payout based on the number of puzzles they solved together; participants could lie and inflate the quantity they had deciphered for a greater monetary reward.

Across all studies and tasks, we found that groups tended to lie. On average, they earned 35.6 percent of the extra profits available to them above what they could make from simply telling the truth. The good news is that there was a limit to this deceit, which suggests people care about moral considerations to some extent. After all, groups did not, on average, earn 100 percent of the extra profits they could have made from their lies. In puzzle tasks, for instance, most teams did not simply pretend to solve every puzzle presented.

Past research suggests that women are penalized more than men for assertive and profit-maximizing behavior in general—for example, when they ask for a higher salary in a job interview. It is possible that this difference is one driver behind women's higher levels of honesty both when working alone and in teams.

Moreover, when studies added ethical costs for dishonesty, such as informing people that lies would harm other participants or have negative consequences for a charity donation, groups lied less. On top of that, we discovered that when it comes to collaborative dishonesty, the gender and age of the group members mattered. The more women that a group had and the older the group members were, the less the group lied. Past research suggests that women are penalized more than men for assertive and profit-maximizing behavior in general—for example, when they ask for a higher salary in a job interview. It is possible that this difference is one driver behind women's higher levels of honesty both when working alone and in teams. This idea is speculative, however, and we'd need further investigation to know for sure.

We also ran an additional analysis that allowed us to study how collaborative dishonesty may escalate and spread over time. More specifically, several studies we analyzed involved asking pairs to roll dice over multiple rounds. One person rolled a die in private and then reported the outcome. Their partner learned about that report and then rolled an independent die before reporting that outcome as well. If both teammates claimed to roll the same number, they received a payout: for example, a 1-1 double might mean each person got $1, a 2-2 double could mean $2 each, and so on. Pairs could choose to be honest and receive payment only when they truly rolled doubles. But over the course of many rounds, some pairs would be tempted to falsely declare a higher or matching roll for greater or more frequent payouts.

For these studies, we first identified whether any participants were obviously deceitful. When the data suggested that certain individuals reported only 6's—the highest roll possible—or only doubles in all rounds of the task, we identified these improbably lucky rollers as "brazen liars." (Given that the chance of honestly reporting 6's or doubles in 20 rounds, the most common number of rounds in the task, is very small—less than 0.001 percent—we felt confident about this classification.)

Then we examined the chances that a brazen liar's behavior might influence their partner. The

data were clear: dishonesty is contagious. Participants were more likely to be brazen liars when their partners were, too. Collaborative dishonesty also escalated over time. In later rounds, compared with earlier ones, the first person to roll a die was more likely to report higher die rolls, and their partner was more likely to report a double.

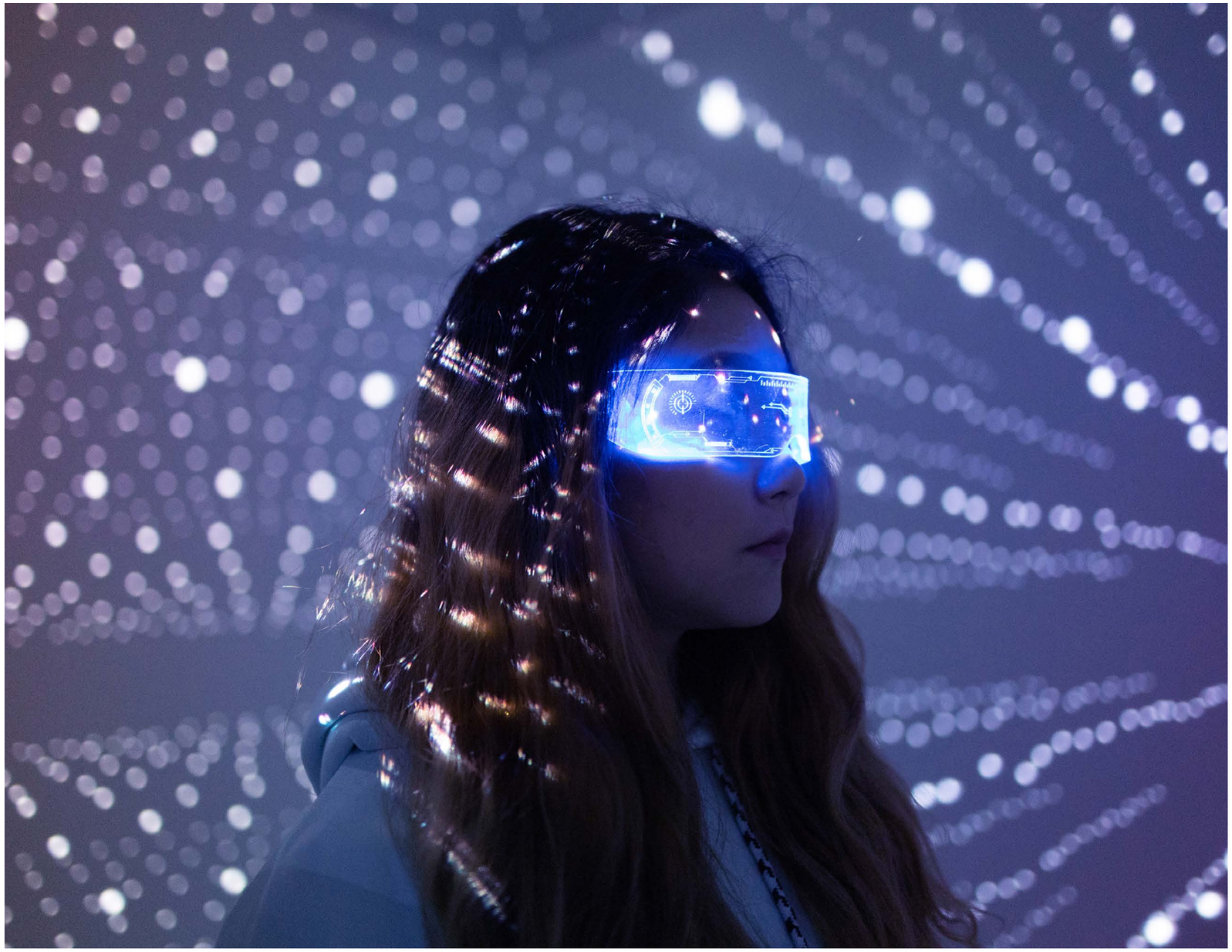
Collaborative dishonesty is clearly a hazard of group work. But our findings point to specific ways people could encourage honesty when groups work together. For instance, our discovery that collaborative dishonesty is contagious and escalates over time suggests that people should detect and act on early signs of dishonesty in groups. Several strategies could help. Managers can implement zero-tolerance policies toward even small acts of deceit to deter its escalation and spread. To increase early detection of dishonesty, they can put policies in place that forgive whistleblowers for their part in wrongdoing when they come forward about dishonest deeds. Finally, just as some managers ask their employees to report mistakes as soon as they occur to avoid larger downstream effects, a similar approach can be adopted when it comes to untruthful behavior. Catching collaborative dishonesty before it spreads could better nip it in the bud.

Knowing that groups are more honest when others are harmed by their lies suggests that we should highlight the negative consequences of collaborative dishonesty more prominently. In the case of Dieselgate, perhaps reminders of how excess pollution wreaks damage on society could have curbed the Volkswagen engineers' willingness to manipulate vehicle engines in the first place.

Rizwan Virk is a computer scientist and video game pioneer, founder of Play Labs @ MIT and author of *The Simulation Hypothesis: An MIT Computer Scientist Shows Why AI, Quantum Physics and Eastern Mystics Agree We Are in a Video Game* and *The Simulated Multiverse*. He is currently at Arizona State University's College of Global Futures. Follow him on Twitter @rizstanford and on the Web at zenentrepreneur.com

The Metaverse Is Coming: We May Already Be in It

As in the world of *The Matrix*, we may not be able to tell what's real and what's not



Qi Yang/Getty Images

A few years ago, while doing research for a virtual-reality (VR) program at the Massachusetts Institute of Technology that I would be running, I donned a VR headset and played a Ping-Pong game. The game was so realistic that it momentarily fooled my brain. When it ended, I instinctively tried to put the paddle down on the "table" and lean against it. Of course, the table didn't exist, and I almost fell over. It was so easy to trick my senses into thinking that the virtual world was real that I began to think about what would happen to humanity if we kept developing this technology.

In 2019 I wrote a book called *The Simulation Hypothesis,* in which I laid out the 10 stages of technology development that would take us to the Simulation Point, where we won't be able to distinguish our virtual worlds from the physical world or AI characters that live in those virtual worlds from real humans. I came to the conclusion that if our civilization could reach this point, then some advanced civilization elsewhere in the real universe had probably already done so and that we are already inside one of their *Matrix*-like virtual worlds.

It turns out that some giants of Silicon Valley have set their sights on building these ultrarealistic simulations, which they call the metaverse. First coined by science-fiction writer Neal Stephenson

in 1992, the metaverse is a set of interconnected virtual worlds that can be used for everything from entertainment to commerce to labor. The metaverse is being called the next generation of the Internet, which we will explore not with a Web browser but via three-dimensional avatars like those in video games such as Fortnite or Roblox.

The metaverse has moved beyond science fiction to become a "technosocial imaginary," a collective vision of the future held by those with the power to turn that vision into reality. Facebook recently changed its name to Meta and committed $10 billion to build out metaverse-related technology. Microsoft just announced that it was spending a record-breaking $69 billion to buy Activision Blizzard, the makers of some of the most popular massively multiplayer online games in the world, including *World of Warcraft*.

This current vision of the metaverse goes well beyond the simple VR of my Ping-Pong game to eventually include augmented reality (or AR, where smart glasses project objects onto the physical world), portable digital goods and currency in the form of nonfungible tokens (NFTs) and cryptocurrency, realistic AI characters that can pass the Turing test, and brain-computer interface (BCI) technology. BCIs will eventually allow us to not only control our avatars via brain waves but, eventually, to beam signals from the metaverse directly into our brains, further muddying the waters of what is real and what is virtual.

I originally estimated it would take us another 100 years or more to get to the Simulation Point. But if Silicon Valley continues its obsession with building the metaverse, we will get there much sooner. This is important because if it is possible for any civilization to ever reach the Simulation Point (in the past or the future, on Earth or another planet), then the chances increase significantly that we are already in an ultrarealistic computer-generated simulated world that we cannot distinguish from physical reality. This would be true whether we were NPCs (or nonplayer characters, or AI) within the simulated world or whether we are players who exist outside of the game, role-playing avatars within the game (as was the case with Neo or Morpheus in *The Matrix*).

Called the simulation argument, this was proposed by University of Oxford philosopher Nick Bostrom in 2003. He stated there were several mutually exclusive possibilities, which I have simplified to two: (1) that no civilization ever reaches this point and no such simulations are created or (2) that at least one civilization reaches this point and creates not just one but many simulated worlds.

If option 1 is true, then there is no chance that we are already inside a simulation because these types of simulation may not be possible. On the other hand, if option 2 is a possibility, then it's likely that a more advanced civilization (imagine one that is hundreds or thousands of years ahead of us) already got there. They would then create billions of simulated worlds with billions of simulated beings who do not realize they are in a simulation.

Statistically speaking, if there are billions more simulated worlds and only one physical world, which are you more likely to be in? This is the argument that led Elon Musk in 2016 to state that the chances that we are in base reality (that is, not in a simulation) is "one in billions." Both Musk and Bostrom assumed we were likely NPCs, so we couldn't get out of the simulation by our own volition. Even if we are players who are locked into an avatar within the simulation, then our ability to exit will depend on the nature of the simulation so as not to affect the realism for those still in the simulation. This was reflected not only with *The Matrix* but in a recent episode of the series *Rick and Morty*, where a character steps into a Virtual Reality Life Simulator and lives out what seems like an entire life and only exits the game when the character dies.

As we get closer to building out the full technosocial imaginary of the metaverse, we will be proving not only that option 2 is possible but also that it is likely. If we can get there within 100 years of inventing computers, then it is likely in a physical universe that is billions of years old that some other civilization has already gotten there and has already created billions of simulated worlds. Bostrom's argument was that if this was the case, the probability we are one of these simulated beings in a simulated world is much higher than being in the single, lone physical reality.

While some of us might be players from the "outside" world, trapped in the metaverse playing characters in this virtual reality, like in *The Matrix,* most of us, statistically speaking, would be simulated AI characters in a simulated virtual world, thinking we are actually in the "real world." If that sounds a little strange, perhaps the only appropriate reaction is the one Keanu Reeves's character Neo gave in the original *Matrix* film 23 years ago: Whoa.

Zhara Astra is a screenwriter, producer and a professor at Arizona State University, where she teaches a course she created on understanding neurodivergent women.

We Need Better Diagnostic Tests for Autism in Women

Diagnostic criteria are developed using white boys and men, failing to serve many neurodivergent girls and women

Maljuk/Getty Images

"You don't look autistic."

This is what people say when I first tell them I'm on the spectrum. But I do look autistic. The problem is that people, especially medical professionals, don't know what to look for when it comes to identifying and diagnosing autism in women and girls.

I am a professor, a screenwriter, producer, mother and a woman who has autism. The challenges I have had in getting my diagnosis lead me to believe that we have to develop a more accurate standard autism test and better diagnostic criteria specifically for women and girls. This test and these criteria need to be co-created by autistic women and psychologists who understand how autism manifests differently in women and girls.

The current assessment is a prime example of gender bias in medicine and an example of how diagnostics are rife with gender and racial biases. The latest diagnostic criteria for autism were set forth in the 2013 *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-5*). This version has extremely restrictive requirements for an autism diagnosis, such as showing deficits in nonverbal communication, displaying social issues, using repetitive speech, and difficulty maintaining relationships.

These diagnostic requirements are outdated and more specific to the white male experience of autism, and until recently, most psychological testing done to diagnose autism was developed using the experiences and symptoms of cisgender white males. The *DSM* doesn't distinguish between sub-

types of autism, including Asperger's syndrome. This means when women and girls visit their doctors with symptoms that lead them to think they have autism, they don't fit the diagnostic criteria, leading to no diagnosis or an incorrect one.

Developing a more accurate diagnostic test is an issue of safety, as well as quality of life, for so many women silently struggling to understand why they might be different, including myself.

Growing up in the 1990s, I was different from other girls, but I certainly never considered I had autism. Sure, I operated on a different wavelength: I gravitated toward philosophy and books that dissected the meaning of life. I was extremely literal and had a fascination with math and numbers, as is common in autism.

But, less commonly, I didn't like to be touched. I laughed at inappropriate times, ate the same foods every day, and was frequently overstimulated by smells, textures and sounds. We are starting to discover that these traits are more likely to occur in women and girls with autism.

I was undoubtedly different, but because my traits were more subtle than what we typically consider a person with autism to have and because I had become accustomed to masking these quirks (girls with autism and ADHD are masterful at doing this), no one suspected I was on the spectrum.

It wasn't until 2020, when I was in my 30s and researching autism for my son, that I began to suspect I was on the spectrum. There began my troubles. It took me a year to find a psychologist who offered testing for adults, who had an understanding of women with autism, and who wouldn't charge me $5,000 or more for an assessment, because my insurance wouldn't cover the testing.

Most places I called were clueless when it came to diagnosing adult women. These psychologists had little experience diagnosing girls as well. After a year of searching for a competent, available and affordable psychologist, I finally found one and got a diagnosis of autism in 2021. I was told that I had Asperger's syndrome but that since the release of the *DSM-5,* the term had been swept into the general definition of "autism spectrum disorder."

Because of the narrow and gendered diagnostic criteria, we're instead often told by the doctors that we have a menstrual-related mood disorder or anxiety, as I was told, or we're slapped with some other grossly inaccurate label. All through history, women have been mislabeled as hysterical, when I think many were likely just neurodivergent and trying to fit into a neurotypical world.

Because of these false labels and the lack of testing, we have historically been overlooked, misdiagnosed or undiagnosed entirely. Many of us end up self-diagnosing later in life, after years of wondering why we feel so out of place in this world and in our own bodies.

Anxiety and depression are very common in neurodivergent women, especially those who remain undiagnosed. Women with autism are three to four times more likely to attempt suicide than neurotypical women. Comorbidities are very common in autistic women as well and can dramatically enhance the risk. Research indicates that women with autism and attention deficit hyperactivity disorder have an even higher chance of trying to commit suicide.

We may look like "the mom next door," but our inner world tells a different story: a change in plans, a high-pitched sound, a blast of pungent perfume or a stray label in a sweater, and we're suddenly struggling to avoid a meltdown.

It's exhausting, and if you don't have the privilege of understanding why you feel this way, then it can be maddening. Knowing that you have autism (along with other comorbid neurodivergences) and that you're prone to anxiety, depression and burnout can help suffering women get access to the treatment and support they may need.

But better diagnostic criteria are just the beginning. We also need more programs, such as group therapy and support groups for women who are diagnosed with autism in adulthood. Training teachers, doctors and psychologists on what to look for in girls and women and how to accommodate us should also become the new standard.

Understanding autism in girls is also a matter of safety because these girls are three times more likely to be sexually abused. We tend to be more trusting and naïve because we are often very direct and straightforward and expect other people to be the same. Recognizing ill intentions and ulterior motives in others can be difficult for us. This can make us more vulnerable and susceptible to abuse.

Every person deserves the opportunity to succeed and rise to their greatness, including women with autism. As more girls and women recognize they are neurodivergent, having accurate testing and the accommodations means we have a better chance to do our best.

Susana Martinez-Conde and **Stephen Macknik** are professors of ophthalmology at the State University of New York and the organizers of the Best Illusion of the Year Contest. They have co-authored *Sleights of Mind: What the Neuroscience of Magic Reveals about Our Everyday Deceptions* and *Champions of Illusion: The Science behind Mind-Boggling Images and Mystifying Brain Puzzles.*

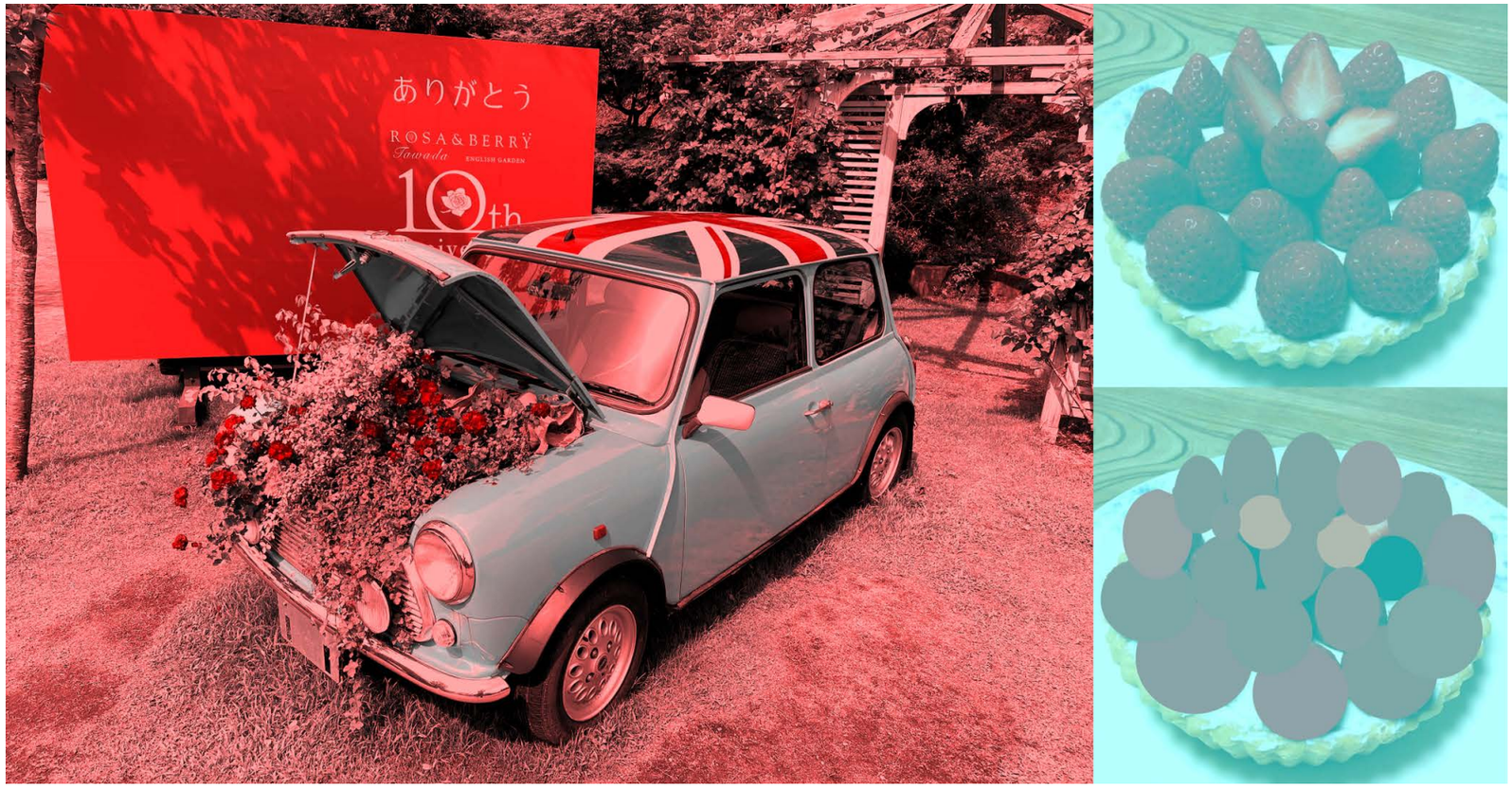
Strawberry Fields

Nothing is real about the colors you see here

Every object we see is a mirror to some extent. The glassy surface of a lake on a windless day is a perfect mirror when it reflects all light faithfully without scatter. But a red strawberry, too, is a mirror, though an imperfect one. The usual reason strawberries appear red is that they reflect reddish and absorb bluish wavelengths. The problem is, sometimes the light that falls on a strawberry does not have any red at all. How do we manage to see red strawberries in the absence of red wavelengths?

In the late 19th century German physiologist Ewald Hering showed that our experience of color is partly the result of our brain interpreting blue as opposite to yellow and red as opposite to green. By the time we perceive a strawberry as red, our perception is far afield from the original light wavelengths. Instead our visual system decides what the surface color of the strawberry probably is based on a process that identifies the light source and then discounts it.

The perceptual consequence of this process is called color constancy because it allows us to see an object's color as constant, irrespective of the illumination conditions. Because of color constancy, strawberries look red at sunset and at noon, under cloudy skies at your local farmer's market, and flooded by fluorescent lighting in your supermarket's produce aisle.



Illusory blues and reds: The car image is composed of red and gray tones. In the fruit plate image, each strawberry is made of tones of gray. Replacing the strawberries with gray blobs does not make them look any less red.

The car photograph, created by vision scientist Akiyoshi Kitaoka with free online software, exemplifies a type of color constancy called the Land effect, after Edwin H. Land, inventor of the Polaroid camera. We see the automobile as blue, but the image contains only red and gray wavelengths.

The plate of strawberries, also created by Kitaoka, illustrates another form of color constancy. Each single berry is actually gray, but your brain begs to differ. Moreover, you do not see the strawberries as red, because you know what color they are supposed to be. Vision scientist Michael Bach modified the original picture by replacing each berry with a gray blob. The resulting image shows that prior knowledge of fruit coloring is irrelevant: even shapeless blobs will take on the color that our visual system assigns them based on our implicit assumptions about the light source.

Akiyoshi Kitaoka (*left and top right*); Michael Bach (*bottom right*)

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