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The Stress Fix

Psychological tools that can increase well-being and prevent burnout

INCLUDING

TARGETING THE ALZHEIMER'S PROTEIN

REMARKABLE INFANT MINDS

NEW TRUTHS ABOUT YOUR AUTHENTIC SELF

WITH COVERAGE FROM nature

FROM THE EDITOR

LIZ TORMES

Whatever Helps You Feel Less Afraid, Tired and Lonely, Do That

In the past several weeks I've often wondered what Bruce McEwen would make of the current state of the world. McEwen was a neuroscientist and endocrinologist at the Rockefeller University who spent his career studying how stress impacts the brain. In 1968 he and his team made the seminal discovery that stress hormones such as cortisol enter the brain and effect neurological function. Exposure to chronic stress factors in the environment creates allostatic load, a term McEwen coined in 1993. Enough stress over long periods leads to measurable changes in brain chemistry and gene expression—and not necessarily for the better. McEwen passed away on January 3 of this year at the age of 81.

I imagine the world events during his career that might have caused McEwen to feel that his work was particularly pertinent, almost painfully relevant: the Vietnam War. The attacks of September 11. I can only guess that he'd feel the same today. Doctors, nurses, administrators, first responders, pharmacists, grocery workers, package delivery personnel, construction workers—they are all dealing with inordinate stress at this time. And so is everyone else—from those working from home alone, parents juggling their jobs and teaching kids full-time from their living rooms, and those who've lost their jobs, worrying over how they're going to survive the coming months. Life is stressful enough in ordinary times, and now we are dealing with heightened allostatic load under the uncertainty and strife of each day.

In this issue, health care worker Ashten Duncan writes that we can't continue to overlook the importance of personal well-being when it comes to how well we (and especially health care providers) are able to function. He has some interesting insights from research on positive psychology on that score (see "How I Broke the Cycle of Stress"). But my (very nonexpert) advice is that this is a time to treat yourself and others very gently. It's a time for nonjudgment, leeway for extra emotions, extra naps and extra ice cream. Whatever helps you feel less afraid, tired and lonely, do that. And do it again. Be well, my friends.

Andrea Gawrylewski
Senior Editor, Collections
editors@sciam.com

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On the Cover

Research on positive psychology may help prevent burnout

RODERICK CHEN GETTY IMAGES

WHAT'S INSIDE

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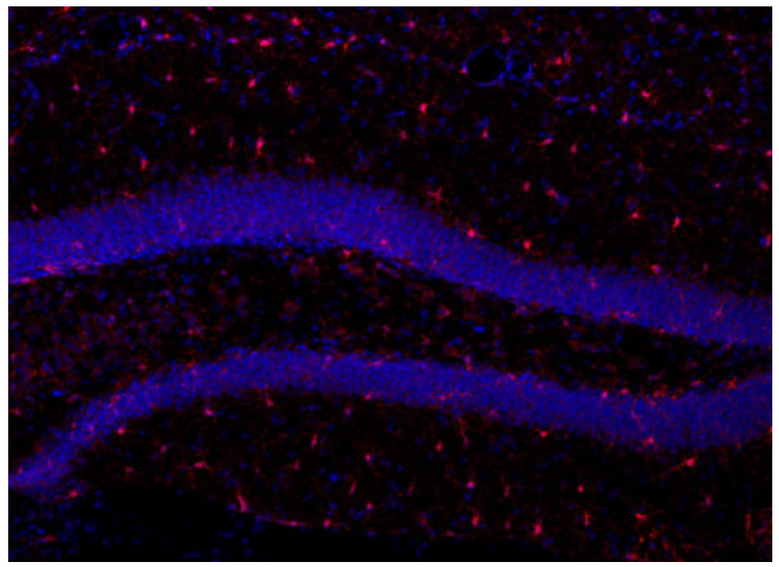
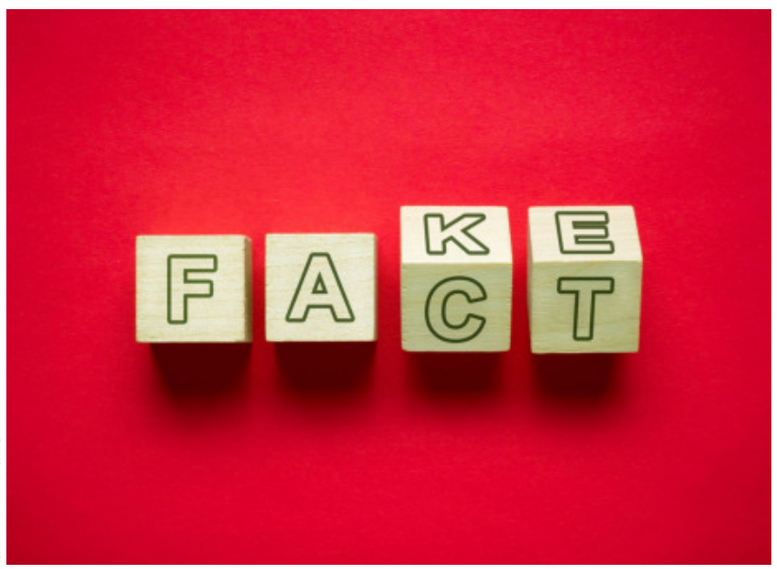


CHAO WANG



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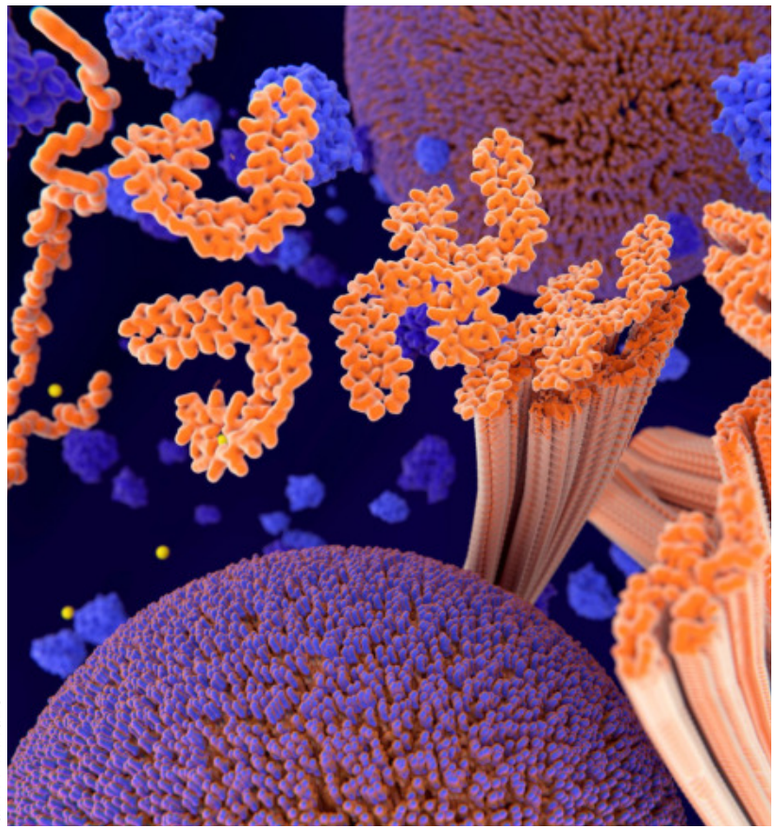

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RODERICK CHEN GETTY IMAGES

Born Ready: Babies Are Prewired to Perceive the World

A study in infants adds to the debate about whether we come into the world prepped for higher cognitive abilities such as face recognition

Neuroscientists understand much about how the human brain is organized into systems specialized for recognizing faces or scenes or for other specific cognitive functions. The questions that remain relate to how such capabilities arise. Are these networks—and the regions comprising them—already specialized at birth? Or do they develop these sensitivities over time? And how might structure influence the development of function? "This is an age-old philosophical question of how knowledge is organized," says psychologist Daniel Dilks of Emory University. "And where does it come from? What are we born with, and what requires experience?"

Dilks and his colleagues addressed these questions in an investigation of neural connectivity in the youngest humans studied in this context to date: 30 infants ranging from six to 57 days old (with an average age of 27 days). Their findings suggest that circuit wiring precedes, and thus may guide, regional specialization, shedding light on how knowledge systems emerge in the brain. Further work along these lines may provide insight into neurodevelopmental disorders such as autism.

In the study, published in March in the *Proceedings of the National Academy of Sciences USA*, the researchers looked at two of the best-studied brain networks dedicat-

ed to a particular visual function—one that underlies face recognition and another that processes scenes. The occipital face area and fusiform face area selectively respond to faces and are highly connected in adults, suggesting they constitute a face-recognition network. The same description applies to the parahippocampal place area and retrosplenial complex but for scenes. All four of these areas are in the inferior temporal cortex, which is behind the ear in humans.

The team used a technique called resting-state functional magnetic resonance imaging (rsfMRI), which measures the level of synchronization of activity in different brain regions to assess how connected they are. The infants were scanned while sleeping and tightly swaddled. "Getting fMRI data from newborns is a new frontier in neuroimaging," says neuroscientist and lead study author Frederik Kamps, now at the Massachusetts Institute of Technology. "You need a participant's head to be still, and a sleeping baby is one that is willing to lie still."

The researchers found that the face regions were highly connected to one another but not to the scene regions, and vice versa, at this young age. It would be months before they became selective for faces or scenes, suggesting connectivity precedes the development of function.

The team also assessed connections between these regions and the part of the brain where visual input first arrives from the retina: the primary visual cortex, or V1. This region is structured so that such inputs from the center of the retina arrive at a different area than those from the periphery of the field of vision, forming a map of the visual world. The face network was strongly connected to V1's central area, while the scene network was more tightly linked to its peripheral area. This arrangement likely relates to the fact that we usually fixate on faces, whereas scenes extend across our entire visual field. These networks, present in an infant's earliest days, are therefore connected so as to receive the most appropriate input for the function they will eventually perform.

Does that mean face recognition and scene processing are innate? Researchers disagree on this point. In 2017 neurobiologist Margaret Livingstone of Harvard Medical School published a study of newborn macaques that found connectivity precedes function—but only as far as visual maps. Livingstone, who was not an author of the new paper, thinks sensitivities to specific categories of things, such as faces, arise from accumulating experiences of seeing them. "You are born with these maps, and that's what drives the final organization of the brain," she says. "That's the scaffolding on which experience acts." In another study, she found that monkeys raised without seeing faces did not develop face selectivity.

Others, however, have shown that congenitally blind people have face- and scene-selective regions (using tactile or auditory stimuli, for example), suggesting these functions may be innate—or at least, that they may depend on more than just visual input. Dilks notes that faces are not the only things we fixate on, and other researchers have proposed that "top-down" connections from high-level cortical regions involved in social interaction (between mother and baby, for instance) may also shape the development of face selectivity. This debate shows no sign of being settled soon. "It all boils down to this philosophical question: Are humans special? Do they have parts of their brain predestined to become these special things?" Livingstone says. "Or can we explain it using low-level principles we've inherited from lower animals?"

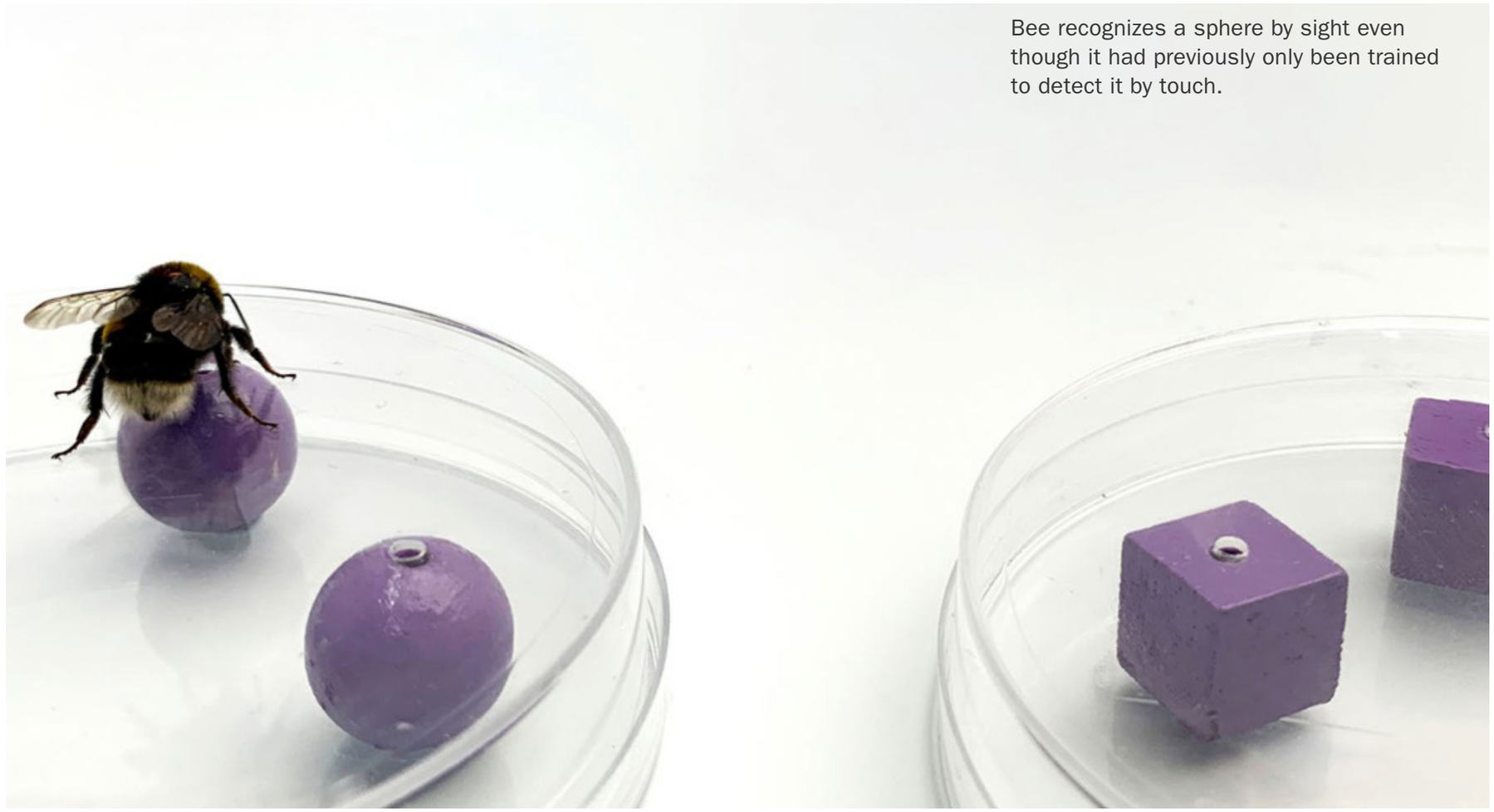
Beyond this theoretical wrangling, Dilks has an eye on possible clinical applications. He is especially interested in two neurodevelopmental disorders thought to involve differences in brain wiring: People with autism have social impairments that may relate to face processing. And a condition called Williams syndrome causes problems with navigation.

Siblings of children with autism could be studied to ask whether connectivity in face regions might predict the onset of the condition, which is usually not diagnosed until at least two years of age. Dilks also hopes to study babies with Williams syndrome to ask whether connectivity between scene-processing regions is a problem. "That's important to know," he says, "because maybe we can harness the incredible malleability of the infant brain to intervene earlier."

—Simon Makin

Bumblebees Solve a 17th-Century Psychological Puzzle

By answering the question posed in Molyneux's problem, the invertebrates may have demonstrated an ability to internally represent objects



Bee recognizes a sphere by sight even though it had previously only been trained to detect it by touch.

LARS CHITTKA

In 1688 Irish philosopher William Molyneux wrote to his colleague John Locke with a puzzle that continues to draw the interest of philosophers and scientists to this day. The idea was simple: Would a person born blind, who has learned to distinguish objects by touch, be able to recognize them purely by sight if he or she regained the ability to see?

The question, known as Molyneux's problem, probes whether the human mind has a built-in concept of shapes that is so innate that such a blind person could immediately recognize an object with restored vision. The alternative is that the concepts of shapes are not innate but have to be learned by exploring an object through sight, touch and other senses, a process that could take a long time when starting from scratch.

An attempt was made to resolve this puzzle a few years ago by testing Molyneux's problem in children who were congenitally blind but then regained their sight, thanks to cataract surgery. Although the children were not immediately able to recognize objects, they quickly learned to do so. The results were equivocal. Some learning was needed to identify an object, but it appeared that the study participants were not starting completely from scratch.

Lars Chittka of Queen Mary University of London and his colleagues have taken another stab at finding an answer, this time using another species. To test whether bumblebees can form an internal representation of objects, Chittka and his team first trained the insects to discriminate spheres and cubes using a sugar reward. The bees were trained in the light, where they could see but not touch the objects that were isolated inside a closed petri dish. Then they were tested in the dark, where they could touch but not see the spheres or cubes. The

researchers found that the invertebrates spent more time in contact with the shape they had been trained to associate with the sugar reward, even though they had to rely on touch rather than sight to discriminate the objects.

The researchers also did the reverse test with untrained bumblebees, first teaching them with rewards in the dark (where they could touch but not see the spheres or cubes) and then testing them in the light (where they could see but not touch the objects). Again, the bees were able to recognize the shape associated with the sugar reward, despite the fact that they had to rely on sight rather than touch in the test. In short, "bees have solved Molyneux's problem," Chittka says.

A substantial body of work has documented the visual pattern-recognition abilities of bees. Researchers previously knew that the insects could recognize complicated color patterns in flowers and even human faces. But most of these pattern-recognition tasks can be done with very simple feature detectors—for instance, neurons' orientation of edges, the field of brightness, and so on. "You could do a whole lot of seemingly advanced pattern recognition without actually having a virtual image floating around in your head, a kind of representation of the object," Chittka says. "So that was always the big question: Is there, in the same way that our perception works, a kind of object representation inside the bees' head rather than simple elements of the image that are, in some way, linked to rewards?"

"So that was always the big question: Is there, in the same way that our perception works, a kind of object representation inside the bees' head rather than simple elements of the image that are, in some way, linked to rewards?"
—Lars Chittka

The fact that the insects were able to discriminate shapes by transferring information across sensory modalities suggests that they represent object features and can access them through sight or touch. "That's why we're excited about this," says Chittka, a bee sensory physiologist and behavioral ecologist.

Experts who were not involved with the study are also intrigued but express some caveats. The experiment shows that bees can transfer a feature that they have identified from one sensory modality to another, says Ludwig Huber, a zoologist at the University of Veterinary Medicine, Vienna, who has studied cross-modal sensory integration in mammals and birds. "But the big question is 'What is this feature, and how abstract is it?'" The bees may be able to discriminate between rounded surfaces and sharp edges by transferring sensory information from one mode to another without recognizing the objects or having an internal representation of them, he argues.

Huber also wonders about the real-world validity of the experiment. In the wild, bumblebees are likely to rely on sight and olfactory cues to recognize flowers, for example. He would like to see a test that is more similar to the kinds of objects and sensory cues that bees are likely to encounter in nature.

Jonathan Birch, a philosopher of science studying animal sentience at the London School of Economics and Political Science, cautions that the bees may have had prior experience associating visual and tactile information about straight edges and curved surfaces in the context of their nests, so it is not possible to eliminate the possibility that some of the cross-sensory integration is learned rather than innate.

For Chittka, the ultimate goal is to find out whether bees have consciousness, which neuroscience and cognitive science often study by focusing on the integration of information from different senses. His earlier work with bumblebees shows that they have sophisticated abilities for learning and memory. "None of these tasks—and the performance of the bees—is a formal indicator of consciousness. In fact, nothing is," Chittka said at his presentation at the recent annual meeting of the Society for Integrative and Comparative Biology in Austin, Tex. "But all of these taken together, I think, nudge the probabilities in the right direction." *—Viviane Callier*

Does Music Boost Your Cognitive Performance?

The answer depends on your personality

Music makes life better in so many ways. It elevates mood, reduces stress and eases pain. Music is heart-healthy because it can lower blood pressure, reduce heart rate and decrease stress hormones in the blood. It also connects us with others and enhances social bonds. Music can even improve workout endurance and increase our enjoyment of challenging activities.

The fact that music can make a difficult task more tolerable may be why students often choose to listen to it while doing their homework or studying for exams. But is listening to music the smart choice for students who want to optimize their learning?

A new study by Manuel Gonzalez of Baruch College and John Aiello of Rutgers University suggests that for some students, listening to music is indeed a wise strategy, but for others, it is not. The effect of music on cognitive functioning appears not to be "one-size-fits-all" but to instead depend, in part, on your personality—specifically, on your need for external stimulation. People with a high requirement for such stimulation tend to get bored easily and to seek out external input. Those individuals often do worse, paradoxically, when listening to music while engaging in a mental task. People with a low need for external stimulation, on the other hand, tend to improve their mental performance with music.

But other factors play a role as well. Gonzalez and Aiello took a fairly sophisticated approach to understanding the influence of music on intellectual performance, assessing not only listener personality but also manipulating the difficulty of the task and the complexity of the music. Whether students experience a perk or a penalty from music depends on the interplay of the personality of the learner, the mental task and the music.

In the study, participants first completed the Boredom Proneness Scale, which is a personality test used to determine need for external stimulation. They then engaged in an easy cognitive task (searching for the letter A in lists of words) and a more challenging one (remembering word pairs). To control for practice and fatigue effects, half of the subjects completed the easy task first, while the other half completed the challenging one first. Participants finished both tasks under one of three sound conditions: (1) no music, (2) simple music or (3) complex music. All of the music was instrumental, and music complexity was manipulated

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by varying the number of instruments involved in the piece. Simple music included piano, strings and synthesizer; complex music added drums and bass to the simple piece.

The data suggest that your decision to turn music on (or off) while studying should depend on your personality. For those with a high need of external stimulation, listening to music while learning is not wise, especially if the task is hard or the music is complex. On the simple task of finding A's, such subjects' scores for the music condition were the same (for simple music) or significantly worse (for complex music) than those for the silent condition. On the complex task of learning word pairs, their performance was worse whenever music was played, regardless of whether it was simple or complex.

For those with a low need of external stimulation, however, listening to music is generally the optimal choice. On the simple task of findings A's, such participants' scores for the music condition were the same (for simple music) or dramatically better (for complex music) than those for the silent condition. On the complex task of learning word pairs, the participants showed a small but reliable benefit with both simple and complex music, relative to silence.

The results suggest that there are substantial individual differences in the impact of music on cognitive function, and thus recommendations regarding its presence in the classroom, study hall or work environment may need to be personalized. Students who are easily bored and who seek out stimulation should be wary of adding music to the mix, especially complex music that may capture attention and consume critical cognitive resources that are needed for successful task completion. On the other hand, students with a low need for stimulation may benefit significantly from the presence of music, especially when completing simple, mundane tasks.

Before students decide to slip in their earbuds, though, they should carefully consider both their musical selection and the nature of the task. All of the music used in the present study was instrumental, and lyrical music will likely be more complex. Complexity appears to increase arousal, and the Yerkes-Dodson law suggests that a moderate level of arousal produces optimal performance. When there is too little or too much arousal, performance drops. Thus, the benefits of music for those with a low need for external stimulation that were observed here could diminish or even disappear with the added complexity of lyrics.

Similarly, increases in the complexity of a cognitive task might also reduce or eliminate the benefit of music. Although the "complex" task used in this study (learning word pairs) was only moderately challenging, the increase in complexity, relative to the simple task, was enough to reduce music's positive effect. With a highly challenging cognitive task (text comprehension or exam preparation), even those with a low need for external stimulation may fail to show such an effect with music.

With the right (low need for stimulation) personality, the right (instrumental) music and the right (low to moderately difficult) task, the presence of music may significantly improve cognitive functioning. Given the many other physical, emotional and psychological benefits of music, that subscription to Spotify just might pay for itself.

—Cindi May

An Alcoholic Parent Can Affect How a Child's Brain Switches Tasks

Such children's neural circuits do not transition properly from an active state to a resting one

One of the strongest predictors of becoming an alcoholic is family history: the offspring of people with the disorder are four times more likely than others to develop it, according to the National Institute on Alcohol Abuse and Alcoholism (NIAAA). But new research shows a family history of alcoholism (FHA) affects more than your desire to drink. It also changes how your brain transitions from one task to the next—going, say, from cooking breakfast to thinking about a work deadline.

A whole line of research has found that having an alcoholic in the family can affect one's mental processes. But these studies have not fully explored what is called executive function—planning, restraint and other behaviors that are impaired with FHA.

To delve further, Enrico Amico, now at the Swiss Federal Institute of Technology in Lausanne, and his colleagues decided to focus on how the brain processes competing cognitive demands—the switching of neural activity from one brain network to another, which is critical to executive functioning. Prior studies acquired "snapshots" of network activity when subjects were either performing a task or resting quietly. But this approach does not provide a continuous record of what is happening in the brain to capture the dynamic transitions from active to resting states that occur constantly throughout the day. So Amico, then at Purdue University, and a team of researchers at Purdue and Indiana University set out to answer how the brain makes these transitions.

The researchers used a functional magnetic resonance imaging (fMRI) scanner to examine the changes in the brains of 54 participants as they performed a task that required them to indicate the direction of an on-screen arrow by pushing a button or to refrain from doing so in response to a stop signal. Afterward, the subjects were instructed to rest while fixing their gaze on a crosshair on the screen.

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The scans showed that individuals without FHA went through a transient period between the game task and the resting state in which some brain regions—frontal, parietal and visual areas, in particular—reconfigured the way in which they communicated with one another. People with FHA experienced fewer changes—even after the researchers controlled for factors such as age, gender, motion in the fMRI scanner, drinking and depression.

"It looks like FHA impacts the mental preparation to switch from performing one task to another," Amico says. "This could be analogous to the process of clearing the cache of your smartphone when you want it to switch faster between apps. The problem is that this 'cache-clearing process' might be impaired in brains with family history of alcoholism."

While a group of 54 participants is a small sample for most studies, Amico maintains it is ample for an fMRI study. "We were very thorough in assessing statistical power and the effect sizes of our claims, so these fMRI results are definitely sufficiently powered," he says. The study was published in January in *NeuroImage*.

FHA did not seem to have an impact on participants' ability to complete the mentally demanding tasks, but deficiencies still may be found in future studies. "What if you are not impaired in doing the task, but then, afterward, you are more stressed or less reactive or even more forgetful or less attentive than a person without FHA?" Amico asks. "This is my hypothesis. And hopefully future studies will tell us more about this fascinating process." Additional investigations are also needed to answer why people with FHA switch between activity and rest in a different way—and whether there may be a genetic basis for its occurrence.

The ability to switch seamlessly from a relatively demanding task (balancing a checkbook) to a less demanding one (binge-watching a TV show that you have already seen) is critical to going about our everyday activities, explains Reza Momenan, director of the Clinical NeuroImaging Research Core at NIAAA, who was

not involved with the research. Carrying out this transition smoothly, Momenan says, helps the nervous system remain in a stable equilibrium state needed for survival. This type of research could provide the basis for better diagnoses for psychiatric disorders than simply interviewing patients to determine the risk, severity or prognosis for alcohol use disorder.

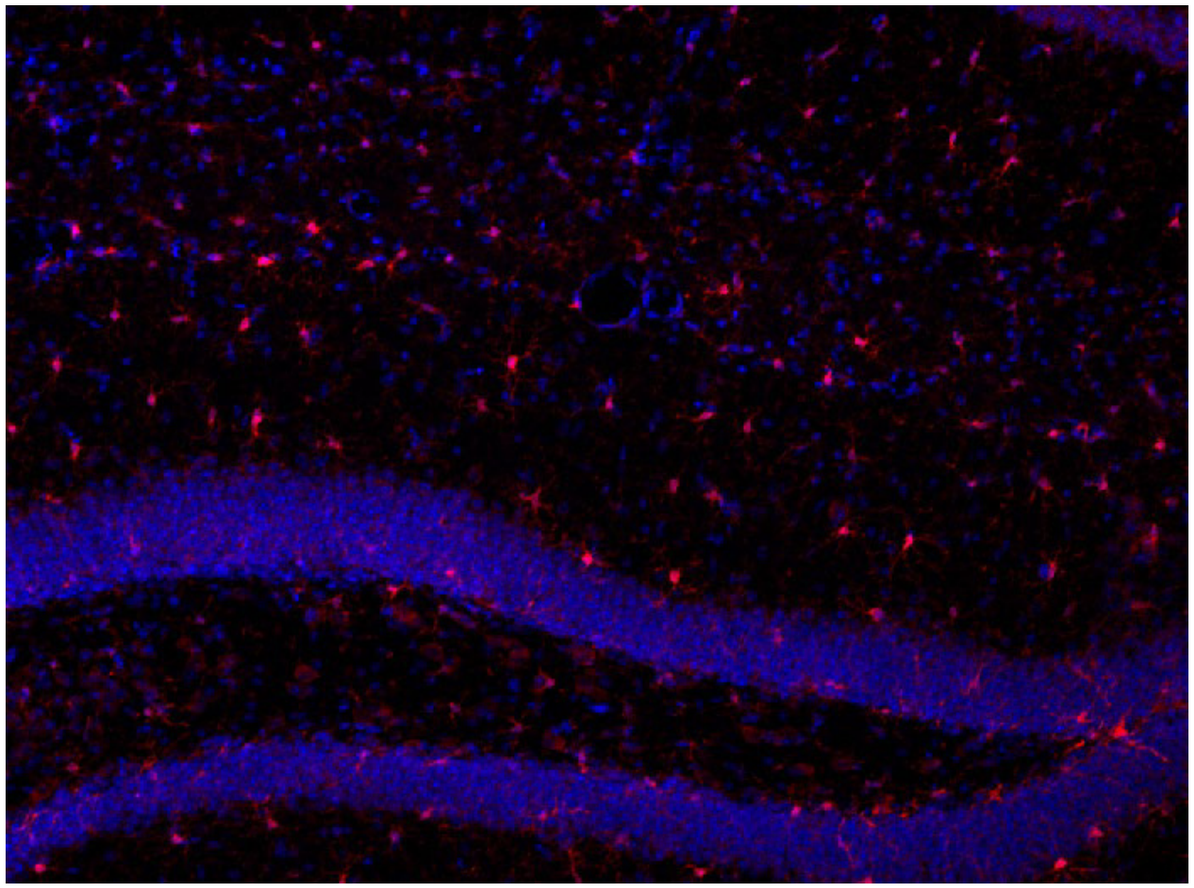
Anita Cservenka, a neuroscientist at Oregon State University, who was also not involved in the research that went into the new paper, found its results to be compelling. "The study's findings point to important new approaches in understanding neural differences between those with and without a family history risk for alcohol use disorder."

Cservenka suggests further research might examine whether these task-to-rest neural measures predict the beginning of heavy alcohol consumption or a capacity to avoid drinking. Another possibility, Momenan says, would be to look at the brain activity of people diagnosed with alcohol use disorder, perhaps providing still deeper insight into the mental-processing impact of having an alcoholic in the family.

—Jillian Kramer

How Does a Mammalian Brain Forget?

A mouse study shows immune cells gobbling up the connections between memory-associated neurons



CHAO WANG

Our memories are imperfect. You can probably recall who you spoke to over dinner last weekend but have likely forgotten the details of the conversation. Remembering too much can have its downsides—in conditions such as post-traumatic stress disorder, a distressing event can remain imprinted in an individual's mind, causing continued anguish. On the other hand, excessive memory loss is also a problem. Alzheimer's disease, for example, is marked by an inability to recollect. Using mice, scientists have now demonstrated that the brain's resident immune cells, microglia, play a critical role in helping the organ to forget.

Microglia were once seen solely as the brain's watchdogs—activated exclusively to guzzle pathogens and dead and dying neurons. That view has changed in recent years, as scientists have amassed evidence that these cells have wide-ranging duties: During development, they seem to help sculpt the brain by trimming away excess synapses—the connections between neurons. And microglia appear to be major players in several neurodevelopmental and neurodegenerative diseases, including autism and Alzheimer's. Yan Gu, a neuroscientist at the Zhejiang University School of Medicine in China, says he and his colleagues were intrigued by the potential link between the work on microglial pruning during early development and prior research indicating that synapses are important for the storage and coding of memories. "We wondered whether microglia can eliminate synapses in the adult brain," he says. "And what is the relationship between loss of synapses by microglia and forgetting?"

To address this question, Gu's group teamed up with other researchers at Zhejiang University in a study, including neuroscientist Lang Wang. They depleted microglia from the brains of mice with drugs administered either through food or injected directly into the brain. To assess memory retention, they used contextual fear conditioning, a technique that involves placing rodents in a cage and giving them mild electric shocks. (When the animals reenter the cage, even in the absence of a shock, the memory of the experience immobilizes them.) The researchers found that although this freezing response diminished after a few weeks in healthy animals, it remained largely intact in their microglia-depleted counterparts.

The team then conducted a series of experiments to pinpoint how, exactly, microglia mediate forgetting. They homed in on the hippocampus, a brain region involved in memory and learning, and tagged neurons that were active during the contextual fear-conditioning task when the animals were making memories. (These memory-associated neurons are thought to fire together when a memory is recalled.) The researchers demonstrated that the reactivation of these cells occurred more frequently in microglia-depleted animals than in healthy ones.

Further tests revealed that forgetting was dependent on the microglia's ability to gobble up synapses—and on the activity of neurons. Suppressing the activation of memory-associated neurons led to more forgetting in the mice, suggesting that microglia-mediated elimination was a mechanism through which less useful memories are lost. The findings were published in February in *Science*.

"This is very exciting work," says Paul Frankland, a neuroscientist at the Hospital for Sick Children in Toronto, who was not involved in the study but has collaborated with some of its co-authors in the past. "This is a brand-new type of forgetting mechanism that's been discovered." According to Frankland, there have been a number of mechanisms of memory erasure proposed over the past decade or so, including work from his group that has suggested that the formation of new neurons, neurogenesis, enables forgetting. Put simply, the idea is that adding neurons introduces new connections and breaks old ones, altering the existing pattern of synapses within engrams—ensembles of neurons where memories are stored—and making them harder to access.

Both the neurogenesis-related and microglia-mediated forgetting could be happening in concert, Frankland adds—at least in parts of the brain where neurogenesis is present. But by looking at areas in the hippocampus where neurogenesis both does and does not occur, Gu and his colleagues demonstrated that microglia-mediated forgetting could be more widespread throughout the brain. "This suggests that microglia-mediated forgetting may be a generalized form of forgetting even in brain regions without neurogenesis [such as the cortex]," Gu says.

"This was a really cool study," says Soyon Hong, a neuroscientist at University College London, who did not take part in the work. She notes that while another group previously demonstrated that microglia are involved in synapse formation during learning, the novelty of the new paper is that it suggests these cells also play a role in synapse elimination in a healthy adult brain. There are still many mysteries that remain about the mechanism underlying this process, however. Prior research has shown that a constituent of the immune system called the complement system is involved in tagging synapses for microglia to prune. Wu and his colleagues demonstrated that this system played a role in microglia-mediated forgetting as well. But more specific questions, such as what factors control which complement proteins will tag neural connections for microglial removal, remain an open question, Hong says.

Gu and his colleagues are now working on further detailing the mechanism through which microglia pinpoint synapses to target and whether such processes go awry in a neurodegenerative disease such as Alzheimer's, in which overactive microglia may play a role. Hong, whose lab is focused on similar work, notes that the answer to these questions may have important implications in the future. "You can imagine, in the long term, for Alzheimer's and other diseases involving memory loss, that this neuroimmune signaling pathway that's implicated in memory could be a really specific and novel therapeutic target," she says.

—Diana Kwon

"Fake News" Web Sites May Not Have a Major Effect on Elections

Voters exposed to such untrustworthy sources also see valid news online, a study finds

During the 2016 election cycle, certain Web sites spread false information across the Internet. But a new study suggests they did not have as much impact as some have feared.

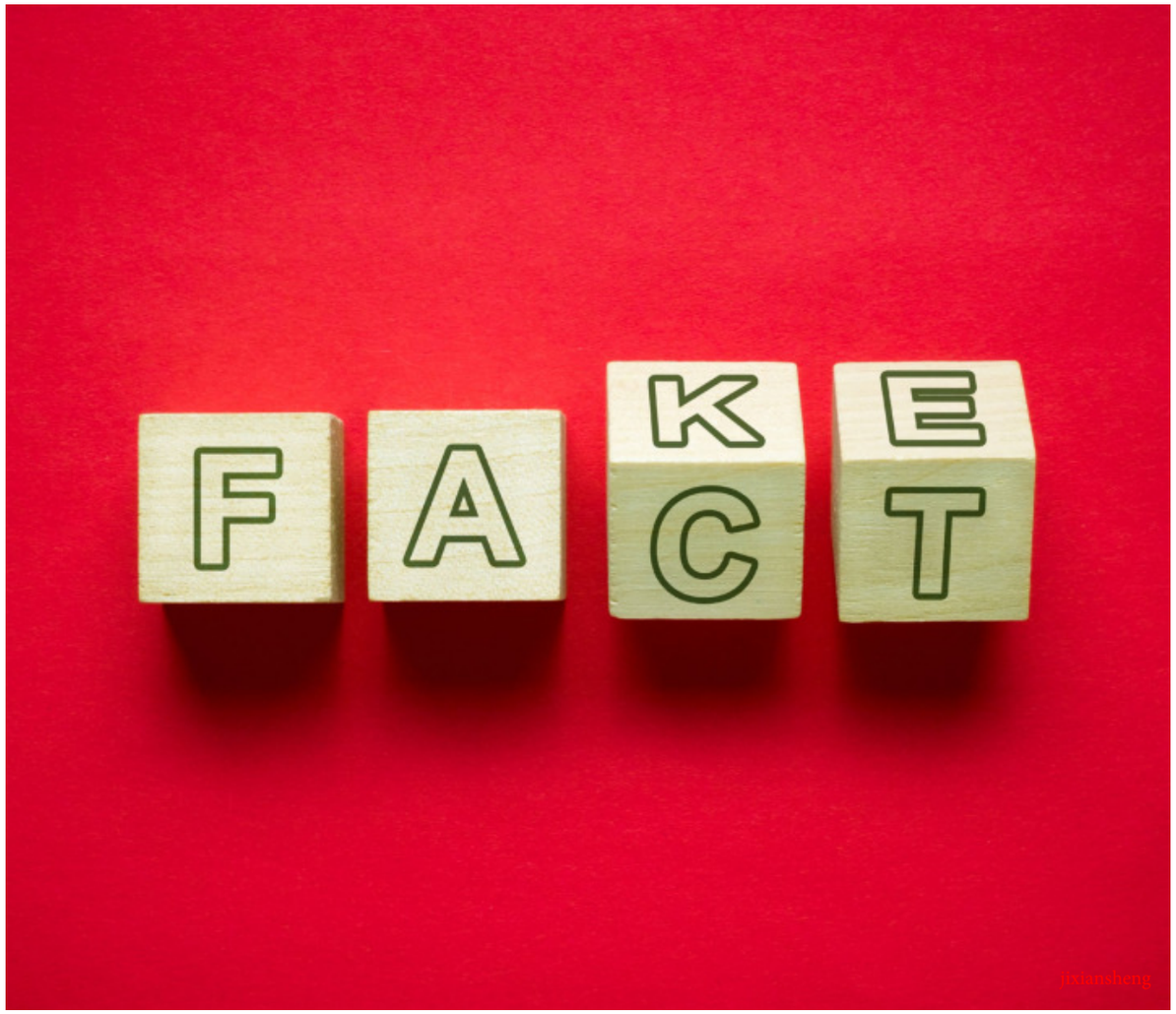
About 44 percent of voters, mostly right-leaning, saw at least one site, the study found. Yet those voters also saw plenty of legitimate news on the Web. "This content, while worrisome, is only a small fraction of most people's information," says Brendan Nyhan, a professor of government at Dartmouth College and one of the three authors of the study, which was published in March in *Nature Human Behaviour*.

The research provided the most systematic examination of people's exposure to these fringe Web sites to date. It showed that while these untrustworthy sources might have a small effect on public opinion, in 2016 they did not substantially move individuals' positions about then presidential candidate Donald Trump or whether to go to the polls.

Emily Thorson, an assistant professor of political science at Syracuse University, says she is not surprised that these sites did not have a huge effect. A single piece of information rarely changes anyone's opinion, "whether it's true—or false," says Thorson, who was not involved in the new study. "That's a good thing." The idea that a handful of unreliable outlets were going to substantially alter views or behaviors "is pretty far-fetched, given what we know about the stability of people's political attitudes," she says.

The research paired responses to an online survey with data about which Web sites participants visited. In 2016 the survey responses were collected from 3,251 volunteers between October 21 and 31, and the Web traffic was recorded between October 7 and November 14. The election was held that year on November 8.

The study "is consistent with, and adds to, prior research that suggests that while a fair number of people had some exposure to 'fake news,' that the exposure was highly concentrated among a small number of conservatives," says David Lazer, University Distinguished Professor of political science and computer and information science at Northeastern University.



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Lazer, who provided feedback for the paper but was not involved in the work, notes that it examined an individual's browsing behavior, whereas previous studies looked solely at sharing false information on Facebook or, in the case of his own research, on exposure to, and dissemination of, such content on Twitter.

In his study, Lazer and his colleagues showed that untrue material accounted for nearly 6 percent of all news consumed on the Twitter. But only 1 percent of users were

exposed to 80 percent of this misinformation, and 0.1 percent shared 80 percent of it.

Nyhan and his colleagues' new research concludes that most people find these untrustworthy Web sites through social media, particularly Facebook. "It shows Facebook as a major conduit to fake news [and] misinformation," Lazer says.

Thorson says that while the *Nature Human Behaviour* study was expensive and difficult to conduct, Facebook already has much of the same information readily available—and should provide more of it to researchers. "One of the big takeaways for me is how important it is to start being able to look inside of what Facebook is doing," she says.

In 2018 voters were less exposed to misleading content than they had been in 2016, Nyhan says. But it is unclear if that reduction is because social media platforms such as Facebook were taking measures to minimize the effects of these fringe sites or whether there was simply less activity during a midterm election year.

Nyhan adds that he and his colleagues conducted the study because of shortcomings they saw in some other research and common misconceptions about the role of these Web sites. "I do worry that people's often incorrect sense of the prevalence of this type of content is leading them to support more extreme responses," he says. Measures to halt the transmission of material can "raise important concerns about the free flow of information and the exercise of power by the platforms over the information that people see."

The main problem with these sites, Nyhan says, is not what they post but the risk that someone in power will amplify their lies. "One implication of our study is that most of the misinformation that people get about politics doesn't come from these fringe Web sites. It comes from the mainstream—it comes from the media and political figures who are the primary sources of political news and commentary," he says.

A Web site might promote unscientific theories about the origins of the coronavirus without changing a lot of minds, Nyhan says. But when someone like conservative commentator Rush Limbaugh talks on air about those same theories, it has a bigger effect, he adds.

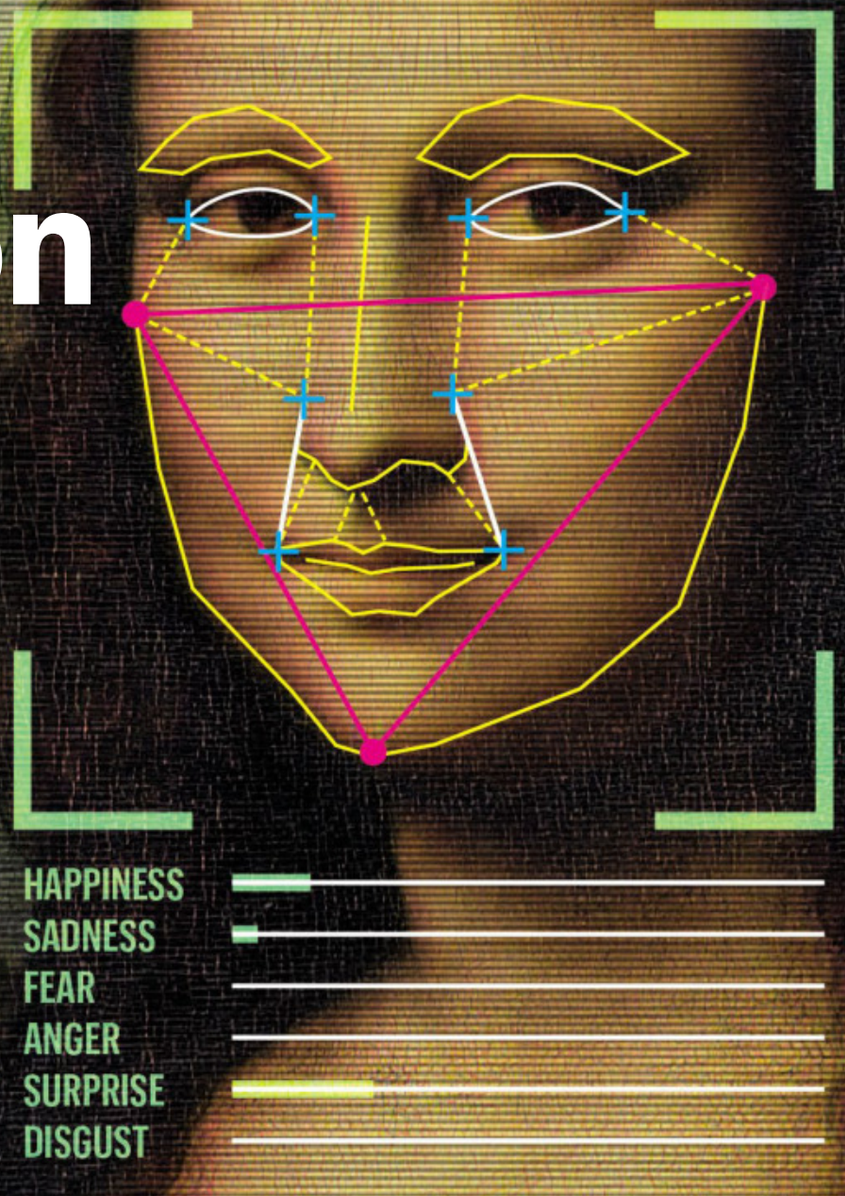
Will the 2020 election prove to be any different than the one in 2016 in terms of the power of these fringe sites? It is too soon to tell, Nyhan says. "The public is at least potentially more aware of the issue, though I don't know of any systematic evidence helping them make better choices," he says. The year "2020 will be the first real test."

—Karen Weintraub

Expression of Doubt

Psychologists can't agree whether facial expressions reliably convey moods. But companies building emotion-recognition software aren't waiting to find out

By Douglas Heaven



Douglas Heaven is a science journalist in London.

Human faces pop up on a screen, hundreds of them, one after another. Some have their eyes stretched wide; others show lips clenched. Some have eyes squeezed shut, cheeks lifted and mouths agape. For each one, you must answer this simple question: Is this the face of someone having an orgasm or experiencing sudden pain?

Psychologist Rachael Jack and her colleagues recruited 80 people to take this test as part of a study in 2018. The team at the University of Glasgow in Scotland enlisted participants from Western and East Asian cultures to explore a long-standing and highly charged question: Do facial expressions reliably communicate emotions?

Researchers have been asking people what emotions they perceive in faces for decades. They have questioned adults and children in different countries and Indigenous populations in remote parts of the world. Influential observations in the 1960s and 1970s by U.S. psychologist Paul Ekman suggested that, around the world, humans could reliably infer emotional states from expressions on faces—implying that emotional expressions are universal.

These ideas stood largely unchallenged for a generation. But a new cohort of psychologists and cognitive scientists has been revisiting those data and questioning the conclusions. Many researchers now think that the picture is a lot more complicated and that facial expressions vary widely between contexts and cultures. Jack's study, for instance, found that although Westerners and East Asians had similar concepts of how faces display pain, they had different ideas about expressions of pleasure.

Researchers are increasingly split over the validity of Ekman's conclusions. But the debate has not stopped companies and governments accepting his assertion that the face is an emotion oracle—and using it in ways that are affecting people's lives. In many legal systems in the West, for example, reading the emotions of a defendant forms part of a fair trial. As U.S. Supreme Court judge Anthony Kennedy wrote in 1992, doing so is necessary to "know the heart and mind of the offender."

Decoding emotions is also at the core of a controversial training program designed by Ekman for the U.S. Transportation Security Administration (TSA) and introduced in 2007. The program, called SPOT (Screening Passengers by Observation Techniques), was created to teach TSA personnel how to monitor passengers for dozens of potentially suspicious signs that can indicate stress, deception or fear. But it has been widely criticized by scientists, members of the U.S. Congress and organizations such as the American Civil Liberties Union for being inaccurate and racially biased.

Such concerns have not stopped leading tech companies running with the idea that emotions can be detected readily, and some firms have created software to do just that. The systems are being trialed or marketed for assessing the suitability of job candidates, detecting lies, making adverts more alluring, and diagnosing disorders from dementia to depression. Estimates place the industry's value at tens of billions of dollars. Tech giants including Microsoft, IBM and Amazon, as well as more specialist companies such as Affectiva in Boston and NeuroData Lab in Miami, all offer algorithms designed to detect a person's emotions from their face.

With researchers still wrangling over whether people can produce or perceive emotional expressions with fidelity, many in the field think efforts to get computers to do it automatically are premature—especially when the technology could have damaging repercussions. The

PRECEDING PAGE: ADAPTED FROM ALAMY

AI Now Institute, a research center at New York University, has even called for a ban on uses of emotion-recognition technology in sensitive situations, such as recruitment or law enforcement.

Facial expressions are extremely difficult to interpret, even for people, says Aleix Martinez, who researches the topic at the Ohio State University. With that in mind, he says, and given the trend toward automation, "we should be very concerned."

SKIN DEEP

The human face has 43 muscles, which can stretch, lift and contort it into dozens of expressions. Despite this vast range of movement, scientists have long held that certain expressions convey specific emotions.

One person who pushed this view was Charles Darwin. His 1859 book *On the Origin of Species,* the result of painstaking fieldwork, was a master class in observation. His second most influential work, *The Expression of the Emotions in Man and Animals* (1872), was more dogmatic.

Darwin noted that primates make facial movements that look like human expressions of emotion, such as disgust or fear, and argued that the expressions must have some adaptive function. For example, curling the lip, wrinkling the nose and narrowing the eyes—an expression linked to disgust—might have originated to protect the individual against noxious pathogens. Only as social behaviors started to develop, did these facial expressions take on a more communicative role.

The first cross-cultural field studies, carried out by Ekman in the 1960s, backed up this hypothesis. He tested the expression and perception of six key emotions—happiness, sadness, anger, fear, surprise and disgust—around the world, including in a remote population in New Guinea.

Ekman chose these six expressions for practical reasons, he told *Nature*. Some emotions, such as shame or

Darwin's treatise on emotions featured plenty of posed expressions, such as these subjects doing their best to imitate grief.

ALAMY

guilt, do not have obvious readouts, he says. “The six emotions that I focused on do have expressions, which meant that they were amenable to study.”

Those early studies, Ekman says, showed evidence of the universality that Darwin’s evolution theory expected. And later work supported the claim that some facial expressions might confer an adaptive advantage.

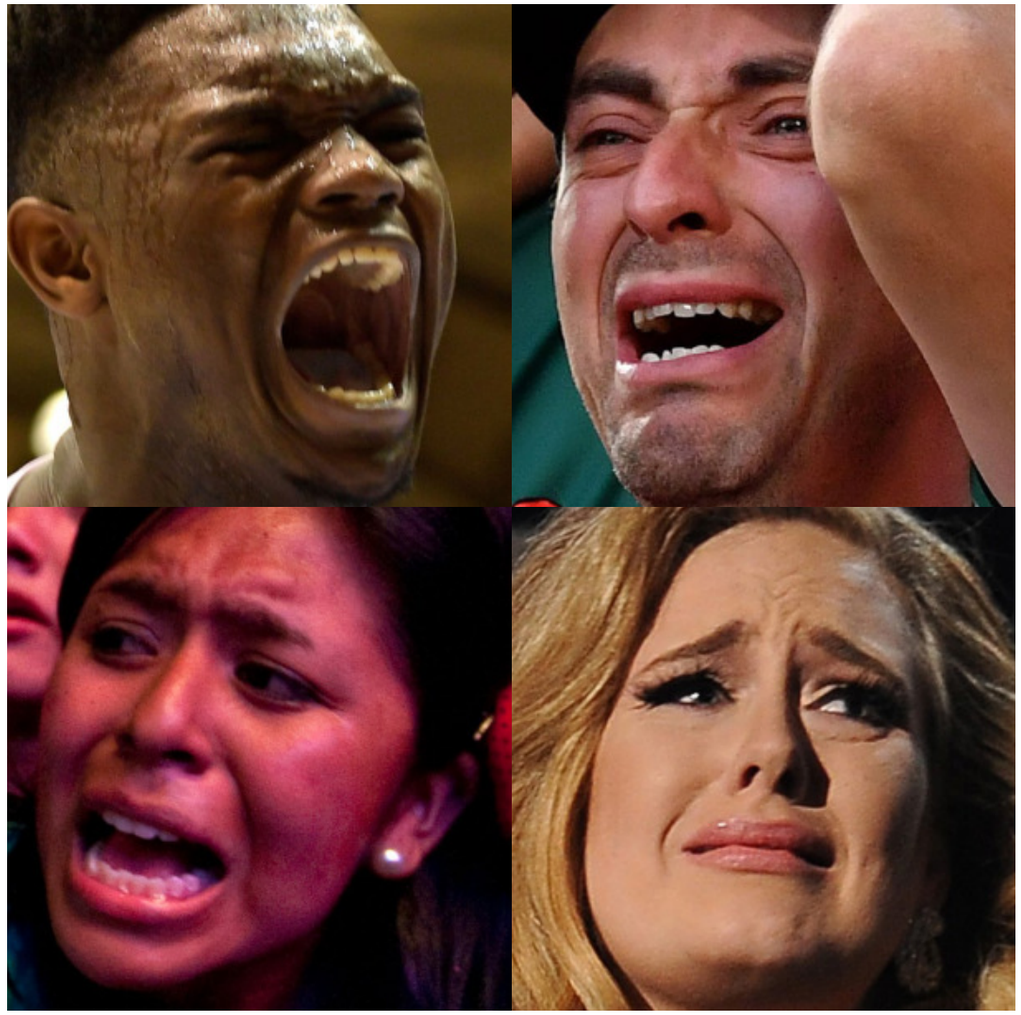
“The assumption for a long time was that facial expressions were obligatory movements,” says Lisa Feldman Barrett, a psychologist at Northeastern University, who studies emotion. In other words, our faces are powerless to hide our emotions. The obvious problem with that assumption is that people can fake emotions and can experience feelings without moving their faces. Researchers in the Ekman camp acknowledge that there can be considerable variation in the “gold standard” expressions expected for each emotion.

But a growing crowd of researchers argues that the variation is so extensive that it stretches the gold-standard idea to the breaking point. Their views are backed up by a vast literature review. A few years ago the editors of the journal *Psychological Science in the Public Interest* put together a panel of authors who disagreed with one another and asked them to review the literature.

“We did our best to set aside our priors,” says Barrett, who led the team. Instead of starting with a hypothesis, they waded into the data. “When there was a disagreement, we just broadened our search for evidence.” They ended up reading around 1,000 papers. After two and a half years, the team reached a stark conclusion: there was little to no evidence that people can reliably infer someone else’s emotional state from a set of facial movements.

At one extreme, the group cited studies that did not uncover a clear link between the movements of a person’s face and an internal emotional state. Psychologist Carlos Crivelli of De Montfort University in Leicester, England, has worked with residents of the Trobriand islands in Papua New Guinea and found no evidence for Ekman’s conclusions in his studies. Trying to assess internal mental states from external markers is like trying to measure mass in meters, Crivelli concludes.

Another reason for the lack of evidence for universal expressions is that the face is not the whole picture. Other things, including body movement, personality, tone of voice and changes in skin tone have important roles in how we perceive and display emotion. For example, changes in emotional state can affect blood flow, and this in turn can alter the appearance of the skin. Martinez and his colleagues have shown that people are able to connect changes in skin tone to emotions. The visual context, such as the background scene, can also provide clues to someone’s emotional state.



Faces alone only reveal so much about mood. See the next page for the full picture.

LANCE KING/HECTOR VIVAS/RONALDO SCHEMIDT/ROBYN BECK/GETTY IMAGES

MIXED EMOTIONS

Other researchers think the pushback on Ekman’s results is a little overzealous—not least Ekman himself. In 2014, responding to a critique from Barrett, he pointed to a body of work that he says supports his previous conclusions, including studies on facial expressions that people make spontaneously, and research on the link between expressions and underlying brain and bodily state. This work, he wrote, suggests that facial expressions are informative not only about individuals’ feelings but also about patterns of neurophysiological activation (see go.nature.com/2pmrjkh). His views have not changed, he says.

According to Jessica Tracy, a psychologist at the University of British Columbia in Vancouver, researchers who conclude that Ekman’s theory of universality is wrong on the basis of a handful of counterexamples are overstating their case. One population or culture with a slightly different idea of what makes an angry face does not demolish the whole theory, she says. Most people recognize an angry face when they see it, she adds, citing an analysis of nearly 100 studies. “Tons of other evidence suggests that most people in most cultures all over the world do see this expression is universal.”

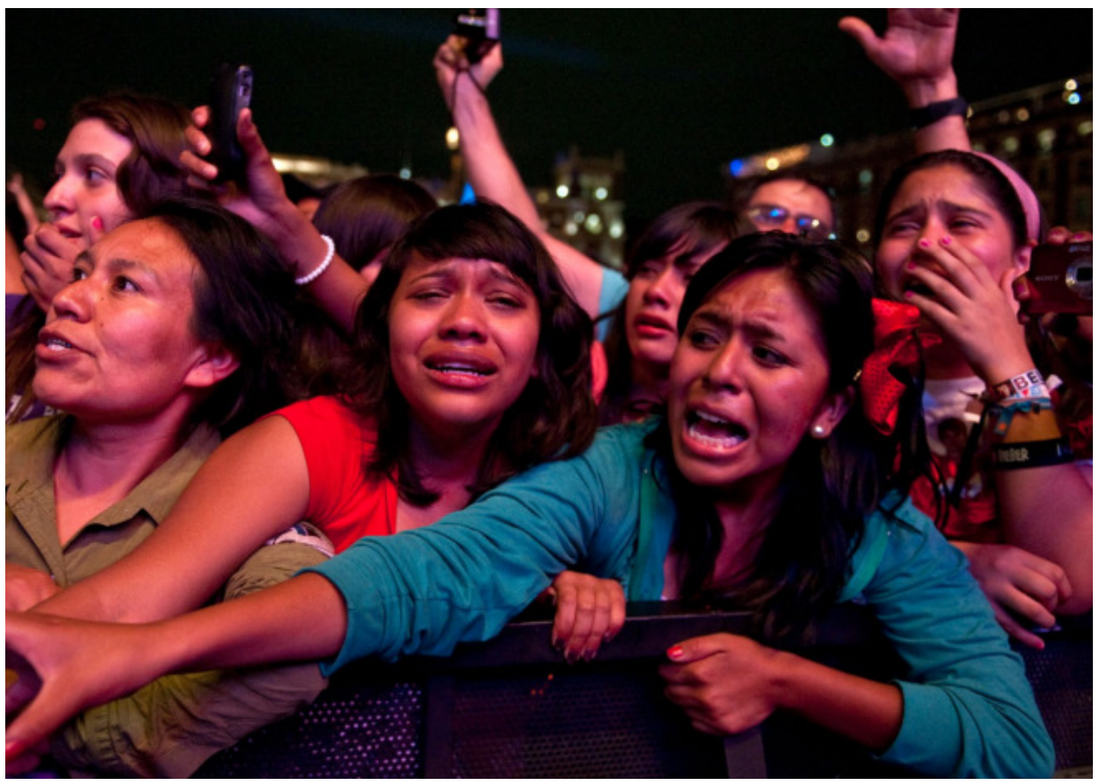
Tracy and three other psychologists argue that Barrett’s literature review caricatures their position as a rig-

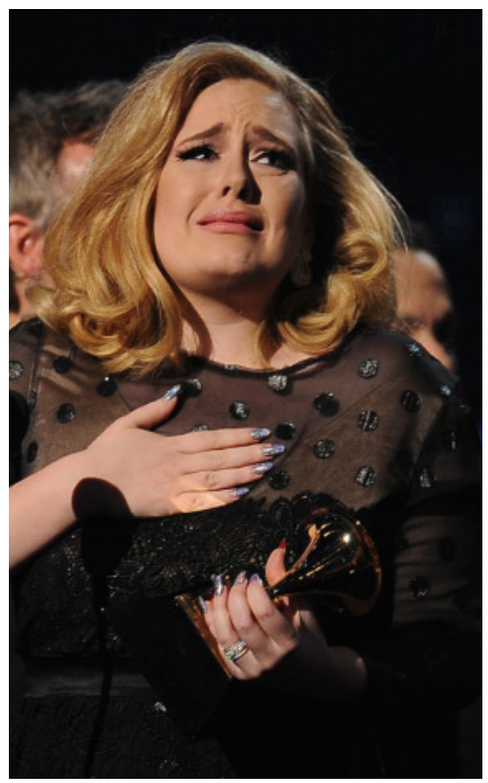
id one-to-one mapping between six emotions and their facial movements. “I don’t know any researcher in the field of emotion science who thinks this is the case,” says Disa Sauter of the University of Amsterdam, a co-author of the reply.

Sauter and Tracy think that what is needed to make sense of facial expressions is a much richer taxonomy of emotions. Rather than considering happiness as a single emotion, researchers should separate emotional categories into their components; the happiness umbrella covers joy, pleasure, compassion, pride, and so on. Expressions for each might differ or overlap.

At the heart of the debate is what counts as significant. In a study in which participants choose one of six emotion labels for each face they see, some researchers might consider that an option that is picked more than 20 percent of the time shows significant commonality. Others might think 20 percent falls far short. Jack argues that Ekman’s threshold was much too low. She read his early papers as a Ph.D. student. “I kept going to my supervisor and showing him these charts from the 1960s and 1970s, and every single one of them shows massive differences in cultural recognition,” she says. “There’s still no data to show that emotions are universally recognized.”

Significance aside, researchers also have to battle with subjectivity: many studies rely on the experimenter having labeled an emotion at the start of the test, so that the end results can be compared. Therefore, Barrett, Jack and others are trying to find more neutral ways to study emotions. Barrett is looking at physiological measures, hoping to provide a proxy for anger, fear or joy. Instead of using posed photographs, Jack uses a computer to randomly generate facial expressions, to avoid fixating on the common six. Others are asking participants to group faces into as many categories as they think are needed to capture the emotions or getting partici-





Clockwise, from top left: Basketball player Zion Williamson celebrates a dunk; Mexico fans celebrate a win in a World Cup group match; singer Adele wins Album of the Year at the Grammys in 2012; Justin Bieber fans cry at a concert in Mexico City.

LANCE KING/HECTOR VIVAS/RONALDO SCHEMIDT/ROBYN BECK/GETTY IMAGES

pants from different cultures to label pictures in their own language.

IN SILICO SENTIMENT

Software firms tend not to allow their algorithms such scope for free association. A typical artificial-intelligence (AI) program for emotion detection is fed millions of images of faces and hundreds of hours of video footage in which each emotion has been labeled and from which it can discern patterns. Affectiva says that it has trained its software on more than seven million faces from 87 countries and that this gives it an accuracy in the 90th percentile. The company declined to comment on the science underlying its algorithm. Neurodata Lab acknowledges that there is variation in how faces express emotion but asserts that "when a person is having an emotional episode, some facial configurations occur more often than a chance would allow" and that its algorithms take this commonality into account. Researchers on both sides of the debate are skeptical of this kind of software, however, citing concerns over the data used to train algorithms and the fact that the science is still debated.

Ekman says he has challenged the firms' claims directly. He has written to several companies—he will not reveal which, only that "they are among the biggest software companies in the world"—asking to see evidence that their automated techniques work. He has not heard back. "As far as I know, they're making claims for things that there is no evidence for," he says.

Martinez concedes that automated emotion detection might be able to say something about the average emotional response of a group. Affectiva, for example, sells software to marketing agencies and brands to help predict how a customer base might react to a product or marketing campaign.

If this software makes a mistake, the stakes are low—an advert might be slightly less effective than hoped. But some algorithms are being used in processes that could have a big impact on people's lives, such as in job interviews and at borders. Last year Hungary, Latvia and Greece piloted a system for prescreening travelers that aims to detect deception by analyzing microexpressions in the face.

"Are AI companies going to continue to use flawed assumptions, or are they going to do what needs to be done?"
—Lisa Feldman Barrett

Settling the emotional-expressions debate will require different kinds of investigation. Barrett—who is often asked to present her research to technology companies, and who visited Microsoft in February—thinks researchers need to do what Darwin did for *On the Origin of Species:* "Observe, observe, observe." Watch what people actually do with their faces and their bodies in real life—not just in the lab. Then use machines to record and analyze real-world footage.

Barrett thinks more data and analytical techniques could help researchers to learn something new, instead of revisiting tired data sets and experiments. She throws down a challenge to the tech companies eager to exploit what she and many others increasingly see as shaky science. "We're really at this precipice," she says. "Are AI companies going to continue to use flawed assumptions, or are they going do what needs to be done?"

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Why Don't People Care That More Men Don't Choose Caregiving Professions?

People attribute the lack of women in STEM fields to external factors but attribute the lack of men in helping professions to internal ones

By Scott Barry Kaufman

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Scott Barry Kaufman is a psychologist at Columbia University exploring intelligence, creativity, personality and well-being. In addition to writing the column Beautiful Minds for *Scientific American*, he hosts The Psychology Podcast and is author or editor of eight books, including *Wired to Create: Unraveling the Mysteries of the Creative Mind* (with Carolyn Gregoire) and *Ungifted: Intelligence Redefined*.

I GIVE A LOT OF TALKS TO EDUCATORS AROUND THE COUNTRY and am always fascinated by the gender imbalance. In a room full of 2,000 educators, I have to look closely to spot the men in the crowd. It's so striking to me, and yet no one seems to be talking about it. Why doesn't anyone care about this gender imbalance? After all, modern society seems to place a great deal of value on gender equality in occupational opportunities, at least when it comes to women. In recent years great strides have been made to remove barriers to women's advancement and representation in science, technology, engineering and math careers (STEM), as well as in leadership positions. For instance, the National Science Foundation has invested $270 million since 2001 to multiple initiatives supporting women in the sciences, and companies invest millions of dollars to support female leaders through programs such as the "10,000 Women" initiative by Goldman Sachs, which provides women entrepreneurs around the world with a business and management education, mentoring and networking, and access to funding.

In stark contrast, men's striking underrepresentation in health care, early education and domestic roles (HEED) has not increased, and even slightly decreased, between 1993 and 2013. Men remain particularly underrepresented in fields such as nursing (10 percent) and elementary education (14 percent), yet researchers, policy makers and the general public seem far less concerned in efforts to promote greater gender balance in these careers.

In a new study, social psychologist Katharina Block and her colleagues attempted to better understand why people might not prioritize gender equality in female-dominated careers relative to male-dominated careers. They found that people think very differently about gender imbalances in a career depending on whether the imbalance concerns an underrepresentation of women or an underrepresentation of men.

Across four studies, people consistently indicated greater support for social action to correct the gender imbalance in male-dominated as compared to female-dominated fields. This asymmetry in support for change was found both in people's explicit reports for social action as well as on a budget allocation task. In particular, the researchers found that people were willing to give $9 million more in funding to promote gender balance in male-dominated than in female-dominated fields.

Why such an asymmetry? Block and her colleagues examined the "lay theories" that people hold about the underlying reasons for gender disparities in each field. They found that people perceived internal factors (for example, lack of motivation, lack of ability) to be the main barrier to men's entry into female-dominated fields, whereas external factors (for example, discrimination, stereotyping) were seen as a larger factor in women's underrepresentation in male-dominated careers. It was precisely this tendency to see internal factors as the main barrier to men's entry into female-dominated fields that explained why people were less likely to support social change when it came to the underrepresentation of males in female-dominated fields.

Also, consistent with a "status value" perspective proposed by Alyssa Croft and her colleagues, the occupations in which men are extremely underrepresented (for example, nursing, elementary education) were viewed as lower in status and therefore less deserving of attention and social action toward change than STEM fields (for example, computer programming, electrical engineering) where women are extremely underrepresented.

Critically, the researchers were able to rule out the possibility that these findings were simply explained by cultural beliefs (for example, traditional gender role attitudes or political conservatism), demographic variables or differential salary opportunities. On average, both men and women were biased in their perception of different gender imbalances based on gender representation of the fields even after controlling for the earning potential of the fields.

Why is any of this important?

Across four studies, people consistently indicated greater support for social action to correct the gender imbalance in male-dominated as compared to female-dominated fields.

IMPLICATIONS

Of course, not all social inequalities are considered a problem, nor should they all be considered a problem. Yet these findings may have importance considering that group differences that are attributed more to external factors (for example, discrimination, stereotyping) than internal factors (low motivation or low ability) tend to receive more support for change, whereas when the underlying cause of a group difference is perceived to be the result primarily of internal factors, people tend to be more satisfied with the existence of the group difference and are more likely to justify existing inequalities.

Undoubtedly, there will be various ways that people will react to this. Some may look at this asymmetry as revealing the double standard we have for gender imbalances in different fields. They may point out how if someone (especially a man) argues that there may be internal reasons (motivation, lack of ability) why there is an underrepresentation of females in male-dominated fields, they can lose their job and be publicly shamed. But when it comes to understanding why there is an underrepresentation of males in female-dominated fields, people seem to be perfectly content reporting that a lack of motivation and ability are the main cause of the gender imbalance, justifying their lack of support for increasing representation of males in such fields.

Those who are upset by this double standard may even go further and say that the truth is that external reasons are way overrated as a cause for the gender imbalance in any field and that we should expect the gender imbalances we witness based on the average differences in values, temperament and ability of males versus females.

Others are sure to react that the lay perceptions are actually correct and that there is rightly more funding and resources directed toward correcting the gender imbalance in STEM fields than in HEED fields because of the historical oppression of women in these fields. These individuals may see nothing wrong whatsoever with the double standard, believing that the true state of affairs is that the underrepresentation of females in STEM fields really is primarily the result of external barriers, whereas men do not truly have as many external barriers to entering female-dominated professions.

I think that all of these extreme interpretations in themselves create a barrier to making important changes in society. The fact of the matter is that both internal and external factors play a role in women's and men's underrepresentation in careers dominated by the other gender. Research has found that personal values and discrimination are both related to women's lack of interest in STEM fields as well as men's lack of interest in HEED fields. Both internal and external factors matter for all genders!

Now, someone may counter that gender equality of outcomes in all fields (50–50) is an impossibility and will never happen even if we address all of the external factors because average differences in values (especially at the tails) will always create gender imbalances across fields.

Even if true (and the data are still out on this issue), I think that a very good case can be made for allocating resources toward increasing equality of opportunity and a sense of belonging for both males and females who have the motivation and ability to enter fields in which their gender is strikingly underrepresented.

TOWARD REAL EQUALITY

"If we're going to get to real equality between men and women, we have to focus less on women and more on elevating the value of care."
—Anne-Marie Slaughter

Much ink has been spilled discussing the need for greater equality of opportunity for women in STEM fields, but what would be gained by a fight toward greater equality of opportunity for men in HEED fields?

Quite a bit, actually!

For one, it is a fact that there are major labor shortages in teaching and nursing. Having more men enter these fields could help to solve those shortages. The labor shortages could be improved by the active recruitment of men rather than the pervasive recruitment efforts targeted almost exclusively to women. Block suggests that seeing a greater proportion of male role models in such fields might enhance men's own internalization of caring values and interest in female-dominated fields. I think that having more male role models in education could also be really important to young children who come from a single parent family and who are primarily raised by a mother.

In general, I think that we underestimate the importance of having caring adult male role models at school for all young boys. Author Peggy Orenstein conducted extensive interviews with more than 100 college and college-bound boys and young men of diverse backgrounds between the ages of 16 and 22.

As she observes in an interview on Fresh Air: "When I was doing the girl book, the kind of core issue with girls was that they were being cut off from their bodies and not understanding their bodies' response and their needs and their limits and their desires. With boys, it felt like they were being cut off from their hearts."

Orenstein notes that the boys she interviewed felt constrained by traditional notions of masculinity. Young boys would benefit from learning that the motivation to care for the welfare of others is not only linked to higher levels of life satisfaction and relationship satisfaction and is actually an essential trait to becoming an "alpha male," but that a communal motivation also affords viable job opportunities in a tight labor market.

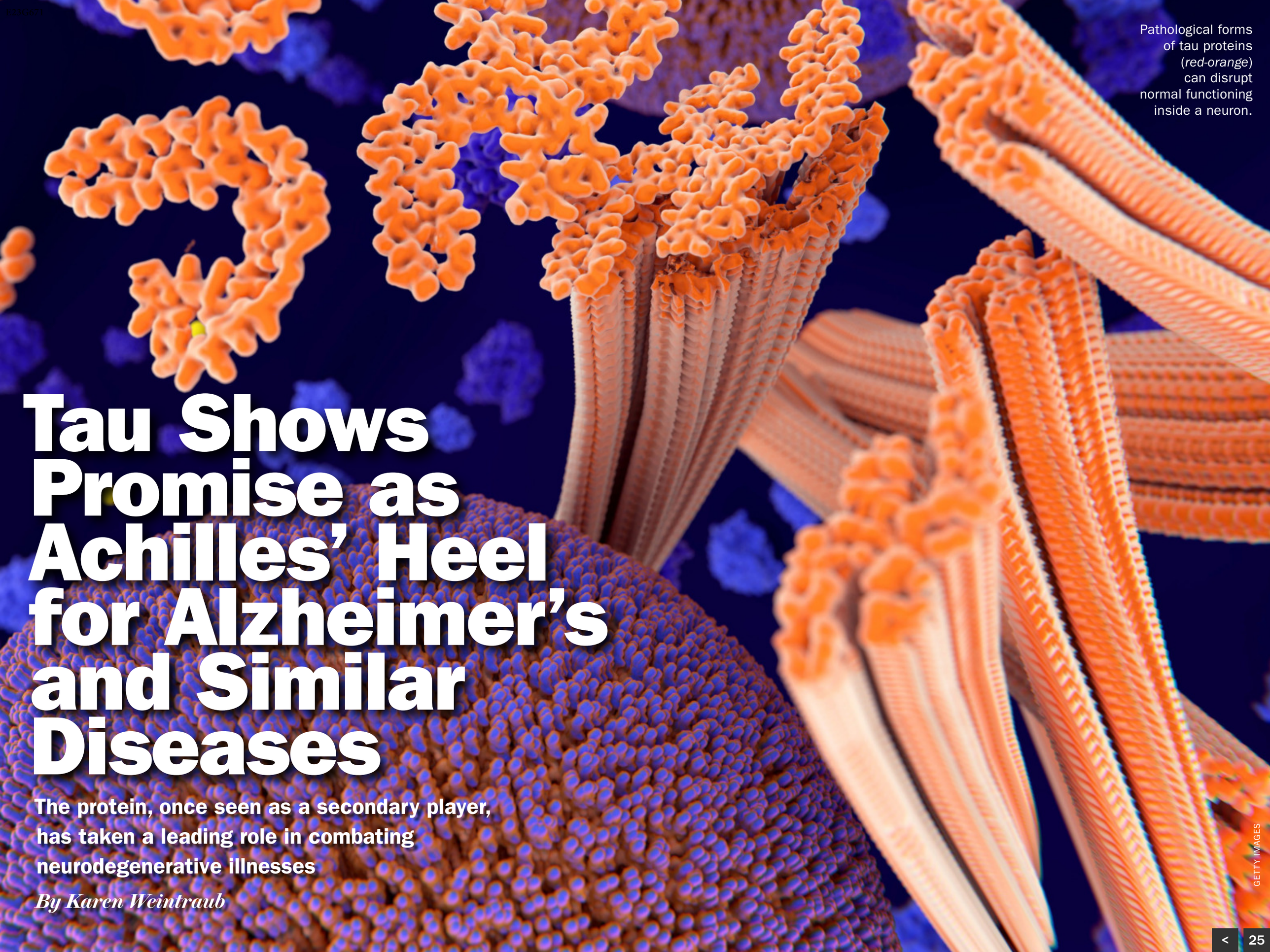
Men's increased participation in HEED fields would also likely benefit the overall gender equality of everyone in society. There is evidence that both women and girls benefit from seeing more men in nontraditional roles and occupations, enabling them to envision themselves in less traditional, complementary roles.

Finally, and perhaps most important, increasing male representation in HEED fields would boost the social status of such fields. According to "status value theory," men's higher status in society means that men's roles and careers are given higher status than those of women. As a result, people value male-dominated domains more than female-dominated domains.

One study found that when men were told that women score higher than men on an obscure trait called "surgency," men assumed this trait had less value to them personally. Increasing the social status of HEED fields would have the consequence of making these fields more attractive to men on average (men are much more driven by social status on average, and this becomes even more striking at the upper tail of ambition for social status).

Also—and this is often underdiscussed—I believe that increasing the social status of HEED fields would also reduce the discrimination many women face for entering HEED fields. It would empower women to enter caring professions and not feel like a failure or be shamed because they did not "lean in" to men's professions. As Ruth Whippman notes, women are constantly confronted with messages to "Lean In!", "Adopt power positions!", "Walk tall!", "Stop apologizing"! "Be assertive!" In other words, women are empowered when they are more like men.

Here's the thing: Women shouldn't have to feel successful only if they enter male-dominated professions, and men shouldn't have to feel successful only if they succeed in male-dominated professions. There is great value in entering a HEED profession, and the more we can create social change to support anyone who wants to enter a field in which their gender is underrepresented, the better off we will all be.



Pathological forms of tau proteins (*red-orange*) can disrupt normal functioning inside a neuron.

GETTY IMAGES

Tau Shows Promise as Achilles' Heel for Alzheimer's and Similar Diseases

The protein, once seen as a secondary player, has taken a leading role in combating neurodegenerative illnesses

By Karen Weintraub

Karen Weintraub is a freelance health and science journalist who writes regularly for the *New York Times*, *STAT* and *USA Today*, among others.

ALZHEIMER'S DISEASE has long been characterized primarily by the buildup of two proteins in the brain: beta-amyloid and tau. Decades of focus on beta-amyloid has failed to significantly help patients. So researchers are turning more attention to the second member of the duo.

"Amyloid hasn't been as successful as we hoped," says Jang-Ho Cha, an executive overseeing translational medicine work at pharmaceutical giant Novartis. "Tau has really emerged as a [potentially] more relevant target."

Tau was long thought to be a secondary actor. Amyloid plaque builds up first, largely outside of neurons, followed by tau tangles—filaments of the tau protein—which clog their insides. But research has found that people can continue to function well with amyloid in their brain. It is only when toxic tau starts to spread that people begin confusing "breakfast" with "baseball," forgetting not just where they left their keys but how to use them.

Now scientists in labs across the world are trying to better understand the role of tau in neurodegenerative diseases and to figure out ways to track and tame it before brain cells—and families—suffer.

Normal tau helps to assemble and maintain the structural scaffolding of brain cells. But various molecular changes can cause the protein to turn toxic and wreak havoc. Toxic tau misfolds like a shoelace tied in a mess of double knots instead of a neat bow. In this contorted state, tau appears to cause the misfolding of other tau proteins, which then clump together. "We think tau is an important target, certainly, in Alzheimer's and potentially other diseases," Cha says. "There certainly a lot of smoke around this fire."

A study published in January in *Science Translational Medicine* showed that where tau builds up in a living brain predicts which areas of the organ will degenerate. This finding suggests that tracking tau over time is feasible and useful, says Anthony Fitzpatrick, an assistant professor of biochemistry and molecular biophysics and a principal investigator at Columbia University's Zuckerman Institute, who was not involved in researching the paper.

In Fitzpatrick's own work, he uses an imaging technique called cryogenic electron microscopy (cryo-EM), which has 10 times the resolution of standard electron microscopy. His research shows that tau tangles form a distinctive shape that is always the same within a single patient and also varies in each of the several diseases it can cause. Alzheimer's tangles look different from those in a patient with frontotemporal dementia. "Each tauopathy has a unique strain particular to each disease," he says, noting that toxic tau is also involved in progressive supranuclear palsy, corticobasal degeneration and chronic traumatic encephalopathy, which affects football players and soldiers. Other neurodegenerative ailments, such as Parkinson's disease, are associated with different toxic proteins.

But it is not yet clear whether these different tau shapes will matter, Fitzpatrick says. Any effective tau treatment may need to be delivered before these filaments develop their distinctive form, he and others say. Researchers are not sure whether an antibody designed to go after one type of tau will stop others as well.

The main problem in deciding which antitau strategy to adopt is that scientists do not yet understand the protein very well. Cryo-EM, for example, provides high-resolution images, but it captures brain tissues from cadavers. So researchers only know what tau filaments look like at the end stage of disease, not as they are beginning to clog brain cells, says Michel Goedert, a research group leader at the MRC Laboratory of Molecular Biology in England.

Researchers have only begun to understand what causes tau to turn toxic. A number of recent studies have suggested that the protein may take an aberrant turn after an inflammatory trigger, such as gum disease or an infection, or different conditions, such as "leaky gut," in which microbes and other particles leak from the digestive system into the nervous system. George Tetz, a consultant at the Human Microbiology Institute, an independent nonprofit research organization in New York City, recently published a study showing that DNA can spur the seed-

ing of toxic tau. “We strongly believe that the starting point for different neurodegenerative diseases is the appearance of certain bacterial DNA in the central nervous system,” he says.

If this theory proves true, it suggests there might be ways to stop the spark of an infection or another untoward event from igniting the raging fire of Alzheimer’s. But it is still very early days, Goedert notes, and more work needs to be done.

Another strategy—besides waylaying a toxic wrong turn—may be to figure out how to address tau buildup. Getting rid of the tangles might slow the progression of Alzheimer’s—or make things worse, explains Einar Sigurdsson, a professor in the departments of neuroscience and physiology and of psychiatry at the New York University Grossman School of Medicine.

There are now at least 20 compounds against tau in clinical trials, including nine antibodies and two vaccine candidates, Sigurdsson says. “No one knows if this is going to work yet,” he adds. So far three antibody trials have been discontinued, and the companies have not been very forthcoming about the reasons, Sigurdsson says. He suspects that in two of the cases, the company was aiming at the wrong target: the drugs were designed to remove tau that is outside of neurons, he says, which is not a primary factor in the non-Alzheimer’s tauopathies that were being treated.

Attacking the tau tangles might actually be detrimental for brain cells, Sigurdsson says. The neurons that have tangles inside of them are still alive, while nearby neurons have been killed off. Targeting the tangle might kill these still functioning neurons, he explains. “If you want to clear the tangle, I think that you’re asking for trouble,” says Sigurdsson, who has spent the past two decades developing ways to go after toxic tau. A better approach, he says, would be to prevent the tau buildup from happening in the first place.

“I would argue that, in general, prevention is probably the way to go. Once people have symptoms, it may be too late.”
—Michel Goedert

Another ongoing challenge has been figuring out how to tell whether toxic tau is present or whether its buildup is getting worse. If it is true that drugs are most effective when they reach the brain before much damage has been done, then early detection is crucial.

A relatively new scanning technology called tau positron-emission tomography (tau PET) can identify signs of tau tangles in the brain and potentially diagnose disease based on whether the protein can be detected and in what form. But Sigurdsson warns that the tau PET technology, not yet approved for clinical use, remains largely untested. The first-generation tau PET screens do not recognize the protein in all diseases that involve aggregated tau. New detection approaches being tested, using fragments of antibodies to bind to tau, have the potential to be even more specific, he says.

Goedert notes it is essential to find a reliable way to identify people most likely to get Alzheimer’s—through tau PET or the detection of some other biological marker. If, when he was 40 years old, someone had offered him a drug therapy that promised to prevent Alzheimer’s decades later, he probably would not have taken it, Goedert says. But if he had been told, at 40, that a biomarker indicated he was at high risk of eventually developing Alzheimer’s, he says he would have opted for the therapy. And preventing any neurodegenerative disease is likely to be easier than treating it. “I would argue that, in general, prevention is probably the way to go,” Goedert says. “Once people have symptoms, it may be too late.”

And even if there is a tau-based treatment, it may only be part of the answer, researchers agree. Combination therapy—perhaps attacking both amyloid and tau simultaneously—may be the only way to beat back Alzheimer’s once both tau filaments and beta-amyloid plaques have begun to accumulate, Sigurdsson says. The government has not allowed combination-drug trials so far—each drug has had to show some effectiveness on its own before it is allowed to be combined with another therapy. But Sigurdsson thinks that such combination approaches are likely to be needed and that trials will be permitted eventually. “That’s where we’re heading,” he says.

Despite the long list of failed therapies, Goedert says he remains optimistic that an effective treatment for Alzheimer’s will eventually be found. There are new ideas being tested—and there is always the chance that luck will strike, he says. Everything we know now, he notes, has been discovered in the past 35 years or so. What keeps him going, Goedert says, is the hope that his research will eventually benefit people with the disease—or prevent them from ever developing it at all. “The fact that nothing has worked well so far must mean that we don’t know enough,” he says.

Sigurdsson agrees that tau research will eventually pay off. “I’m optimistic that, with all these different targets that are out there, we will have something, at least, that will slow progression—hopefully within the next 10 years,” he says.

Ashten Duncan is a third-year medical student OU-TU School of Community Medicine in Oklahoma. He holds an M.P.H. with an interdisciplinary focus and is a researcher in the areas of positive psychology and well-being.

BEHAVIOR & SOCIETY

How I Broke the Cycle of Stress

A technique called goal diversification turned out to be surprisingly effective

BULAT SILVIA GETTY IMAGES

Most of us can likely relate to this experience: you put all that you have into your work for prolonged periods of time and feel physically and mentally exhausted by the end. This common phenomenon is known simply as stress, a natural reaction to facing increasing demands without the necessary resources to meet them. In moderation, stress on our bodies and minds can elicit beneficial responses that enhance well-being, such as increased memory formation. As most of us know, however, there is often an imperceptibly fine line between advantageous stress and toxic stress from being exposed to too much for too long. Sadly, we often cannot control the balance between the two.

Whether it is on social media or our go-to news channels, we hear a lot about stress and deteriorating well-being in our country. In fact, this reality has become so pervasive that some of us probably normalize much of it, writing off the downstream effects of stress as just part of modernity. For adults working in fields associated with above-average levels of psychosocial stress, a vicious cycle can manifest wherein unmitigated chronic stress breaks us down, drains us of our resilience, narrows our perception of what makes life worth living, and leaves us feeling hollow. This whole process is often encapsulated in a single word: burnout.

For some: burnout, schm-urnout! Critics of this concept tend to point out how nebulous it sounds even when someone offers up the definition. A different, more integrated way of understanding the long-term effects of chronic stress on the whole person is a principle called allostatic load. While there is a lot that happens to our bodies when we experience prolonged stress, the central idea of allostatic load theory is that if you apply enough force for long enough on someone without destroying her, you will fundamentally change the way she functions and responds to future stressors through a process called maladaptation.

As a medical student, I see this problem of maladaptation frequently, both in trainees and in trained physicians. Research demonstrates this trend in the alarming number of physicians who quit practicing medicine every year. I think it is because we are so deeply focused on trying to carry out a complex mission of providing care to patients. In our efforts to do this, we often focus on one large goal after another, not allowing ourselves to have much latitude. Whether it is taking a standardized examination or meeting documentation requirements, setting and pursuing less diverse goals like this is problematic: any barriers to goal attainment will cause much more stress than it would if we had other irons in the fire.

Recently major news sources and professional organizations have cited emerging evidence of epidemic levels of burnout among physicians in the U.S. While this is not unique to physicians, there is perhaps a pronounced susceptibility in this population because of how purpose-discordant tasks like navigating electronic medical records hinder progress toward meaningful goals like direct patient care. While much work is being done to streamline these systems-level processes, not enough is being done to examine what goals are not being achieved and why they exist on a cultural level.

People can break their cycles of stress and even flourish outside of the work they regularly do by incorporating new and different goals in their day-to-days.

Doing what is in the best interest of the patient is at the heart of the Hippocratic oath, which represents a major theme in physician culture. The oft-overlooked connection between personal well-being and quality of patient care has an empirical basis: physicians who experience chronic stress and burnout are more likely to make errors that result in disease, disability or death. What is ironic is that physicians who push themselves to deliver the best care possible may be doing so at the expense of this goal!

So, what do we do about this?

We are making strides toward rectifying issues ingrained in health care systems, but progress toward shifting the culture to uphold our mission of optimal care is less robust. Research in positive psychology and organizational dynamics has shown that goal diversification is associated with subjective well-being. This means the act of setting and pursuing different kinds of goals that are meaningful to you is associated with less stress, which decreases the impact of allostatic load on the body and mind. Studies on intervention strategies to promote goal diversification have included mindfulness meditation, hope building and active self-reflection activities.

Hope theory describes how thinking about one's motivation and perceived capability of attaining a goal and about the pathways leading to that goal influence how we set and go after what is important to us. It also suggests that goals, especially smaller ones, can serve as pathways to other larger goals. This theoretical framework is further supported by research showing that goal setting promotes behavioral change, which can improve well-being even in the context of major depression. Moreover, the act of setting goals, particularly those that are diverse and of high personal value, increases productivity at work, which may subsequently help to alleviate stress by decreasing the demands of one's work environment.

One of the most significant hurdles in health care is that clinical practice generally has a substantial workload and numerous legal constraints that force clinicians to stick to a script. Thus, if the current practice environment largely opposes per-

sonal goal setting and goal diversity, how do we work around this? National research on health care quality offers some ideas: decreasing daily workplace activity, adopting collaborative care models and allowing employees to work on quality-improvement projects. A common thread in all of these ideas is that health care providers can focus on more than just the same repetitive goals, which allows them to feel that they are fulfilling their professional purpose more often. Additionally, this method can limit stress and prevent much of the maladaptation that comes with it.

People can break their cycles of stress and even flourish outside of the work they regularly do by incorporating new and different goals in their day-to-days. Our best shot at getting ahead of the problems that stress produces in our country is to look at where our finite energy is going and ask the tough questions: "Why?" and "At what cost?" We are not machines; it is not sustainable for us to push ourselves at the cost of our well-being. Whether it is in medicine or any other field, we must ensure that our cultures nurture goal diversity and being more than just your work because, at the end of the day, stress occurs when we feel that we lack the resources to meet the demands around us.

Jennifer Beer is a professor of psychology at the University of Texas at Austin.

BEHAVIOR & SOCIETY

The Inconvenient Truth about Your "Authentic" Self

To actually feel authentic, you might have to betray your true nature

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Everyone wants to be authentic. You want to be true to yourself, not a slavish follower of social expectations. You want to "live your best life," pursuing your particular desires rather than falling in line with whatever everyone else thinks happiness requires. Studies have even shown that feelings of authenticity can go hand in hand with numerous psychological and social benefits: higher self-esteem, greater well-being, better romantic relationships and enhanced work performance.

But authenticity is a slippery thing. Although most people would define authenticity as acting in accordance with your idiosyncratic set of values and qualities, research has shown that people feel most authentic when they conform to a particular set of socially approved qualities, such as being extroverted, emotionally stable, conscientious, intellectual and agreeable. This is the paradox of authenticity: to reap the many benefits of feeling authentic, you may have to betray your true nature.

From a psychological science standpoint, a person is considered authentic if she meets certain criteria. Authentic people have considerable self-knowledge and are motivated to learn more about themselves. They are equally interested in understanding their strengths and weaknesses, and they are willing to honestly reflect on feedback regardless of whether it is flattering or unflattering.

Most important, authentic people behave in line with their unique values and qualities even if those idiosyncrasies may conflict with social conventions

or other external influences. For example, introverted people are being authentic when they are quiet at a dinner party even if social convention dictates that guests should generate conversation.

But a number of studies have shown that people's feelings of authenticity are often shaped by something other than their loyalty to their unique qualities. Paradoxically, feelings of authenticity seem to be related to a kind of social conformity.

In these studies, people are first asked to characterize the qualities that reflect their true self. Afterward, they complete assessments—daily or once a week over a period of multiple weeks—about the extent to which their behavior reflected their qualities and the extent to which they felt authentic. We would expect that people feel most authentic on days where their behavior closely matches their unique pattern of values and qualities.

Consider two people who differ in the degree to which they avoid quarreling with other people. Let's say that Jane is agreeable, and John is antagonistic. On a day where each quarrels with someone, Jane would be expected to report feeling less authentic than John because she has engaged in a behavior that is inconsistent with her idiosyncratic qualities.

Instead research finds that people report feeling most authentic when their behavior conforms to a specific pattern of qualities: namely, when they are extroverted, emotionally stable, conscientious, intellectual and agreeable. That is, we feel most authentic when we act like a cross between the perfect party guest and the perfect co-worker. Therefore, despite their personality differences, research suggests that both Jane and John would report feeling inauthentic on a day where they quarrel with someone.

In our lab and other labs that study authenticity, we tend to study people from countries where parenting practices and institutions play a role in reinforcing behaviors that are socially outgoing, even-keeled, dependable, competent and pleasant to others.

Research has shown that we view people as less than fully human when they fail to conform to societal conventions. For example, people with soiled clothes do not conform to societal conventions surrounding hygiene, and they tend to be treated as less than completely human.

So, when it comes time to actually make a judgment about our own authenticity, we may use criteria that are closer to how we judge the authenticity of an object such as food. A passion fruit tiramisu may be unique, but the authenticity of tiramisu is judged by its conformity to a conventional recipe. Similarly, it appears that the more we conform to social conventions about how a person should act, the more authentic we feel.

We want to believe that authenticity will bring us benefits. It's not surprising that businesses such as Microsoft, BlueCross BlueShield, and Gap have worked with consultants to leverage authenticity in the workplace. But until we learn more about whether being authentic reaps the same benefits as feeling authentic, we are left with a tough decision between loyalty to our true selves and conformity to social convention.

Charles Zanor is a psychologist practicing in Connecticut.

COGNITION

Living with No Sense of Direction

For those who have developmental topographical disorientation, ordinary travel is extraordinarily difficult

We all know people who say they have "no sense of direction," and our tendency is almost always to minimize such claims rather than take them at full force.

Yet for some people that description is literally true and true in all circumstances: If they take a single wrong turn on an established route, they often become totally lost. This happens even when they are just a few miles from where they live.

Ellen Rose had been a patient of mine for years before I realized that she had this lifelong learning disability.

I was made aware of it not long after I moved my psychology office from Agawam, Mass., to Suffield, Conn., just five miles away.

I gave Ellen a fresh set of directions from the Springfield, Mass., area that took her south on Interstate 91 to Exit 47W, then across the Connecticut River to Route 159 in Suffield. I thought it would pose no problem at all for her.

A few minutes past her scheduled appointment time she called to say that she was lost. She had come south on Route 91 and had taken the correct exit, but she got confused and almost immediately hooked a right onto a road going directly north, bringing her back over the Massachusetts line to the town of Longmeadow.

She knew this was wrong but did not know how to correct it, so I repeated the directions to get on 91 South and so on.

GETTY IMAGES

Minutes passed, and then more minutes passed, and she called again to say that somehow she had driven by the exit she was supposed to take and was in Windsor, Conn. I kept her on the phone and guided her turn by turn to my office.

When I asked her why she hadn't taken Exit 47W, she said that she saw it, but it came up sooner than she expected so she kept going.

This condition—developmental topographic disorientation (DTD)—didn't even have a formal name until 2009, when Giuseppe Iaria reported his first case in the journal *Neuropsychologia*.

To understand DTD, it is best to begin by saying that there are two main ways that successful travelers use to navigate their environment.

The first is to follow a prescribed route from here to there. Cognitive psychologist Barbara Tversky describes route navigation as a series of paths and choice points that is basically egocentric: it is constructed for the purpose of reaching one particular goal from a fixed starting point, and the entire journey is explained from the point of view of the traveler.

Start here. Go straight for one mile and take a right onto Elm Street. When the road splits, go toward the flagpole and follow that road over the bridge. Go to the first traffic circle and take the second exit. The restaurant is two miles down the road on the left.

The second navigational strategy involves a bird's-eye view—a map—of the general area.

Maps are overviews, "surveys of a space of possibilities," that lay out a variety of possible paths. Maps almost always rely on cardinal directions, usually east-west and north-south, that anchor them to a larger space.

When we use a map to get somewhere, it is up to us to figure out the best route, or the array of alternatives, for ourselves.

So how does this work out in the real world?

In her 2019 book, *Mind in Motion,* Tversky acknowledges that most of us do not carry a file drawer of maps in our heads.

Instead we use a combination of methods to get where we are going: part turn-by-turn directions, part bird's-eye view, and part general map-like information (*it's somewhere near the center of town; we'll be traveling toward Omaha; the midday sun is on our left, so we are still heading west*) and helpful landmarks.

For this reason, Tversky refers to our wayfinding plans not as "cognitive maps" but as "cognitive collages," and her research demonstrates that when we spontaneously impart directions to another person we almost always use a stitched-together description.

But it is important to note that most navigational directions of moderate complexity depend in part on the ability to understand a map perspective.

Sometimes maps just make for better directions, but they are essential if we make a mistake and have to figure out how to correct our course.

The problem for Ellen is that she is not able to create a bird's-eye view on her own and, likewise, can't really make good use of one when it is provided by others.

Like other people with DTD, she can follow a route in pieces, but it never becomes part of a larger spatial understanding. That's because she does not have a larger spatial understanding of her environment.

A couple of years ago, for example, Ellen was driving in the town of West Springfield and unintentionally wound up crossing the Connecticut River into Springfield. She landed on Carew Street, only one mile from the hospital where she worked and two and a half miles from Winchester Square, where she grew up.

Lacking even a sketchy map perspective of that part of town, she could not establish her bearings and did not know where to turn. So she drove around randomly, as if she was a stranger in a strange place. Fortunately, she eventually spotted a landmark close to the bridge that crossed the river back into West Springfield.

This experience was not a fluke. When I asked Ellen to indicate the relative positions of Holyoke, Granby and Belchertown on a blank sheet of paper, her rendition was totally wrong. This in spite of the fact that the towns line up one after the other on a 13-mile stretch of U.S. Route 202, which is well known to her.

I asked her to draw a diagram of the second floor of the house she shares with her daughter and son-in-law. It was a difficult task for her (she lives on the first floor but is very familiar with the second).

She described her effort not as a bird looking down from above but as a spider crawling across the paper tracing a route from one room to the next.

Like dyslexics who learn how to adapt to a world of street signs, restaurant menus and official forms, people with DTD learn how to navigate

in their environment without having a mental blueprint of where they are going.

For 20 years Ellen was able to function successfully as a school bus driver by relying solely on a route strategy. She carried detailed notes with her every day, consulted them religiously and added little mnemonics to keep herself on track.

Ellen has always wondered what was wrong with her. She knew that when others ascribed her problems to simply not paying attention they were mistaken. She worried that her problems traveling might be a sign of something more ominous than just getting lost easily but had no idea what that might be.

Finding out that she had developmental topographic disorientation was a relief. Knowing that something has a name can be a liberating experience. All of a sudden it is a thing, a concept with defining characteristics and boundaries. It is, in a way, a kind of map.

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*.

Eyebomb Your Brain

How googly eyes hack your visual circuits

In January 2017 Adam decided that the six-month Scandinavian winter had lasted for too long already, and he must do something—anything—to combat his boredom. So as one does, he bought himself a bunch of googly eyes and stuck them all over his hometown of Uppsala, Sweden, to the amusement of passersby.

According to the Googly Eyes Foundation, which has the noble mission of spreading the trend "all over the world," eyebombing is a form of urban art, consisting of sticking googly eyes "onto an inanimate object in the public sphere, in a way that cleverly lends the object the appearance of a living creature." The movement, which has been around for more than a decade, has reached countless metropolitan locations, including the streets of Paris, London, and Sofia, Bulgaria, where the artist Vanyu Krastev searches for "things that are broken, ruptured, punctured, tangled, crumbling or twisted" as the best candidates for eyebombing.

Whereas the practice of eyebombing may not suit everybody's taste, the anthropomorphic illusions that result are remarkably powerful. Why

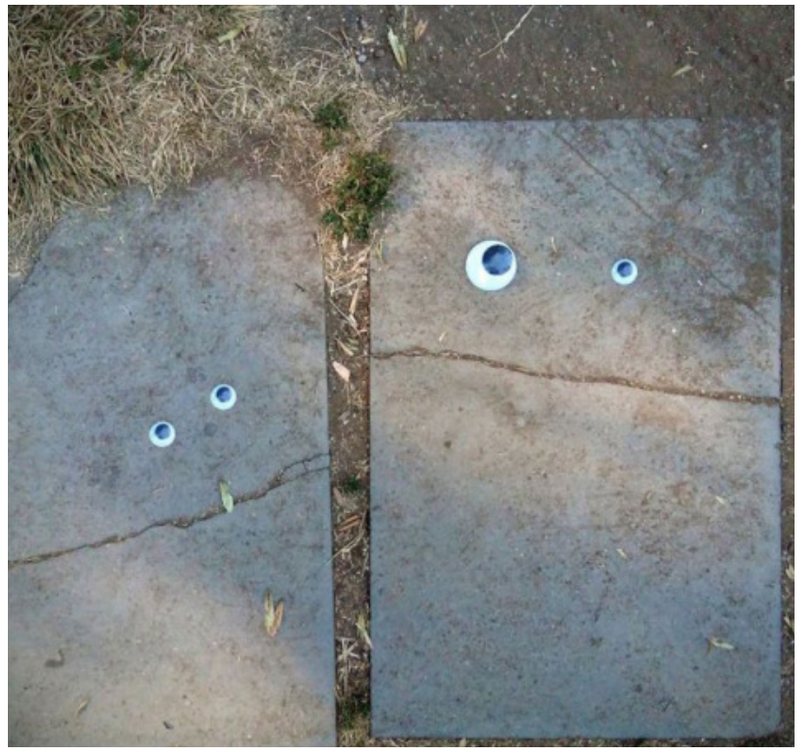
VANYU KRASTEV

should a mere pair of googly eyes change a tea kettle into an Emperor penguin or transmute a tree trunk into a bewildered, long-nosed man?

The answer lies both in our brain's ability to extract meaningful—though not necessarily accurate—information from the endless chaos that bombards our senses, as well as in our visual system's obsession with faces and gazes. Pareidolia, our peculiar ability to detect faces in water stains, clouds and even grilled cheese sandwiches, arises from our exquisitely sensitive face-detection neurons, located in a specialized brain region called the fusiform gyrus. Damage to this area results in face blindness, or prosopagnosia, which in the most severe cases makes sufferers unable to recognize themselves in pictures and even mirrors.

In the healthy brain, face-detection circuits are finely tuned to eyes and eye-shaped objects. Not long after birth, babies display strong interest in cartoon faces consisting of eyes and mouths only. Similarly, eye-tracking experiments reveal that we do not observe people's faces in general, but we direct our gaze most intensively to the eyes and mouths of those around us.

It follows that googly eyes—no matter how cartoonish—generate so much activation in our face-detection circuits that the ingenious addition of a few cracks and splotches (on a lamppost, say, or on a brick wall) suffices to complete our perceptual experience of an expressive face. Which goes a long way to explain why the character Forky from *Toy Story 4* is not only compelling but also instantly believable.



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