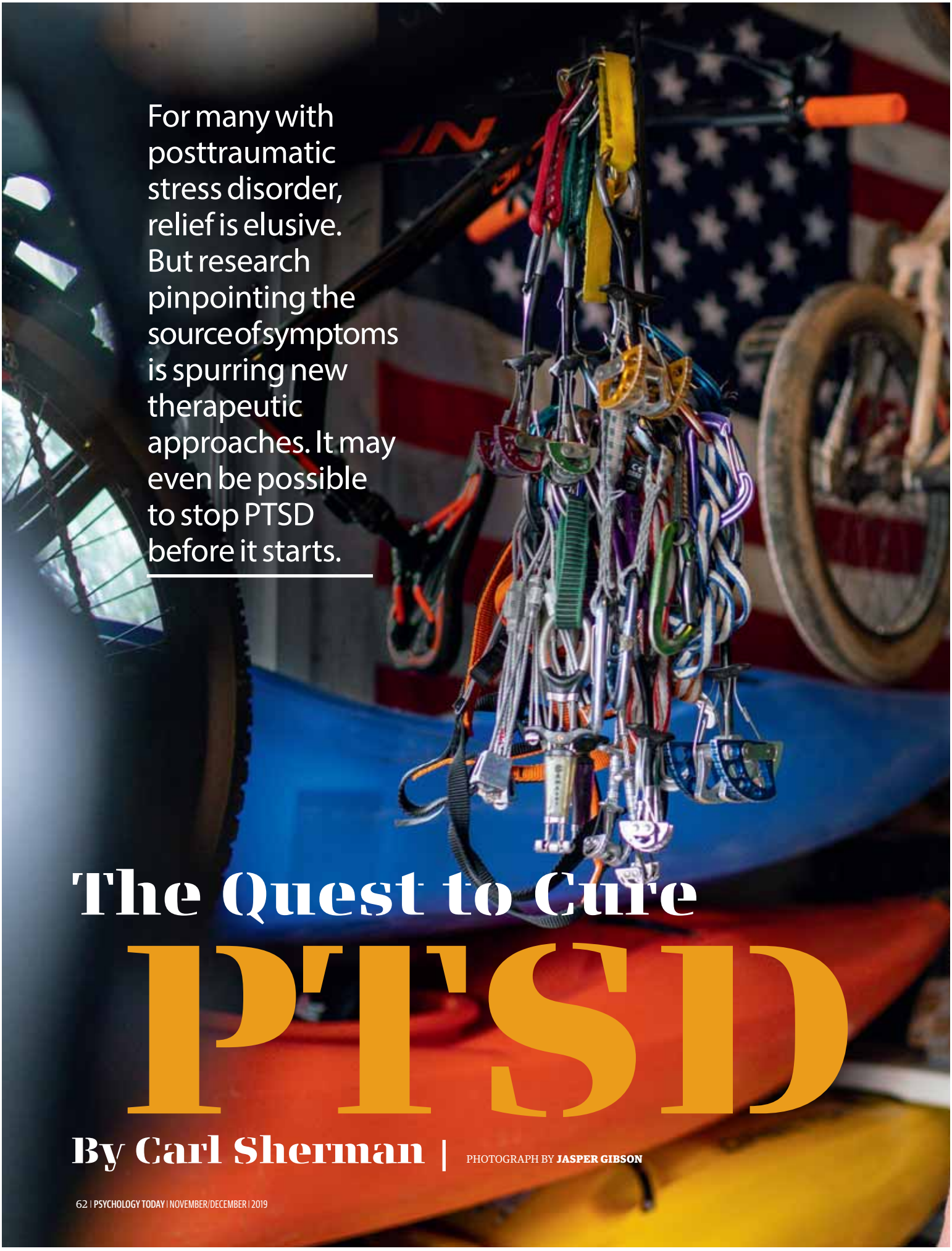
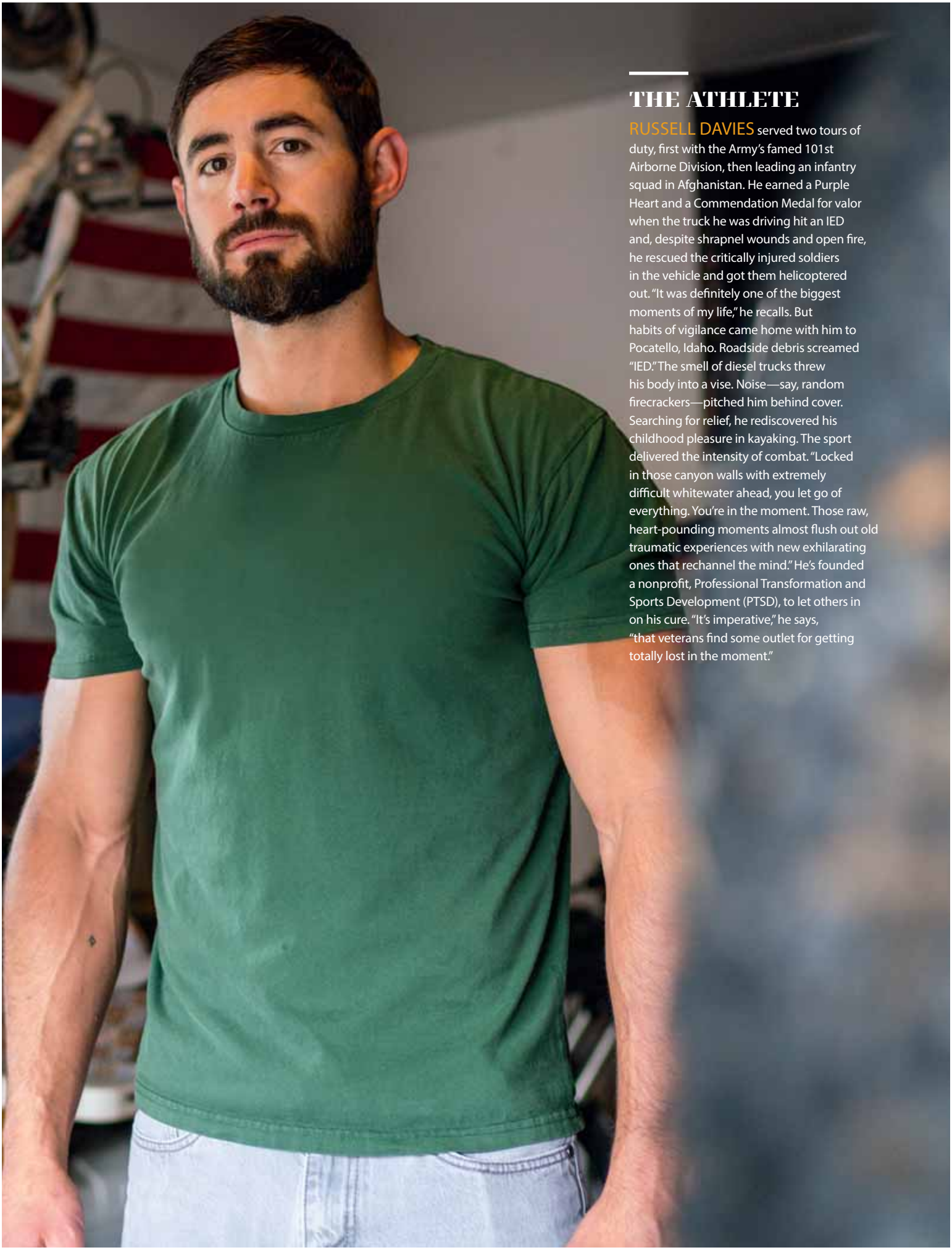


For many with posttraumatic stress disorder, relief is elusive. But research pinpointing the source of symptoms is spurring new therapeutic approaches. It may even be possible to stop PTSD before it starts.

The Quest to Cure PTSD

By Carl Sherman | PHOTOGRAPH BY **JASPER GIBSON**



THE ATHLETE

RUSSELL DAVIES served two tours of duty, first with the Army's famed 101st Airborne Division, then leading an infantry squad in Afghanistan. He earned a Purple Heart and a Commendation Medal for valor when the truck he was driving hit an IED and, despite shrapnel wounds and open fire, he rescued the critically injured soldiers in the vehicle and got them helicoptered out. "It was definitely one of the biggest moments of my life," he recalls. But habits of vigilance came home with him to Pocatello, Idaho. Roadside debris screamed "IED." The smell of diesel trucks threw his body into a vise. Noise—say, random firecrackers—pitched him behind cover. Searching for relief, he rediscovered his childhood pleasure in kayaking. The sport delivered the intensity of combat. "Locked in those canyon walls with extremely difficult whitewater ahead, you let go of everything. You're in the moment. Those raw, heart-pounding moments almost flush out old traumatic experiences with new exhilarating ones that rechannel the mind." He's founded a nonprofit, Professional Transformation and Sports Development (PTSD), to let others in on his cure. "It's imperative," he says, "that veterans find some outlet for getting totally lost in the moment."

As a 21-year-old tank commander in the Israel Defense Forces, Yuval Neria saw comrades and close friends badly hurt and killed in the 1973 Yom Kippur War. He himself suffered serious injury when his tank was hit, but that didn't keep him from taking command of other tanks, for which he received the Medal of Valor, Israel's highest combat award. He served again in 1983.

His experience on the Sinai front in 1973 vividly informs *Fire*, a war novel he wrote that captures the terror, courage, frustration, and confusion of battle. It also decreed his life's work.

"The Yom Kippur War taught me a lot about the devastating effect of severe combat," says Neria. "I understood fear very well, extreme fear, fear for your life," he says. "I knew a lot of people who eventually developed PTSD; I felt very connected to them, I wanted to be involved." He became a clinical psychologist specializing in trauma, then a researcher probing its roots. In 2001, in the immediate wake of the World Trade Center attacks, New York's Columbia University recruited him to head its Research and Treatment Program for PTSD.

He saw it as "an opportunity to follow what I'd felt was my destiny because of my experience in war." Neria never had post-traumatic stress disorder, but "what I carry with me, in addition to the horror and the fear of war, is an understanding of what patients are going through and a commitment to their treatment."

War, of course, is not the only experience that stamps the brain so powerfully that it remains constantly vigilant to threats, sees them where they may not exist, and fetches memories of fearful events so readily and vividly they overwhelm everyday activities. Nor is it the sole catastrophe that turns up the emotional torment at night, taunting sleep with the faces or cries of children, or spouses, or comrades who could not be saved from harm.

Fires, hurricanes, plane crashes, motor vehicle accidents, sexual abuse—any sudden, violent disruption, even a life-threatening illness like cancer—can leave a mark. And so Neria has conducted studies not only of veterans and prisoners of war and civilians under missile attack but also of earthquake survivors, those who've endured sexual assault, people who lost loved ones on 9/11, and those directly exposed to the 9/11 attacks in New York City.

At Columbia, Neria is focused largely on the neural mechanisms underlying PTSD. His work spotlights areas of the brain involved in identifying threats and storing memories of fearful events. Neria and colleagues have pinpointed abnormalities in how these areas look, how they work, and especially how they fail to work together.

From his ongoing studies, and those of many other researchers, effective treatments are emerging. They target specific biochemical processes and brain circuits.

Not all of the treatments are new. Exposure therapy, for example, has been around for decades, but combined with targeted biological treatments involving specific drugs and delivered in novel ways, it promises relief for the nearly 50 percent of sufferers left behind by current approaches, their whiplash reactivity driving them to withdraw from the world, or to navigate it with suspicion or anger, or to numb themselves with substances that exchange one kind of pain for another. There is also great new hope that there are ways to prevent PTSD from ever occurring.

Three Months, Three Years—or Forever

THE EXISTENCE OF PTSD was formally recognized in 1980, when it was first included in psychiatry's *Diagnostic and Statistical Manual*, then in its third edition. The condition, however, has been around likely since the first hunter was mauled by a lion or the first temblor shook the earth.

PTSD is a response to experiencing or witnessing an event or series of events involving the threat of death or serious bodily harm. People with PTSD suffer from classic anxiety symptoms, like insomnia and worry, and are often hypervigilant—constantly alert to possible dangers. They characteristically have an exaggerated startle response: Unexpected sounds, movements, or contact can provoke a strong, even violent reaction.

PTSD is characterized by intrusive memories: The traumatic event(s) is recalled spontaneously in flashbacks with the same panic, dread, and terror it originally evoked. Distressing moods and thoughts persist. They can take the form of anger, guilt, shame, or a feeling of detachment from others. Thoughts like "Nothing good can happen to me" and "No one can be trusted" are common. To evade reminders of the trauma, sufferers may avoid leaving the house.

The disorder "is not merely fear based," stresses psychologist Paula Schnurr, executive director of the National Center for PTSD, a unit of the Veteran's Administration. It can show up as depression—complete with shame, guilt, and apathy—or as anger and aggression.

The Inside Story of PTSD

IN ONE SENSE, PTSD is an adaptive process, meant to help the body respond quickly to threatening circumstances when they recur. But it comes at a high cost, the stress response locked into perpetual, screeching overdrive. The condition can last three months or three years. Or it can become a chronic disorder that lasts a lifetime.

When sensory areas of the brain detect a potential threat, nerve impulses are immediately routed through the thalamus to the amygdala. Aroused, the amygdala generates the sensation of fear and signals the adrenal glands to secrete adrenalin, raising heart rate and blood pressure to mobilize the body for sudden action.

For more sustained mobilization, the hypothalamic-pituitary axis swings into gear, tripping off a cascade of hormones culminating in the release of cortisol, which extends the mobilization reaction. It also keeps the amygdala activated, maintaining the state of high alert. In such an aroused state, strong memories are readily formed, and they have staying power.

Under normal conditions, the thinking brain brakes amygdala activation, bringing

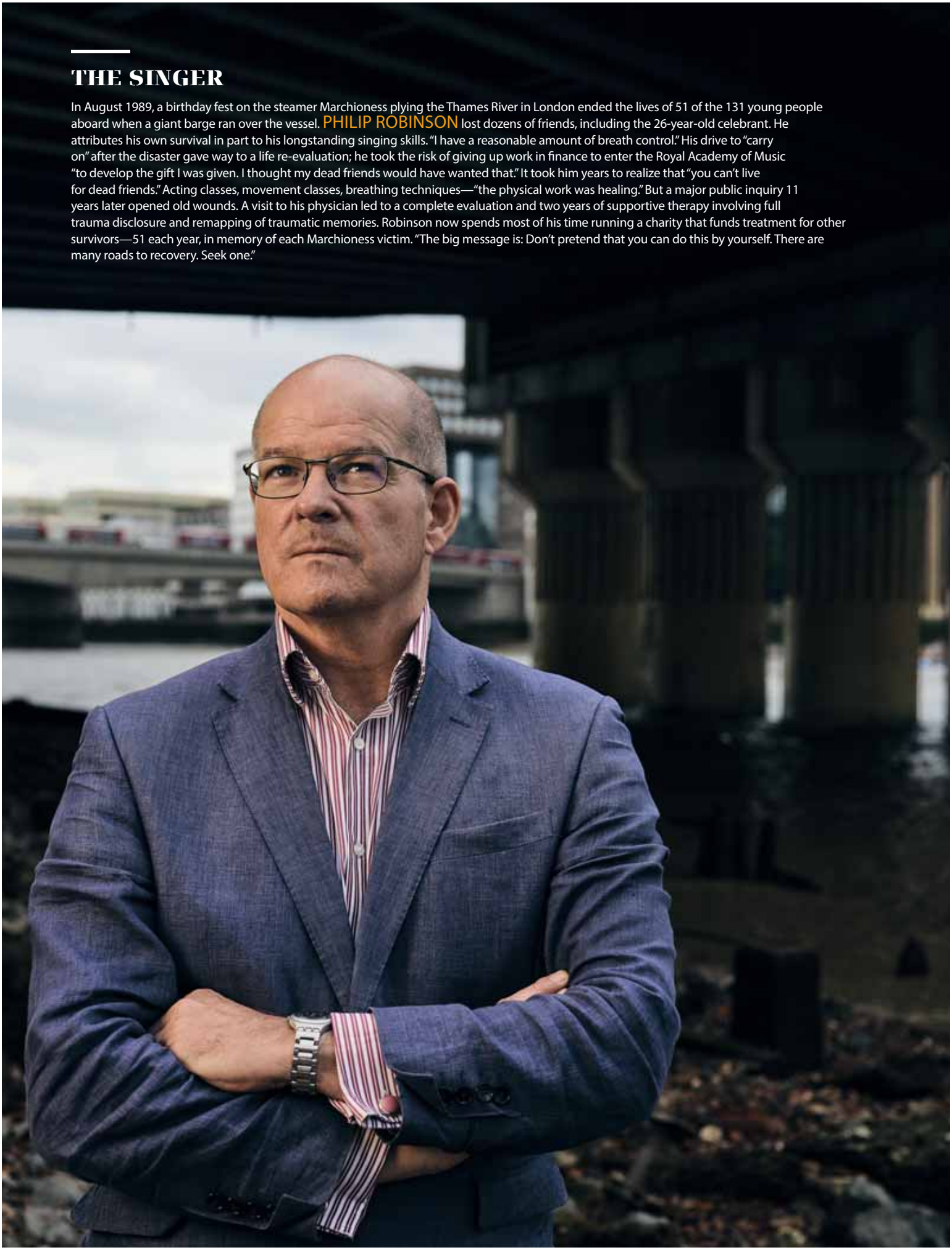
PHOTOGRAPH BY **NICK HAGEN**

THE PARENTAL RIGHTS ACTIVIST

LATAGIACOPELAND-TYRONCEwas holding her baby when she answered the door in 2013. That's how she learned that her husband was sexually abusing their five other girls. The infant was pulled from her arms and, with the others, taken into protective custody. She left her husband and fought the child-welfare system single-handedly, while also attending college and battling insomnia, nightmares, and flashbacks. The children were never returned. "I was the nonoffending parent penalized for someone else's actions," says Copeland-Tyronce, who is still haunted by nightmares. "In them, I'm trying to save my kids, one or two at a time, and I can't." Nor can she glimpse cartoons or hear music the children liked. They're triggers. "As an African-American female—there are too few of us willing to share our stories—who was raised in a single-mother low-income family, there was a lot of trauma in my life, from sexual abuse to domestic violence. But none compares to the trauma that led to my PTSD." What keeps her afloat is writing about child-welfare reform for Medium and helping other parents deal with the system. With a master's in social work, "I handle my symptoms through child-welfare advocacy."

THE SINGER

In August 1989, a birthday fest on the steamer Marchioness plying the Thames River in London ended the lives of 51 of the 131 young people aboard when a giant barge ran over the vessel. PHILIP ROBINSON lost dozens of friends, including the 26-year-old celebrant. He attributes his own survival in part to his longstanding singing skills. "I have a reasonable amount of breath control." His drive to "carry on" after the disaster gave way to a life re-evaluation; he took the risk of giving up work in finance to enter the Royal Academy of Music "to develop the gift I was given. I thought my dead friends would have wanted that." It took him years to realize that "you can't live for dead friends." Acting classes, movement classes, breathing techniques—"the physical work was healing." But a major public inquiry 11 years later opened old wounds. A visit to his physician led to a complete evaluation and two years of supportive therapy involving full trauma disclosure and remapping of traumatic memories. Robinson now spends most of his time running a charity that funds treatment for other survivors—51 each year, in memory of each Marchioness victim. "The big message is: Don't pretend that you can do this by yourself. There are many roads to recovery. Seek one."



mobilization to a halt when it concludes that danger is past, and the hippocampus puts the episode in the context of past experience. With PTSD, people remain hypervigilant, on the lookout for danger even in everyday circumstances. Fear memories are easily awakened—ordinary sounds, sights, or even thoughts trigger recollection of the traumatic event so vividly that it feels as if it's happening again.

Armand Cucciniello III was a diplomat at the U.S. Embassy in Baghdad during the Iraq War, living and working in the Green Zone, a compound secured by tall concrete walls topped by barbed wire. "But rockets and mortars lobbed or fired overhead had no problem penetrating it," recalls Cucciniello. Attacks began during the troop surge of spring 2007, six months after he arrived. "My first exposure was the worst: I heard a woman die just meters away."

There was no pattern to the attacks. "You never knew what would happen or when. After a year of off-and-on bombardment, I was very tense, highly emotional. I would well up as if I wanted to cry, for no reason," Cucciniello recalls.

A psychiatrist told him he had PTSD and prescribed an antidepressant. The drug helped his emotional control, but even years later, "loud noises, doors slamming, anything like a boom would trigger me. Time would stop for a few seconds, and I'd be incapacitated," he says. On a visit to family in New York City, the dull thump of a taxi going over an iron plate covering street construction—not loud, but "the exact pitch of a rocket exploding"—could provoke a flashback.

He had trouble sleeping for years, and even now, if he tries going off his medication, "everything comes back—the tense feeling, the welling up of tears." Cucciniello has gone on with his life and is now an advisor to four-star Army General Robert Abrams, who heads the United Nations Command in South Korea.

There's been a great surge of interest in biological markers that identify the changes caused by PTSD and that could be used to predict and diagnose the disorder, Schnurr reports. With brain-imaging tools like magnetic resonance imaging, researchers are getting a dynamic picture of the flashback memories, the fear, and other mood disturbances typical of the disorder. The National Center now also maintains a brain bank, a repository of postmortem tissue samples from PTSD sufferers, to facilitate investigation into the molecular machinery giving life to the symptoms.

"We see at least three regions involved," Neria reports. They include the amygdala, which regulates emotion and is ground zero for processing fear; the hippocampus, where memories are processed for storage and retrieval; and areas of the prefrontal cortex, the planning and decision center of the brain, which normally has the capacity to dampen amygdala activity.

In the wake of a traumatic event, he says, circuits of communication among the three regions are disrupted, accounting for the toxic vitality of traumatic memory. "In PTSD, the amygdala is hyperactivated and the prefrontal cortex and hippocampus are underengaged, leaving patients overly anxious and haunted by their traumatic experiences, the memories appearing and reappearing involuntarily" with an intensity untouched by time.

"Trying to gain control over those memories and their related anxiety, nightmares, and flashbacks, we see a lot of avoidance—people avoid talking about their trauma, trying to control their anxiety level," says Neria. They shun situations that might trigger recollection. "Numbing of emotion comes later—patients become more depressed than aroused." Fifty percent of people with PTSD, in fact, also suffer from clinical depression.

Neurobiologist Benjamin Suarez-Jimenez, a member of Neria's lab, employs virtual reality to explore the tendency to see danger where there is none. While in an MRI scanner, subjects video-walk through a meadow picking flowers. In some areas, they are stung by bees—represented by mild electric shocks. In others, they are not. "Healthy controls learn to distinguish between safe and dangerous locations, becoming hyperaroused only in areas where they were stung. People with PTSD overgeneralize; they don't discriminate accurately between safe and threatening areas," Suarez-Jimenez finds.

He is trying to pinpoint the brain areas responsible for the overgeneralization of threat. In earlier work, he identified the brain networks activated when healthy subjects make safe-dangerous distinctions, and is now collecting data on PTSD patients. "We want to compare brain activity, physiology, and self-ratings of anxiety in people who have never experienced severe trauma, those who have and developed PTSD, and those who were resilient."

Although most brain-imaging work provides fundamental insights, some findings have direct clinical application. Several studies in his lab and elsewhere suggest that "the size of the hippocampus is a key to response to therapy," says Neria. "We found that patients who have a larger hippocampus develop less PTSD over time and do better." Tests revealing a small hippocampus might well signal the need for medication and psychotherapy aimed at reprocessing their memories.

IN ONE SENSE, PTSD IS AN ADAPTIVE PROCESS, MEANT TO HELP THE BODY RESPOND QUICKLY TO THREATENING CIRCUMSTANCES WHEN THEY RECUR.

Psychotherapy was instrumental for Philip Robinson. "Being a survivor is quite difficult," says Robinson, who, 30 years ago last August, embarked on the steamer *Marchioness*, along with 130 others, most in their 20s, to celebrate the birthday of a London friend. He was below deck when

PHOTOGRAPH BY **JAMES HOLE**

a huge barge riding high in the Thames essentially ran over the boat and sent it down in seconds. "I was struck in the shoulder and hit by flying bottles. I just swam and swam. I'm a professional singer, and I kept hold of my breath. I got out through a broken window." Fifty-one others didn't.

After a day in the hospital to repair a dislocated shoulder and flesh wounds, "I just wanted to carry on." He went back to his job in finance. "Then the funerals came. I sang at the funerals. I started drinking heavily." He found the trivialities of life increasingly irritating. He re-evaluated his life and followed his dream: He entered the Royal Academy of Music. Movement classes, acting classes, counseling, and breathing techniques, all routine in his program, were the very things now known to help survivors.

And Robinson did well until, 11 years after the disaster, a public inquiry got underway. "We had to relive the accident. There were interviews, investigations. My relationship broke down. I was having trouble at work." A visit to his GP led to a full psychiatric assessment. "I was suffering from depression. My normally robust coping mechanisms had been challenged and overwhelmed." Two years of work with a therapist followed. He was encouraged to let go of the belief that "I was singing for dead friends." He now sings for himself. "Singing is a way that my soul can talk to tragedy."

Because Robinson is the first to acknowledge how fortuitously the elements of his life worked for him, he's set up a charity to assist other victims of single-incident disasters get whatever help they are found to need. Every year his charity, the Antonio Vasconellos Fund, gives out 51 grants—each in the name of a *Marchioness* victim.

The Stricken and the Spared

NOT EVERYONE exposed to catastrophic or life-threatening events develops PTSD. Even among veterans of combat, which can deliver a barrage of disturbing events under conditions of high emotional arousal, rates of the disorder range from 10 to 30 percent.

Researchers have been dissecting exactly what constitutes resilience ever since the late sociologist Emmy Werner began tracking the development of every infant born on the island of Kauai in 1955 and discovered that only a minority of those delivered into highly adverse circumstances wound up troubled or in trouble. For the most part, says psychiatrist Adriana Feder of New York's Mt. Sinai Medical Center, resilience research has sought answers in psychosocial factors like family stability and social support, which foster emotional regulation. Only recently has it deepened to include biology.

Most research into exactly what goes awry in stress circuitry in PTSD looks at individuals who already have the disorder. But the most useful studies, Feder observes, would look at people before they experience trauma—such as military personnel pre-deployment and civilians beginning work in police and fire departments—and follow them.

A large national collaborative study named AURORA is doing the next best thing. Researchers are gathering data, including brain scans, on people seen in emergency rooms immediately after trauma exposure and seeking patterns of brain activity that predict how they fare over time. Feder herself is leading studies of police, construction workers, and others who responded to the World Trade Center attacks, comparing those who went on to develop PTSD with those who did not.

The 9/11 attacks, tragic as they were, are serving as a living laboratory illuminating the natural course of PTSD. Overall, studies show, among people exposed to the trauma, PTSD rates declined over the first few years.

Volunteer first responders were significantly more likely to develop PTSD than professionals, such as police and firefighters. Volunteers not affiliated with rescue organizations like the Red Cross were particularly hard hit, with PTSD rates of nearly 30 percent, vs 13 percent for the pros.

Those data confirm earlier findings: Individuals with a history of trauma exposure or mental difficulties and those with poor social support and recent or ongoing life stress are at high risk of PTSD. An important new finding was that physical impairment or job loss raised the risk of PTSD.

Psychotherapy, including exposure therapy employing virtual reality, was generally effective. New data found that children responded well to psychotherapy provided in school or the community.

IMAGEN is the acronym for a large European study tracking how a wide range of factors during adolescence influences brain development and adult mental health. One of the findings so far is that adolescents who are doing well, despite the presence of major stressors in their life, react in a distinctive way when shown pictures of fearful or angry faces, normally a stress-inducing scenario.

Notably, there is little activation of the amygdala. In addition, studies show that these youth have more grey matter in the prefrontal cortex. Circuitry involved in cognitive reappraisal—the ability to reinterpret an event's meaning—appears associated with more controlled, less excessive responses.

Can resilience be fostered? Stress-inoculation therapy, often a component of cognitive behavioral therapy, counts on it. It aims to fortify people in advance of difficult experiences by exposing them to a progression of challenging circumstances through imagery and video simulations. It seeks

THE 9/11 ATTACKS, TRAGIC AS THEY WERE, ARE SERVING AS A LIVING LABORATORY, ILLUMINATING THE NATURAL COURSE OF PTSD. OVERALL, RATES OF THE DISORDER DECLINED OVER THE FIRST FEW YEARS.

to help people develop coping skills; to maintain cognitive flexibility so that difficulties can be seen as challenges to be mastered and opportunities for growth; and to inculcate a sense of control, the realization that it's possible to shape the stress response by such perceptions. The therapy is often used with people who will be exposed to combat.

It may be that specific drugs given to people immediately before exposure to life-threatening conditions or immediately after can also forestall development of PTSD. Among the agents under study is neuropeptide Y (NPY), a chemical found throughout the nervous system and best known for promoting food intake.

In the brain, NPY is also associated with resilience to the harmful effects of stress, says neuroscientist Esther Sabban of New York Medical College. There is some evidence that NPY is an all-around inhibitor of nerve action, so that it takes a stronger dose of danger to overactivate stress-circuit neurons and dysregulate them. In the amygdala, its release mutes the response to stress.

Studies show that people with PTSD have lower blood levels of neuropeptide Y than those who don't develop PTSD. It is impossible to know yet whether the difference predates their response to trauma or is a result of it, although genetic studies suggest it's pre-existing.

In one of her own experiments, conducted on rats, Sabban and colleagues subjected animals to a strong and prolonged stressor—the rodent equivalent of trauma. Animals got NPY either 30 minutes before the stress exposure, immediately after it, or a week later, when severe stress effects had already set in. NPY given before or immediately after exposure to stress completely blocked development of PTSD-like responses. It had no effect on full-blown symptoms.

Human studies with NPY are few. One small clinical trial found that the neuropeptide given intranasally (to go directly to the brain, averting unwanted effects on the body) reduced the anxiety symptoms of PTSD. Sabban and her colleagues are now conducting research that, she hopes, will lead to a clinical trial large enough to establish whether giving the drug within two days after trauma can forestall progression of distress to PTSD.

THE ACTRESS

"I thought PTSD occurred only among those coming back from combat," says HAYLEY GRIPP. That was until 2014, when the car the young actress was driving was hit broadside. Trapped and suffocating on the fumes, she passed out. She came to "consumed by gratitude" at being alive, despite injuries to her legs. "Everything was taken from me, including my livelihood," she reports. "I could no longer stand on a set." Two weeks later, "I heard a loud car horn, and I screamed. I was always the girl attacked in a film. I knew how to scream. I thought I was going crazy." And a disorder she had learned to control years before—Tourette's syndrome—came roaring back, alongside PTSD. "You can't overcome PTSD the way you can Tourette's," she discovered. The thought of driving triggered massive anxiety. Getting into a car—unavoidable in Los Angeles—led to panic attacks. So "I left everything behind and moved to New York City," where her PTSD symptoms, she says, are 50 percent better, and her tics are 65 percent better. "I accept PTSD. I'm not letting it win."

The Opposite of Stress

NPY IS NOT the only chemical hope against PTSD. Compounds of interest include ketamine, an anesthetic that has a shady past as a club drug called Special K but which has recently been approved for use to treat severe, unremitting depression, especially when accompanied by thoughts of suicide. Delivered intravenously, it acts rapidly, within hours, although no one knows exactly how. After years of testing, esketamine (one of two nearly identical forms of ketamine) was FDA-approved for resistant depression early this year.

"A couple of patients we treated for depression had PTSD, and their symptoms seemed to get better as well," Adriana Feder reports. "This led to our first study, in 2014, with a single intravenous infusion of ketamine." Treatment resulted in improvement in all symptom groups of PTSD—re-experiencing the traumatic incident, avoidance, anhedonia, and hyperarousal—measured 24 hours later. Feder is now leading a clinical trial in which patients receive six doses of the drug over a two-week period, "to see whether we can replicate these initial findings and maintain the response."

There are strong indications that ketamine fundamentally alters nerve

PTSD *continued on page 90*

PHOTOGRAPH BY **KARJEAN LEVINE**

PTSD *continued from page 69*

connectivity within the brain. "We published a neuroimaging study in depressed patients, which found increased connectivity in emotional regulation regions after ketamine administration," Feder reports. Her group is now conducting a similar study in patients with PTSD.

Neuroscientist Ronald Duman, professor of psychiatry and director of molecular psychiatry at Yale University, contends that PTSD is fundamentally a "synaptic deficit disorder"—blunting communication between individual neurons. "A lot of brain imaging work demonstrates decreased volume in brain regions implicated in PTSD. This led to the idea that a loss of synaptic connections could be involved."

A shortage of connections between nerve cells would compromise neuroplasticity, impeding learning and keeping those exposed to trauma stuck in their over-the-top response, with no neural escape route—no pathway for extinguishing the fear response. Animal research has shown that synapses in the hippocampus and prefrontal cortex dwindle after chronic stress. But evidence that the same thing happens in PTSD has been elusive. "These are technically very difficult studies to do," Duman observes.

There's some indirect evidence of synaptic loss in humans with PTSD. In studies of tissue samples from the PTSD Center's brain bank, researchers have found differences in genes regulating synapse formation between individuals with PTSD and those without.

The findings, if confirmed, could help explain how ketamine works—both in depression and PTSD. "Ketamine produces an effect opposite to stress: It increases synaptic connections in the prefrontal cortex, even after a single dose," Duman says.

Synaptic plasticity—the growth of new inter-neuron connections—is the foundation of memory and learning. And, in its unraveling, it is the source of the memory-changing processes that go awry in PTSD.

Ordinarily, the link between a memory and the emotions associated with it can be extinguished; over time, the emotional response component weakens and dissipates. What's more, scientists know that every time a memory is brought to mind, it can be modified and reframed, a process known as reconsolidation. That paves the way for talking about a bad experience with friends in pleasant surroundings to send the memory back into storage in less disturbing form.

But in PTSD, memories resist both kinds of change, making them nearly ineradicable. "The memory is always stored in its original form—they're being raped again, with all the emotions of the original event," explains clinical psychologist Ilan Harpaz-Rotem, also of Yale.

Prolonged exposure and cognitive reappraisal are known to be two of the most effective psychotherapies. They work by advancing memory modification—the very process crippled by PTSD. "Patients need a nudge, and enhanced neurogenesis after ketamine may open a window of reconsolidation," says Harpaz-Rotem.

The Yale researcher is gearing up to provide that nudge, with a clinical trial that combines ketamine with prolonged exposure therapy. The combo could do in seven days what, under the best of circumstances, might otherwise take months. Before-and-after MRI studies will explore whether and how the treatment changes the way parts of the brain work together.

That's one possibility—the rapid-acting way. If Ronald Duman is right, there are other ways to restore synaptic connectivity and psychological flexibility. Prime among them is physical activity, which is known to directly stimulate the growth of new neuronal connections.

"Maybe a Door"

PAUL ASCNURRI is excited about the use of ketamine to "potentiate and enhance the power of the most effective psychotherapy." It's an instance of taking something that works well and making it work even better. Another chemical agent that fits that bill is the psychedelic drug MDMA, aka Ecstasy. "It catalyzes the psychotherapeutic process," says psychiatrist Michael Mithoefer, who has spearheaded two decades of research on MDMA. Intense interest in its potential has spurred the FDA to designate MDMA a "breakthrough" treatment for PTSD, and the agency is fast-tracking it toward approval. MDMA is already approved for use in Israel.

An international Phase III clinical trial—a big step toward approval—is already underway. An analysis of six small clinical trials showed that the agent brought about symptom improvement double that of control groups. In the standard protocol, patients are given MDMA before each of three therapy sessions of eight hours or longer, conducted by two specially trained therapists and spaced a week apart.

"We don't tell people to talk about trauma, but whatever comes up," says Mithoefer. Unstructured as the sessions are, elements of standard trauma therapy—exposure to traumatic material and cognitive restructuring—are generally engaged. "We emphasize that MDMA is different from most psychiatric medications in that it is not designed to repress symptoms but to help process underlying causes; sometimes symptoms get worse before they get better."

As a neuroscientist researching trauma for three decades, psychologist Rachel Yehuda was skeptical of MDMA case reports. "Having been in the field for so long and having research experience with many treatments, I couldn't fathom the claim that after one or two sessions people with chronic PTSD no longer had it," says Yehuda, director of the Traumatic Stress Studies

THOSE OF US TRYING TO UNDERSTAND TRAUMA HAVE BEEN LOOKING FOR A WINDOW TO HELP PEOPLE. MDMA MAY BE A FLOOR-TO-CEILING WINDOW, MAYBE A DOOR.

Division at Mt. Sinai Medical Center.

That was before she went to Israel. "I began to understand this was an approach to trauma therapy that has to do with inducing a very safe and cocooned state for a person." The drug, she says, "creates an open, warm feeling of self-compassion, and the therapist provides an environment for understanding the material that is coming up, making it safe to see from different angles." It removes the barriers where people normally get stuck in psychotherapy—"where it hurts, the core where they don't want to go."

Yehuda herself underwent a session of treatment, which she says gave her an inside understanding of how the accelerated psychotherapeutic experience fosters accessing and processing the events of one's life. "It's like learning you can take a plane from New York to Los Angeles, rather than having to walk there."

"Those of us who have tried to understand trauma have been looking for a window to help people," Yehuda says. "This may be a floor-to-ceiling window, maybe a door."

"We know MDMA decreases activity in the amygdala, and increases it in the prefrontal cortex, which fits really well with what we see clinically: People can suddenly talk about their trauma without being overcome by emotion." Mithoefer says. "A vet who underwent treatment said, 'Iraq changed my brain, and MDMA changed it back.' There's brain-imaging data to show that."

Regaining Control of Their Own Brains

ALL THE IMAGING studies exploring the neurobiology of PTSD have helped identify "which brain areas need to be turned up and which turned down," says Paul Holtzheimer, deputy director for research at the National Center for PTSD. And that opens the way for highly targeted treatments, including neurofeedback.

"When you fear something, the amygdala becomes activated; in PTSD it's activated more," says Ilan Harpaz-Rotem. With neurofeedback, patients learn to reduce symptoms by dialing back brain activity by themselves. Especially after being at the mercy of unpredictable triggers anytime and anywhere, "it's empowering for them to take control of their own brains," he says.

Harpaz-Rotem is leading a clinical trial in which individuals with PTSD lie in an MRI scanner, watching a pointer that tracks blood flow—an indication of amygdala activity—while they are read a script and hear sounds evocative of the precipitating trauma. They are taught techniques to reduce fear and, by watching the pointer, can determine which ones dampen amygdala arousal.

The hope is that they will apply the techniques whenever they feel overwhelmed, "not to erase the memories but to learn to tolerate them," he says. Before-and-after MRIs will reveal any altered connectivity between the amygdala, the hippocampus, and the prefrontal cortex and any correlations with symptom reduction.

Another promising treatment takes direct aim at the faulty circuitry of PTSD and gives it a reboot. Transcranial magnetic stimulation, which applies a shifting magnetic field to generate small electric currents in relevant spots, is already in use for drug-resistant depression and obsessive-compulsive disorder.

In PTSD, it targets a key neural node—the dorsolateral prefrontal cortex. The goal is to jack up cognitive control so the brain can better regulate emotion, decreasing the intensity of undesired experiences. "The effects may carry over to a number of symptoms—avoidance, even flashbacks," says Holtzheimer.

Brain stimulation is being tested as a psychotherapy booster, too. Applied just prior to weekly sessions of cognitive reprocessing therapy, the treatment, Holtzheimer stresses, is still very much a work in progress. "If it follows the same timeline as that for depression, maybe in five years we'll see a pivotal clinical trial that opens the door to broad availability."

The ability to treat PTSD effectively is advancing in lockstep with new understanding of the disorder. Terrible events will continue to happen; even if war were to stop tomorrow, nature delivers its own random blows. Emotional aftershocks will inevitably reverberate in the minds and brains of those exposed. But while pain is inevitable, lasting suffering is not. Putting an end to it is no longer an impossible goal. ■

CARL SHERMAN *is a science writer who is based in New York City.*

EXPOSURE *continued from page 77*

their sense of well-being and belonging. Supporting the theory that these extended relationships are a form of social compensation, a study led by Wim Meeus at Utrecht University found that the more interactions that introverts have with "online-only" friends, the higher their self-esteem and the lower their rate of depression.

"Just as a diverse financial portfolio makes people less vulnerable to market fluctuations," Sandstrom speculates, "a diverse social media portfolio might make people less vulnerable to fluctuations in their social network." Remote ties offer freshness and variety, low emotional intensity, and the chance to interact outside of our routine roles. They offer a sense of social support we might otherwise lack.

There are limits, of course. For emotional well-being, online acquaintances obviously can't replace more intimate time with close friends and family. Context collapse remains a problem—anything you say and do may still be linked with the identity your future boss sees—and the bandwidth spent on making wider connections on social media may be better invested at a networking party or the local pub. On most days, my social-media cap is 30 minutes, the limit after which mental health takes a downward turn, according to a study published in the *Journal of Social and Clinical Psychology*.

But the giver mentality inspires a new metric that centers on depth and engagement. Not just how many friends or followers you have on social media, but how many you've actually interacted with that day. Not just the number of people who "like" your content, but how much of an effort you've made to like others. Not just how widely your content circulates, but how free you feel to express yourself. Not just what social media does for your brand, but what it does for your whole self. ■

JENA PINCOTT*'s most recent book is* Wits Guts Grit: All-Natural Biohacks for Raising Smart, Resilient Kids.