



collaboration

leverage multidisciplinary expertise | join forces to maximize impact | share tools and techniques

Brain Research Foundation funds research that impacts our understanding of all diseases and disorders of the brain.

ALS (Lou Gehrig's disease) | Age-related macular degeneration (AMD)

Aggressive disorder | Alcoholism | Alzheimer's disease | Anorexia nervosa

Anxiety disorders | Aphasia | Arteriovenous malformation | Asperger syndrome

Attention deficit disorder | Autism spectrum disorder | Batten disease | Bell's palsy

Bipolar disorder | Blindness | Brain aneurysm | Brain cancer | Brain development

Brain tumors | Bulimia | Cerebral palsy | Charcot-Marie-Tooth disease | Concussion

Conduct disorder | Creutzfeldt-Jakob disease | Dandy-Walker syndrome | Dementia

Depression | Developmental disorders | Down syndrome | Dravet syndrome

Dystonia | Eating disorders | Encephalopathy | Epilepsy | Essential tremor

Fatal familial insomnia | Fragile X syndrome | Frontotemporal lobar degeneration

Guillain-Barré syndrome | Hemifacial spasm | Huntington's disease

Learning disability | Lewy body dementia | Locked-in syndrome

Manic-depressive illness | Meningitis | Mental retardation | Migraine headaches

Motor neuron disease | Multiple sclerosis | Muscular dystrophy | Myasthenia gravis

Narcolepsy | Nicotine addiction | Neuropathy | Obsessive-compulsive disorder

Opioid addiction and dependency | Panic disorder | Parkinson's disease

Pick's disease | Post traumatic stress disorder (PTSD) | Prion disease

Restless legs syndrome | Rett syndrome | Schizophrenia | Sleep apnea

Smith-Magenis syndrome | Spinal cord injury | Spinal muscular atrophy | Stroke

Substance abuse disorders | Tay-Sachs disease | Tourette syndrome

Transient ischemic attack | Traumatic brain injury (TBI) | Trigeminal neuralgia

Tuberous sclerosis | Williams syndrome

collaboration

It's the foundation of the field of neuroscience, which relies on expertise across a range of disciplines from neurology and psychology to computer science and engineering.

Our approach to funding brain research is built on that foundation. We identify the most visionary scientists regardless of their specialty or disease focus and provide the funding they need to build the collaborations necessary to achieve the next breakthroughs.

Dear Friends,



Like everyone in 2020-2021, Brain Research Foundation (BRF) was focused on getting through a pandemic and facing unknowns that we have never faced in our 68 years. Our Trustees and staff were trying to navigate uncertainties that could affect our mission of funding the nation's most pioneering neuroscience research. We were not sure how COVID-19 would impact our contribution levels, our investment income and even the researchers that we support.

But what we did know was that fulfilling BRF's mission came from a combination of: the passion of our donors, Trustees and staff; the expertise from our Scientific Review Committee; and the innovation from research grant recipients. All these critical pieces needed to work together in a collaboration toward discoveries.

In our Impact Report, we have highlighted some incredible stories of perseverance and advancement. You will read a lot about scientific collaboration, but one of the most important collaborations is with our donors. Without donors, BRF could not have navigated the pandemic and supported the most cutting-edge neuroscience research in the nation. We are extremely grateful for your continued generosity.

While we are still amid uncertain times, BRF always looks forward. We support innovative neuroscience today for new treatments and eventual cures in the future. I am so proud to say that even during the pandemic, 2020-2021 was an extremely productive time for the Foundation.

- BRF contributed over **\$3.6 million** for research and educational programs.
- BRF ensured that **100%** of every dollar donated is used directly for research.
- BRF **increased the amount of grants awarded** above budget, funding an additional seven grants in FY2020-2021.

While we are extremely proud of these accomplishments, we continue to see outstanding research projects to fund and will strive to increase our support to answer important questions about the human brain. Our mission has never wavered, and the ultimate goal remains the same—to help everyone who is struggling with devastating brain disorders.

I know there are many worthy nonprofits. I want to personally thank you for collaborating with us.

A handwritten signature in black ink, reading "Terre A. Constantine". The signature is fluid and cursive, with a long horizontal flourish extending to the right.

Terre A. Constantine, Ph.D.
Executive Director and CEO



At our annual meeting this fall I will be stepping down as Chairman of the Board. The board's achievements over these past six years provide an opportunity for reflection, and also an opportunity to look ahead.

First and foremost, I want to thank my Executive Committee members: Norm Bobins, Vice Chair; Dave Fishburn, Treasurer; David Olson, Secretary. Their management and leadership provided streamlined and proficient operations on all levels. To my fellow board members, we simply would not have been as successful without your guidance and support. My sincerest thanks for everything you did for BRF over these past six years. Finally, I would like to thank the people that I collaborated with the most during my tenure, the office staff: Dr. Terre A. Constantine, Executive Director and CEO;

Sandra Jaggi, Director of Philanthropy and Janie Jenkins, Bookkeeper.

Brain Research Foundation is formidable in the field of neuroscience. Their venture capitalist approach is what drew me to this organization, when I first joined the board in 1983, lured by the co-founder of the Foundation itself, William Fay, Jr. At that time, we funded only Chicago scientists. Since then, I've watched the Foundation grow and establish itself as a neuroscience research leader in the nation. My focus while Chair was three-fold: grow a diverse board, increase awareness, and focus on fundraising. I am confident that as I leave my position all three of those goals have been achieved.

Looking ahead, I am thrilled that Scott Serota will be taking over the helm of this truly extraordinary foundation. Scott is a capable and dynamic leader who I know will lead the Foundation into many more years of growth and success. I look forward to working together with him.

Finally, I would like to send my thanks to our greatest collaborators...our readers, our donors, and our friends. Without you we would simply not be able to accomplish the great work that gets done daily, in labs across the country, as we race to find cures to debilitating diseases and injuries. Thank you for your support and the confidence you place in our Foundation.

Sincerely,

A handwritten signature in black ink, appearing to read 'P. Pond', with a long, sweeping horizontal line extending to the right.

Peter Pond
Chairman, Board of Trustees



Introducing Scott Serota, BRF's next Chairman of the Board of Trustees

We are exceptionally pleased to announce that the next Chairman of the Board will be Scott Serota, former president and chief executive officer of the Blue Cross Blue Shield Association (BCBSA).

Scott accepted the BRF Frederic A. Gibbs Discovery Award for Community Service on behalf of BCBSA in 2016 and joined the Board of Trustees shortly thereafter.

"As someone who has committed his entire career to healthcare, I have a special appreciation for the terrific work Brain Research Foundation has enabled for almost seven decades," states Mr. Serota. "I am grateful to Peter Pond for the excellent leadership during his tenure, and I am confident we can continue the momentum towards discoveries and cures."

Please join us in welcoming Scott.

maximize

Collaboration is the key to decoding how billions of brain cells orchestrate a myriad of daily tasks and how disruptions to those complex interactions contribute to brain disease and disorders. Cracking that code requires multi-talented teams and cross-institution partnerships.

For almost 70 years, Brain Research Foundation (BRF) has recognized the importance of collaboration to drive progress in neuroscience. Strong relationships between BRF, our passionate donors and the leading scientists on our Scientific Review Committee have been essential to our success. Grants from BRF have enabled our visionary grantees to assemble boundary-breaking teams and build new tools that are accelerating the pace of discovery. Alliances with other nonprofits are helping further extend BRF's impact and bringing answers one step closer to treatments and cures.

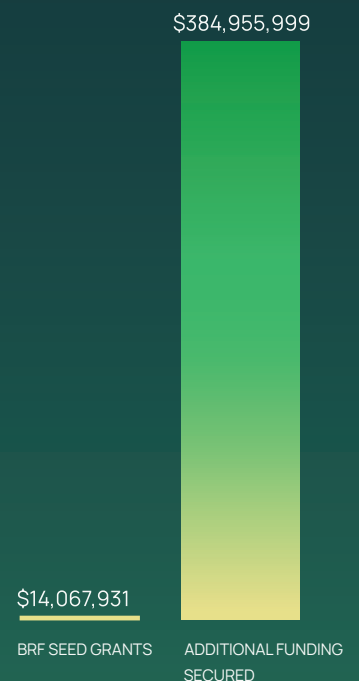
impact

Many of BRF's donors are passionate and empathetic people who have deep personal connections with someone who has experienced brain disease. To make sure each of their donations goes as far as possible, we maintain a small staff and lean operational costs that are entirely funded by investment income. This allows 100% of each donation to go toward funding research.

Through our Seed Grant Program, we have awarded \$14,067,931. On average, every one of those grant dollars leads to about \$27 in additional funding for the investigator. Those researchers have obtained \$384,955,999 in additional funding. That's a 1:27 return on investment, bringing these cutting-edge labs many steps closer to breakthroughs.

By making the most of each donation and funding collaborative researchers and multidisciplinary projects, we have provided more than \$47 million for neuroscience and supported 691 bold projects. Our work is having a transformative impact on the field of neuroscience.

Since 1981, we have awarded over \$14 million in **Seed Grants**, leading to a **1:27 return on our investment:**



To date, we have awarded more than **\$47 million** to advance neuroscience

leverage

To find researchers doing the most innovative work, BRF asks the top universities across the country to nominate their most promising researcher each year. These visionary scientists each describe their project and how they think it will lead to new insights on the brain or neurologic diseases.

The leading scientists on BRF's Scientific Review Committee (SRC) review those proposals. They offer their time and expertise to help the BRF in our mission to accelerate brain research that will one day lead to novel ways to prevent and treat neurological diseases and disorders. Working together, SRC members leverage their diverse backgrounds and years of experience to identify the most promising nominees and projects with the greatest potential to propel brain research forward.

The SRC looks not only for projects that could lead to immediate breakthroughs in neuroscience, but also projects that are likely to yield collateral benefits for many years to come. It identifies projects that are producing new research tools, launching the careers of promising young scientists, or supporting collaborative scientists whose work has the potential to revolutionize the field.

expertise

BRF Scientific Review Committee

Tracy L. Bale, Ph.D.
University of Maryland School of Medicine

Scott T. Brady, Ph.D.
SRC Chair
University of Illinois Chicago

Monica J. Carson, Ph.D.
University of California, Riverside

Yamuna Krishnan, Ph.D.
The University of Chicago

Daniel A. Peterson, Ph.D.
Rosalind Franklin University

Kerry J. Ressler, M.D., Ph.D.
McLean Hospital,
Harvard Medical School

Nenad Sestan, M.D., Ph.D.
Yale University

Gordon M.G. Shepherd, M.D., Ph.D.
Northwestern University

BRF Seed Grants provide early career scientists the support they need to establish laboratories and begin testing their ideas. The Seed Grants provide \$80,000 over two years. They enable young investigators to generate the preliminary data they need to compete for larger grants from traditional funding sources to keep their research moving forward.

BRF Scientific Innovations Awards (SIAs) are designed to support established neuroscience researchers taking a chance on an innovative or collaborative project that could yield big gains. The awards provide \$150,000 over two years to support projects that may be viewed as too risky by some traditional funders but have a high potential to yield important insights in a short period of time.

accelerate

2020 Scientific Innovations Award Recipients

Sandeep Robert Datta M.D., Ph.D.

Harvard University

"Probing Sensation and Behavior in Autism Spectrum Disorder Models"

APPLICATIONS: AUTISM SPECTRUM DISORDERS, SENSORY PROCESSING, OLFACTORY PERCEPTION

[Carl & Marilyn Thoma Foundation Scientific Innovations Award](#)

Samuel J. Pleasure M.D., Ph.D.

University of California, San Francisco

"Autoantibody Discovery in Neuropsychiatric Disease"

APPLICATIONS: SCHIZOPHRENIA, AUTOIMMUNE DISORDER

2021 Scientific Innovations Award Recipients

Dr. Gregory Scherrer

The University of Carolina, Chapel Hill

"Mechanisms of Affective States and Drug Discovery at the Intersection of Chronic Pain and Opioid Addiction"

APPLICATIONS: CHRONIC PAIN, DRUG DISCOVERY, OPIOID ADDICTION

Dr. Shigeki Watanabe

Johns Hopkins University

"Intrinsic and Extrinsic Mechanisms Underlying Synaptic Proteostasis"

APPLICATIONS: ALZHEIMER'S DISEASE, NEURODEGENERATIVE DISEASES, NEURONAL "WASTE MANAGEMENT," PARKINSON'S DISEASE

Dr. Ilana Witten

Princeton University

"A Role for Dopamine During Rest and Sleep in Memory Consolidation"

APPLICATIONS: ALZHEIMER'S DISEASE, DOPAMINE, SLEEP, MEMORY, MEMORY DISORDERS

2020 Seed Grant Recipients

Christian R. Burgess, Ph.D.

University of Michigan

"Dopaminergic Contributions to Dexterous Skill in Cortex and Striatum"

APPLICATIONS: PARKINSON'S DISEASE, MOTOR CORTEX

Natalia V. De Marco Garcia, Ph.D.

Cornell University

"A Circuit Mechanism for the Development of Cortico-cortical Connectivity"

APPLICATIONS: AUTISM, NEURONAL CIRCUITS, DEVELOPMENT

Laura A. DeNardo, Ph.D.

University of California, Los Angeles

"Defining the Role of Early Life Experience in mPFC Circuit Assembly"

APPLICATIONS: AUTISM, DEVELOPMENT, STRESS

Sung Han, Ph.D.

Salk Institute for Biological Studies

"The Neural Basis of Opioid-induced Respiratory Depression"

APPLICATIONS: OPIOID OVERDOSE, OPIOID-INDUCED RESPIRATORY DEPRESSION

Anirvan S. Nandy, Ph.D.

Yale University

"A New Paradigm for the Neuroscience of Navigation"

APPLICATIONS: AUTISM, SOCIAL NAVIGATION, BEHAVIOR

[The Serota Family Seed Grant](#)

Won Chan Oh, Ph.D.

University of Colorado

"Role of Inhibitory Synapses in Shaping Excitatory Circuits"

APPLICATIONS: AUTISM, EXCITATORY AND INHIBITORY SYNAPSES, SYNAPTIC PLASTICITY

Cody A. Siciliano, Ph.D.

Vanderbilt University

"Neural Mechanisms of Inferential Learning"

APPLICATIONS: ADDICTION, PREFRONTAL CORTEX, LEARNING CIRCUITS

[Michael Lee Ciardullo Seed Grant](#)

discovery

Emily L. Sylwestrak, Ph.D.

University of Oregon

"Linking Cell Type to Disease: Mapping Gene Expression and Neural Activity in Pathological Reward Processing"

APPLICATIONS: NEURAL BASIS OF BEHAVIOR, REWARD, OPIOIDS, ADDICTION

[Women's Council Seed Grant](#)

2021 Seed Grant Recipients

Lindsay M. De Biase, Ph.D.

University of California, Los Angeles

"The Role of Microglial Lysosomes in Selective Neuronal Vulnerability"

APPLICATIONS: PARKINSON'S DISEASE, AGING, NEURODEGENERATION

[Peter Pond Seed Grant](#)

Stephen W. Flavell, Ph.D.

Massachusetts Institute of Technology

"How the Nervous System Constructs Internal Models of the External World"

APPLICATIONS: NEURAL CIRCUITS, BEHAVIOR, SENSORIMOTOR

Xiaojing Gao, Ph.D.

Stanford University

"When Neural Circuits Meet Molecular Circuits: Quantitative Genetic Manipulation with Single-cell Consistency"

APPLICATIONS: ALZHEIMER'S DISEASE, NEUROGENETIC DISORDER

[Dementia Society of America Seed Grant](#)

Rafiq Huda, Ph.D.

Rutgers University

"Conducting the Orchestra of Movement—Functional Role of Striatal Astrocytes in Health and Disease"

APPLICATIONS: PARKINSON'S DISEASE, ASTROCYTES

Ethan G. Hughes, Ph.D.

University of Colorado

"Rethinking Remyelination: The Role of Mature Oligodendrocytes in Remyelination"

APPLICATIONS: MULTIPLE SCLEROSIS, MYELIN, REGENERATION

Joseph G. Makin, Ph.D.

Purdue University

"Decoding Speech from Electrocorticography"

APPLICATIONS: BRAIN-MACHINE INTERFACE, SPEECH, MACHINE LEARNING

Anna V. Molofsky, M.D., Ph.D.

University of California San Francisco

"A Zebrafish Model to Study Microglial-Extracellular Matrix Dynamics During Synapse Development"

APPLICATIONS: : AUTISM, SCHIZOPHRENIA

[Carl & Marilyn Thoma Foundation Seed Grant](#)

Ashleigh E. Schaffer, Ph.D.

Case Western Reserve University

"Epistasis Screening for Neuronal Mechanisms of Secretory Protein Trafficking"

APPLICATIONS: NEUROLOGICAL DISEASE, STEM CELL

Sarah Stern, Ph.D.

Max Planck Florida Institute

"Cortical Processing of Interoceptive and Exteroceptive Signals"

APPLICATIONS: BEHAVIOR, PSYCHIATRIC DISORDERS, SENSORY PROCESSING, FEEDING MOTIVATION

[Women's Council Seed Grant](#)

Sharon A. Swanger, Ph.D.

Virginia Tech

"Targeting Intrinsic Versus Synaptic Mechanisms in the Epileptic Brain"

APPLICATIONS: EPILEPSY, SEIZURES

Dr. Jai Y. Yu, Ph.D.

The University of Chicago

"Understanding Memory Association

Through Modulation of Hippocampal-Cortical Communication"

APPLICATIONS: MEMORY, MEMORY DISORDERS, PTSD

Xinzhu Yu, Ph.D.

University of Illinois Urbana-Champaign

"Astrocyte Contributions to Cortical Synaptic Plasticity"

APPLICATIONS: ALZHEIMER'S DISEASE, HUNTINGTON'S DISEASE, AUTISM, MAJOR DEPRESSIVE DISORDER

“Without BRF’s funding I wouldn’t have been able to take a chance on testing a brain-machine interface in non-human primates, which provided insight on how movement is encoded in the brain that helped us develop a brain-machine interface for humans.”

**Nicholas Hatsopoulos, Ph.D., BRF Seed Grant Recipient
The University of Chicago**

A 2002 BRF Seed Grant allowed Nicholas Hatsopoulos, Ph.D., to study the code used by brain cells to control reaching movements in non-human primates—a step toward creating a brain-machine interface.

“Once you understand the code you can develop a decoding algorithm, which is necessary for creating a brain-machine interface,” Hatsopoulos explains.

Another BRF Seed Grant in 2008 helped him study the code that enables even more complex movements in the animals. The results from the two BRF-funded studies helped him secure an additional \$4.2 million to further refine his work.

Now, he and a multi-institution, multi-disciplinary team of scientists are collaborating to apply what he learned from those early experiments in a clinical trial of a brain-machine interface that might one day help people with spinal cord injuries control a robotic arm with their brains.

Collaborating to restore movement and touch

Two-Time BRF Seed Grant Winner Dr. Nicholas Hatsopoulos Co-Leads a Multisite Clinical Trial of a Brain-Controlled Prosthetic Arm

From vision to reality

BRF's foresight in recognizing the potential in Dr. Nicholas Hatsopoulos' early investigation is now paying off with the clinical trial of a device that may one day change the lives of people with paralysis.

The trial began at the University of Pittsburgh, where a team was working to create a robotic prosthetic arm that a person could control with their brain. After that team was successful at creating and testing the prosthetic in one patient, they decided to expand the trial to a second location and partnered with Hatsopoulos and his long-time collaborator, Sliman Bensmaia.

Together, the two groups secured a \$7 million grant to expand the clinical trial to at least four patients. Having a multisite trial will enable the team to further refine the device

and demonstrate that the success can be replicated at other sites in other patients.

"We want to make this device clinically viable, something that can be used by patients to help them," Hatsopoulos said.

John Downey, who earned his Ph.D. in biomedical engineering at the University of Pittsburgh while working on the project, then joined the team. Downey, who serves as the project lead for the trial site in Chicago, brought with him the software used at the University of Pittsburgh. In addition to Downey, neurosurgeons, neuroscientists, physiatrists, statisticians, and computer scientists from the universities are also participating in this multidisciplinary effort.

"The collaboration really helps accelerate everyone's work," Downey added. "We have

such broad expertise to draw from."

Scott Imbrie, the first patient participant to sign on to the trial in Chicago, is also a key member of the group. Imbrie broke his neck in a car accident in 1985 when he was 22 years old. After his accident, he was told he would be quadriplegic, but he was ultimately able to regain some mobility. He said he was motivated to volunteer for Hatsopoulos' trial by a desire to help others regain abilities like he had.

"I've always had a real positive attitude about everything in life," he explained. "I'm content with the way I am, but I wanted to help someone else out."

Brain-machine interface

In October 2020, Imbrie underwent surgery to implant electrodes in his brain. The



Two-time BRF grantee Dr. Nicholas Hatsopoulos, professor of organismal biology and anatomy at The University of Chicago, has an ongoing clinical trial underway testing a brain-machine interface in people with paralysis.



Clinical trial participant, Scott Imbrie, has a device connected to electrodes implanted in his brain. The device allows Hatsopoulos and his colleagues to record electrical signals from Imbrie's brain.



Dr. John Downey, the project lead on the study, and Dr. Hatsopoulos observe the electrical signals from each electrode (represented by a square in the computer screens) in Imbrie's brain.

electrodes are an improved version of the electrodes that Hatsopoulos used in his BRF-funded studies in non-human primates. Those studies helped show that the electrodes can last for extended periods without causing infections. The clinical trial is also using a refined version of the brain signal decoding algorithms that Hatsopoulos developed for his primate studies.

"These electrode arrays we implant are improved but they are essentially the same ones I used 20 years ago," Hatsopoulos explained.

Currently Imbrie comes to The University of Chicago three times each week to practice using electrical signals transmitted from his brain through the electrodes to manipulate an arm in what looks like a virtual reality video game.

The ultimate goal is to teach Imbrie to use a mechanical prosthetic arm. But first they must recreate sensations, so he can feel what he is moving with the arm. Hatsopoulos said that touch is essential for successfully completing a task like picking up and holding a coffee cup. He explained it helps you determine how much pressure is necessary

to prevent the cup from slipping and prevents you from using so much pressure you break the cup. They've already made substantial improvements since the first trial participant in Pittsburgh. Through careful placement of the electrodes in Imbrie's brain and by sending electrical signals through the electrodes to his brain, they've been able to recreate sensation in his fingertips.

"We are trying to recreate the feeling of natural touch," Hatsopoulos said. Imbrie's verbal feedback on what he experiences when his brain is stimulated has been essential to the team.

"It's been very exciting, even when it's not a successful day, they still get data from my brain," Imbrie said. "It is totally the biggest thing I've ever done in my whole entire life."

Now Dr. Hatsopoulos and his colleagues are recruiting more patients to the trial as they continue to record and process the data from Imbrie and the participants in Pittsburgh. They are using the data to refine the computer algorithms that convert the electrical signals from participants' brains into commands that control the arm. Eventually, Imbrie and the other participants will transition to using a robotic arm instead of a virtual one.

Having a diverse team of experts collaborating at two sites is helping to accelerate the work on the device, said Downey. "We can more rapidly iterate through ideas and processes that will improve participants control of the arm."

That progress means that 20 years after Dr. Hatsopoulos' first BRF Seed Grant, the basic research it funded is on the verge of yielding a brain-machine interface that could help people with paralysis. It may also help those with strokes or movement disorders like amyotrophic lateral sclerosis. Eventually, the technology might also be used to create more sophisticated prosthetics for people with amputations or to help people with paralysis regain the ability to move their own limbs.

"This clinical trial will not only help people with movement disorders, but it will also expand our basic understanding of the brain," Hatsopoulos said. Those insights may yield even more breakthroughs on treating brain disease and movement disorders in the future, providing an even greater return on BRF's initial investment in his work.



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Imbrie wears a virtual reality visor that allows him to see the virtual arm he is trying to manipulate using signals sent through the electrodes in his brain.



The screen shows the virtual arm Imbrie manipulates using his brain. To recreate the 3-dimensional effect, each eye sees a slightly different image as shown on the screen.

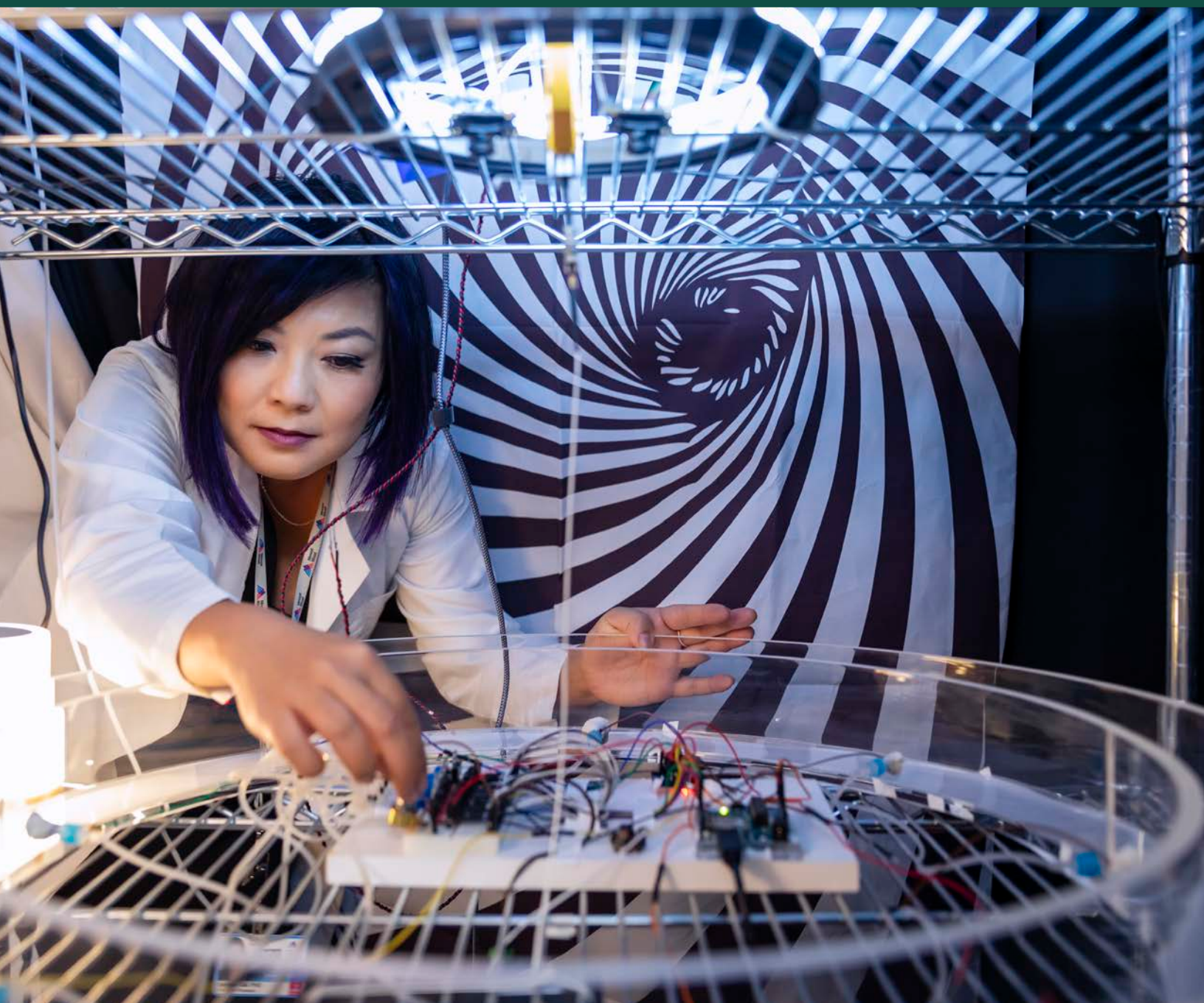
“The fact that a potentially life-changing device for people with spinal cord injury is currently being tested in a clinical trial because of the two BRF Seed Grants Dr. Hatsopoulos received is a testament to BRF’s mission to identify and fund the most innovative research that will lead to eventual treatments and cures.

The BRF grants provided the support Hatsopoulos needed to test and refine components of the brain-machine interface, and to build the collaborations that have made this tremendous advance possible. It has been our privilege to be part of a journey that has the capability to restore movement and touch to people with paralysis and other movement disorders.”

Terre A. Constantine, Ph.D.
BRF Executive Director and CEO

“We’re hoping that by democratizing neuroscience tools we created with BRF-funding, we will be able to increase innovation and our understanding of the brain so we can develop better treatments for brain diseases faster.”

Denise Cai, Ph.D., BRF Seed Grant Recipient, Icahn School of Medicine at Mount Sinai.



Dr. Cai is adjusting the Miniscope (miniature microscope) that will be used to visualize hippocampal activity in a freely-behaving rodent as it learns to spatially navigate in a new maze.

Tools for collaboration

Dr. Denise Cai Leverages a BRF Seed Grant to Build Free Tools for Neuroscience Research

Denise Cai, Ph.D. was excited to start her own lab. The next step was to get grant funding but that was taking longer than she expected. She questioned whether she would be successful. Then she was awarded a BRF Seed Grant which solidified her academic career in neuroscience.

"Beyond the monetary support, it was a vote of confidence that we were on the right track, that I was someone worth investing in," Cai explained.

BRF's investment in the state-of-the-art research Dr. Cai was pursuing has paid big dividends. She has secured an additional \$6 million in external grants to fund her research on the memory processes underlying conditions like post-traumatic stress disorder (PTSD). She has also become a leader in building and sharing free tools that are used by neuroscientists around the globe.

"The BRF Seed Grant supported us asking a scientific question and developing new technology to help us answer that question," added Cai, who explains that traditional funding sources like federal grants often don't provide support for the development of new tools.

The question Cai was trying to answer was how memories—specifically unpleasant ones—are updated and stored in the brain. Her study looked at what happened in the brains of mice after a mild electric shock to the foot comparable to a carpet static shock. To peer into the mice brains and observe the memory-formation and recall processes, they needed to develop a new miniature microscope that can record different colors at the same time. So, her team and collaborators created a thumb-sized one, simply from a couple of cellphone camera chips and melted plastic.

Using the Miniscope (miniature microscope), Cai found that after experiencing the mild shock the mice would reactivate the memory of the experience and search other memories. Then, they would link some memories together. She likened it to what happens after you develop food poisoning and you try to remember what you ate the day before to avoid becoming sick in the future.

"When something bad happens to you want to look back in time and you want your brain to link the

two experiences, so you know to avoid that in the future," she explained. "We are really interested in understanding the circumstances where this is beneficial and when it becomes harmful."

Understanding these processes could have important implications for treating people with PTSD who may experience traumatic memories that resurface during benign activities. She and her team are now studying the reactivation of memories during sleep. This is important because many people with PTSD have disturbing nightmares and struggle to sleep well. Cai wants to know if these sleep disruptions contribute to maladaptive memory storage and reactivation. If they do, Cai and her team think that developing therapies that help people sleep better after a traumatic experience may help reduce PTSD symptoms.

Cai and her colleagues are also continuing to develop new tools for neuroscience research and are making them freely available for other researchers online. For example, they improved their miniature microscope and shared the instructions for building it online. With support from the BRF grant, her team also created free software that researchers can use to analyze the data. Similar commercial software costs \$30,000 and would be too expensive for many labs to afford.

"We try to take things that are commercially available and then break them down into the most affordable and simplest parts," Cai explained. "Then we teach other labs how to build it, how to implement it, and how to use it in research."

The BRF Seed Grant has helped fund the development of these free neuroscience tools that are now being used by researchers around the world. This is helping researchers, who may not have the capacity to purchase expensive tools, to tackle a wide range of neuroscience questions from an array of perspectives.

Cai hopes that this will accelerate the pace of neuroscience discovery. "We're hoping that by democratizing neuroscience tools we created with help from BRF-funding, we will be able to increase innovation and our understanding of the brain so we can develop better treatments for brain diseases faster."

Making memories

BRF SIA Recipient Dr. Ilana Witten Explores What Makes Memories Last

A 2021 BRF Scientific Innovations Award (SIA) is allowing Ilana Witten, Ph.D., to answer a fundamental question in neuroscience—what makes some memories lasting and others fleeting?

In support of this line of inquiry, Witten's lab has long studied the role of dopamine, an important chemical messenger in the brain, in learning. With a 2021 BRF \$150,000 SIA, which is designed to help established researchers take on new high-risk high-reward projects, she is pursuing a whole new line of inquiry focusing on the role of dopamine in memory consolidation. It's a rare opportunity, Witten explained, because most funding sources only support well-established projects that have a proven track record of success.

To answer this question of what makes some memories lasting and others fleeting, Witten is using the latest generation of a cutting-edge technique called optogenetics. She will use light to turn on and off individual brain cells that have been genetically engineered to be light sensitive. This precise level of control is essential to reproduce the complex interactions of individual brain cells, which some in the field liken to an orchestra. "This new technique allows you to make each brain cell fire exactly when you want it to rather than having a group of neurons firing together," she explained. "This is much more realistic."

She and her colleagues are using this tool to test the effects of dopamine when an animal replays

an experience to learn from it or perhaps to form a memory. Witten wants to find out what happens if they turn on brain cells that produce dopamine during replay. Will the dopamine make the replayed memory stronger or cause it to be replayed more? Will the animal like the memory more if dopamine, which creates pleasurable feelings, is released during replay? The answers are not only key to understanding diseases that affect memory, but also to understanding fundamental aspects of human neuroscience.

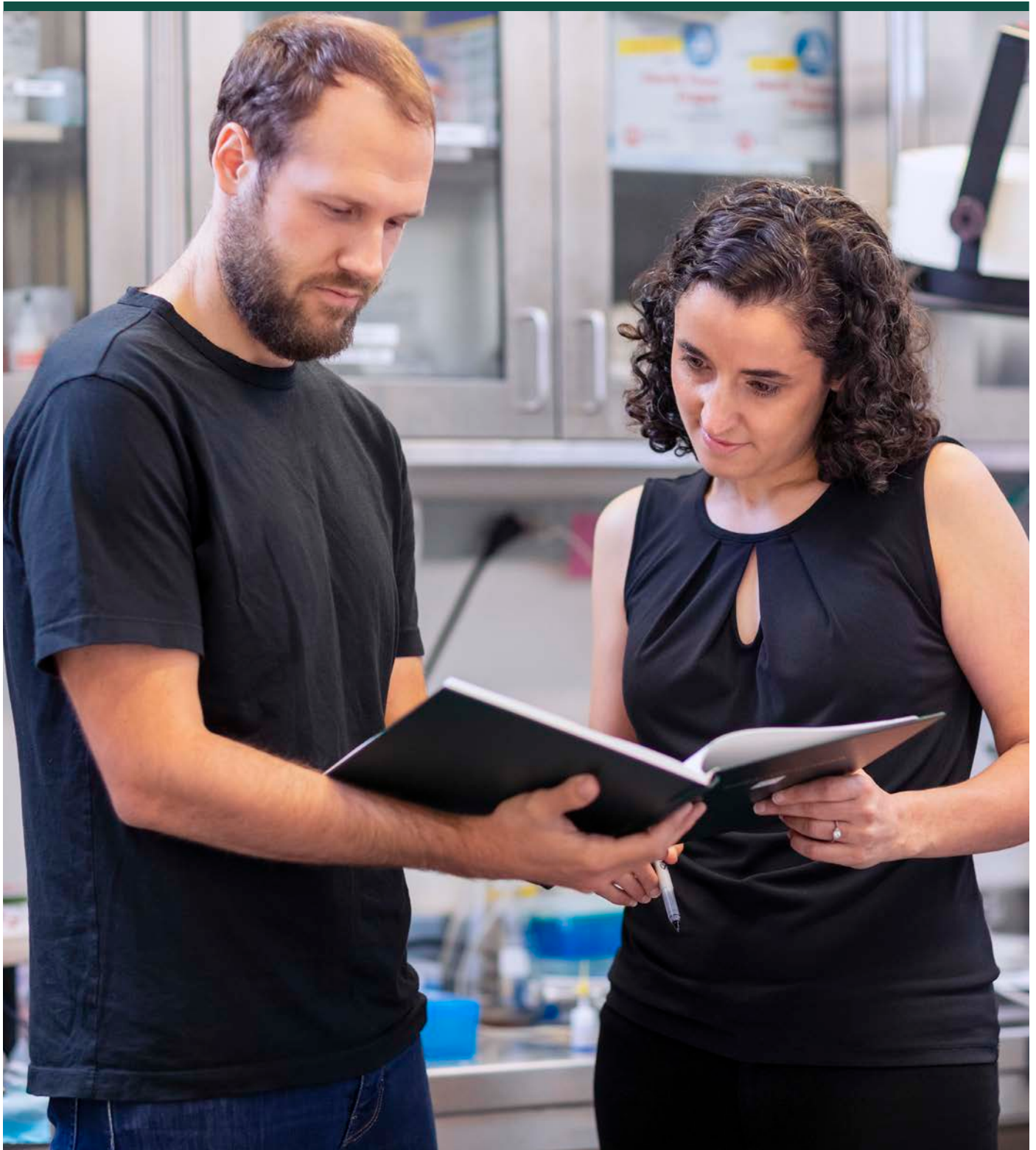
"We're made up of memories," Witten said. "Memories make up a lot of our personality. They are necessary to function in life and to make decisions. They are one of the most fundamental things that make us human."

By supporting the work of visionary and collaborative scientists like Witten, BRF is working to accelerate the pace of discovery throughout the field of neuroscience and speed the development of new approaches to treatment.

"This award from BRF is allowing us to pursue a new direction that we think will have a lot of implications for diseases that affect memory. If dopamine plays a role in determining which memories are permanent and which are forgotten, it could have important implications for diseases like addiction in which memories are too strong, or conditions like dementia in which memories are lost."

"The future of neuroscience depends on synergy and collaboration between scientists and funders like BRF who are willing to take a chance on a new idea."

**Ilana Witten, Ph.D., BRF Scientific Innovations Award Recipient
Princeton University**



In addition to investing in this kind of ground-breaking research, BRF prides itself on identifying and supporting collaborative scientists whose work is likely to have ripple effects on the field of neuroscience. In Witten's case, those ripples extend to both undergraduates and graduate students in her laboratory. According to Witten, "undergraduates bring a lot of energy, enthusiasm, and different perspectives to the lab. They are the future."

Understudied brain cell may

BRF Seed Grant Propels Dr. Rafiq Huda's Ground-Breaking Work

"I've been dreaming about having a lab for ten years," said Rafiq Huda, Ph.D., who just launched his laboratory in January 2020. "One of the great things about being a new principal investigator is you can go in new directions, but the scary, risky thing is that these new ideas are completely untested."

Receiving his first grant—a 2021 BRF Seed Grant—not only gave Huda the monetary support he needed to hire a team and begin conducting experiments, it also gave him the confidence of knowing that the leading neuroscientists on BRF's Scientific Review Committee thought his idea could provide valuable insights for the field of neuroscience.

"It was really critical for me to get that feedback from a prestigious entity like Brain Research Foundation—that it's worth seeing where this line of inquiry takes us," he explained. **Since receiving his BRF grant, he's secured three more grants from foundations and has applied for a National Institutes of Health grant that could support the project long-term.**

His idea is that an understudied type of brain cells called astrocytes, which are currently thought to play a supporting role in the brain, may play a central role in modulating movement and could be key to developing treatments for movement disorders like Parkinson's disease.

Huda's work focuses on testing how astrocytes located in part of the brain called the striatum help coordinate movement and how this goes awry in diseases like Parkinson's disease. The striatum receives information from all over the brain and acts as a control center for movement. In patients with Parkinson's disease, neurons that send messages to the striatum via a chemical messenger called dopamine die off. As the dopamine disappears, people with Parkinson's disease begin to develop slowed movements or difficulty speaking or walking.

Using a cutting-edge imaging technique called two-photon microscopy, Huda and his team are observing signaling in astrocytes in live mice. They look at what the astrocytes are doing in both healthy mice while they are moving and mice with a Parkinson's disease-like movement disorder. Then, they will see if they can alleviate movement deficits in the mice by directly stimulating the astrocytes.

To be successful, the project requires multidisciplinary collaboration between Huda, experts in Parkinson's disease, as well as partners with both surgical and computer expertise.

"Neuroscience is a diverse field that marries a lot of different techniques," Huda said. "Bringing all these techniques together at a high level to be able to execute a complex project like this requires people to collaborate. That's really a critical component to any neuroscience study."

If the study shows that Huda is right about the role of astrocytes in coordinating movement, it could lead to new treatments for Parkinson's disease or other movement disorders that target the astrocytes.

"My hope is that we can come up with a more nuanced framework for understanding how the various types of cells in the brain really work together to enable critical functions like movement."



offer clues to Parkinson's disease

“Neuroscience is such a diverse field that marries a lot of different techniques together. Bringing all these techniques together at a high level to be able to execute a complex project like this requires people to collaborate. Without BRF's vision and support, that kind of collaborative science wouldn't be possible.”

Rafiq Huda, Ph.D., BRF Seed Grant Recipient, Rutgers University

Since receiving his BRF grant, Dr. Huda has secured three additional grants to support his project.



“A lot of nonprofits don’t want to collaborate with other nonprofits because they look at them as competitors. I don’t look at it that way. Why not partner with an organization like BRF that has decades of experience identifying and funding the most ground-breaking brain research?”

Kevin Jameson, Founder and President, Dementia Society of America



The first grant funded by the Dementia Society of America could one day have important implications for treating Alzheimer's disease.

Collaborating for a shared purpose

The Dementia Society of America and Brain Research Foundation Team Up to Support Brain Health Research

Kevin Jameson founded the Dementia Society of America in 2013 after experiencing first-hand the challenges families face when a loved one has dementia. When his wife and partner of 20+ years, Ginny, began experiencing symptoms of dementia, it took years of running through a gauntlet of different physicians to get a diagnosis. In the process, Jameson learned a lot about the condition and realized there was a need for more accessible information.

"I really started to dig in and learn about dementia and thought nobody is really telling this story the way I think it needs to be told," said Jameson, who now serves as the organization's president.

Now, an innovative partnership between Brain Research Foundation and the Dementia Society of America is helping accelerate research on brain health and dementia.

The collaboration will leverage BRF's nearly 70-years of experience in identifying and funding innovative, high-impact brain research and fostering the careers of promising scientists. The Society will provide additional funding for projects helping to expand BRF's research grants.

"This unique collaboration will allow BRF to fund even more ground-breaking brain research and advance both organizations' missions," said Terre A. Constantine, Ph.D., Executive Director and CEO of BRF.

"Working with BRF allows us to continue focusing on what we do best—sharing easy to understand information about dementia—while also allowing us to invest in research on brain disease," Jameson said.

The first grant funded by the Dementia Society of America is a 2021 Seed Grant for Xiaojing Gao, Ph.D. at Stanford University to support his work refining the delivery of gene therapy in the brain, which could

one day have important implications for treating Alzheimer's disease. Its Board of Directors chose the project from a selection of options identified by the BRF's Scientific Review Committee.

"We are relying on BRF's expertise to present us with the best of the best in terms of Seed Grant opportunities," Jameson explained. This will allow the Dementia Society of America to expand its reach into funding research without taking resources away from the organization's core education mission.

The Society focuses on educating the public about what Jameson calls the "dementias."

"Dementia is plural because it's not a disease; it's a syndrome with multiple causes," explained Jameson. Though he and his wife Ginny never learned the exact causes of her dementia, they did learn she had multiple risk factors including having been hospitalized for a concussion, undergoing hours of anesthesia during back surgery, and taking medication associated with a higher risk of dementia. To help others, the Dementia Society of America shares information about protecting brain health to prevent the disease.

The Society also creates programs and resources to help improve the quality-of-life of people with dementia and their caregivers. Jameson said that too often people with dementia and their caregivers hear the condition described in "horrific terms." Caregivers are told their loved one's life is over and that they are not the same. But Jameson said that's the wrong message. He said he learned from Ginny, who asked immediately after her diagnosis where they were going for lunch, that quality of life is what's most important. After her diagnosis the two of them traveled to China and India, Egypt, Sweden, Ireland, and England and took advantage of simpler pleasures like holding hands and going for walks.

"It's how you live in the moment."

gratitude

Some of Brain Research Foundation's most valuable collaborators are our donors. Their passion and generosity provide crucial support for the bold research needed to make breakthroughs. Every contribution counts and helps the nation's brightest scientists pave the way to new cutting edge discoveries. We are honored by the trust our donors have placed in BRF and are grateful for their support as we try to advance neuroscience in the most inventive and effective way possible.

Thank you.

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We do our best to accurately recognize all of our donors. If you see an error or omission, please contact us at 312.759.5157.

Letter from the Treasurer

Brain Research Foundation continues to fund ground breaking research thanks to the increasingly generous contributions of our donors and our superior investment performance. During the last two years, more than 100% of our annual donor contributions have been used to fund research and educational programs in neuroscience. We are proud of having achieved these results, on average, over the last nine years.

BRF continues to fund the most innovative neuroscience research in the most beneficial ways to advance the understanding of the brain. As we review all of our programs, we funded over \$3.6 million of projects in the last two years. That amount exceeded our contributions by \$1.1 million, thus exceeding our objective of investing at least 100% of our annual support in worthy neuroscience programs. We are proud of our ability to be good stewards of our donor dollars.

We have included a summary of our income and major expenses and a condensed balance sheet for fiscal years 2020 and 2021. We encourage you to review our audited financial statements on our website or contact the BRF office.

The Board of Trustees and staff continue to work hard to sustain your support to fulfill our mission. As we start our 68th year, we look forward to building our donor base and funding more researchers who are focused on improving life through innovative neuroscience research.

Sincerely,

A handwritten signature in black ink, reading "David H. Fishburn". The signature is fluid and cursive, with the first name "David" and last name "Fishburn" clearly legible.

David H. Fishburn
Treasurer

Statement of Activities and Changes in Net Assets

Highlights of Income Statement year ended June 30, 2020 and 2021

	2020	2021
Beginning Net Assets	\$ 17,347,004	\$ 18,748,138
Contributions	1,325,468	1,192,915
Interest and Dividends	404,805	399,420
Net Realized and Unrealized Gains on Investments	1,648,027	6,289,457
Total	\$ 20,725,304	\$ 26,629,930
Expenses		
Program Services	\$ 1,580,930	\$ 2,039,292
Supporting Services	396,236	501,979
Total	\$ 1,977,166	\$ 2,541,271
Total Net Assets	\$ 18,748,138	\$ 24,088,659

Statement of Financial Position

As of June 30, 2020 and 2021

Assets	2020	2021
Cash	\$ 177,668	\$ 86,465
Investments	19,134,371	24,761,584
Contributions Receivable	-	-
Prepaid Expenses and Other Current Assets	15,000	-
Security Deposits	5,200	5,200
Property and Equipment - Net	1,179	-
Total Assets	\$ 19,333,418	\$ 24,853,249

Liabilities and Net Assets	2020	2021
Liabilities		
Accounts Payable and Accrued Expenses	\$ 60,236	\$ 52,033
Deferred Rent Expense	15,044	7,557
Grants Payable	510,000	705,000
Total Liabilities	\$ 585,280	\$ 764,590

Net Assets		
Net Assets Without Donor Restrictions	\$ 16,610,676	\$ 21,386,200
Net Assets With Donor Restrictions	2,137,462	2,702,459
Total Net Assets	\$ 18,748,138	\$ 24,088,659

Total Liabilities and Net Assets	\$ 19,333,418	\$ 24,853,249
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