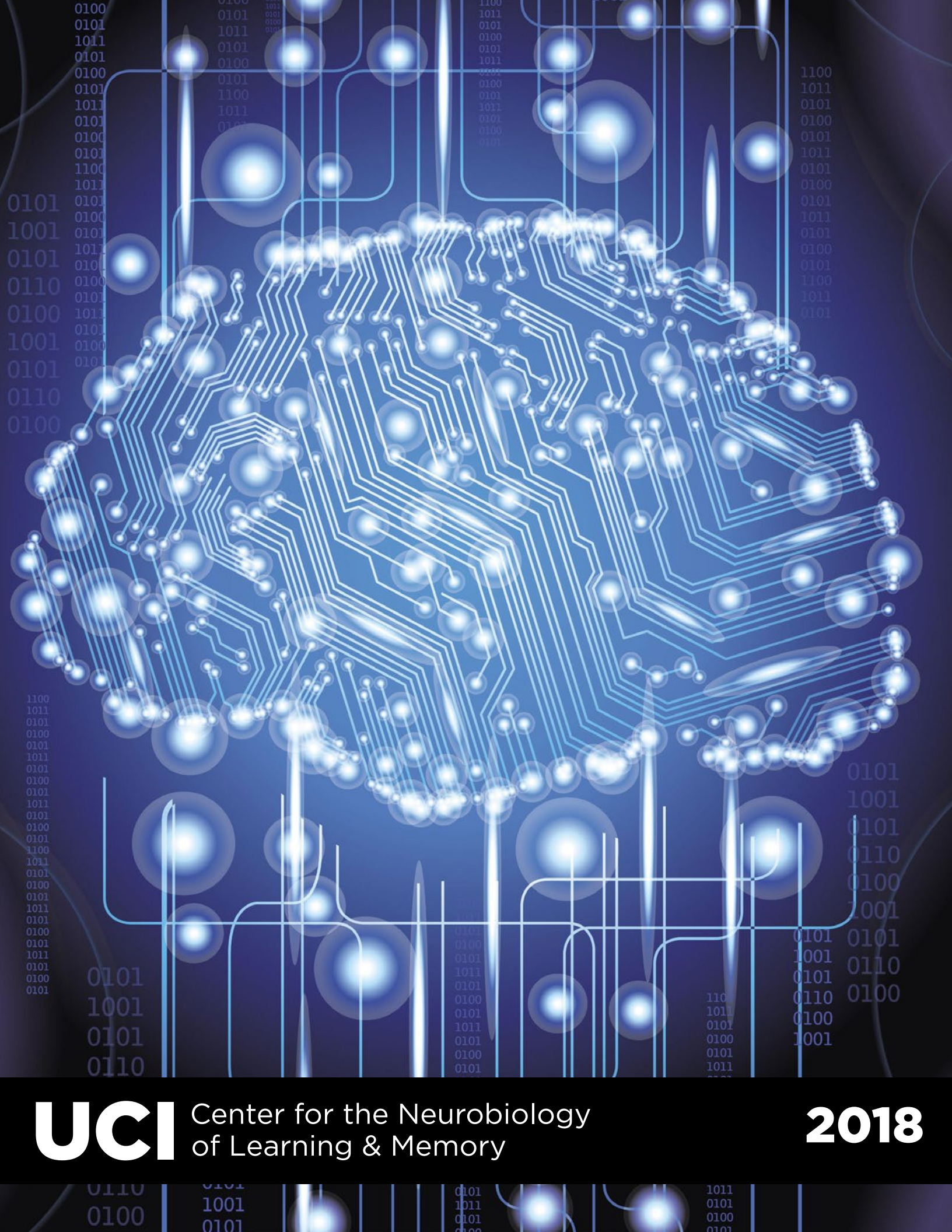


UCI Center for the Neurobiology of Learning & Memory

2018

Cracking the Memory Code since 1983

Contents

Center for the Neurobiology of Learning and Memory
University of California, Irvine

Director
Michael Yassa

Associate Director
Sunil Gandhi

Director of Outreach and Education
Manuella Yassa

Administrative Support
Michael Gomez

Faculty Fellows

UCI Fellows

Michael Alkire
Pierre Baldi
Tallie Z. Baram
Kevin Beier
Ruth Benca
Sven Bernecker
Mathew Blurton-Jones
Aaron Bornstein
Gregory Brewer
Jorge Busciglio
Susan Charles
Susana Cohen-Cory
Karina Cramer
Steven Cramer
Barbara Dosher
Lisa Flanagan
Norbert Fortin
Christie Fowler
Ron Frostig
Christine Gall
Sunil Gandhi
Charles Glabe
Douglas Granger
Kim Green
John Guzowski
Gregory Hickok
Robert Hunt
Kei Igarashi
Autumn Ivy
Susanne Jaeggi
Claudia Kawas
Jeffrey Krichmar
Frank LaFerla
Julie Lauterborn
Michael Lee
Michael Leon
Frances Leslie
Linda Levine
Charles Limoli
Jack Lin
Elizabeth Loftus
Angela Lukowski
Gyorgy Lur
Gary Lynch
Mark Mapstone
Steven Mahler
Bryce Mander
Elizabeth Martin
James McGaugh
Bruce McNaughton
Sara Mednick
Raju Metherate
Bin Nan
Andrea Nicholas
Diane O'Dowd
Andre Obenaus
Jodi Quas
Uma Rao
David Reinkensmeyer
Steven Small
Robert Spitale
Craig Stark
Oswald Steward
Mark Steyvers
Andrea Tenner
Leslie Thompson
Theodorus van Erp
Craig Walsh
Marcelo Wood
Xiangmin Xu
Michael Yassa

External Fellows

Ted Abel, Univ of Iowa
Ralph Adolphs, Caltech
Timothy Allen, FIU
Stephan Anagnostaras, UCSD
Michel Baudry, Western Univ
Federico B.Rattoni, UNAM
Kasia Bieszczad, Rutgers Univ
Jennifer Bizon, Univ of Florida
Tim Bredy, Univ Queensland
Sara Burke, Univ of Florida
Robert Clark, UCSD
Laura Colgin, UT Austin
Michael Fanselow, UCLA
Joaquin Fuster, UCLA
Paul Gold, Syracuse Univ
Ivan Izquierdo, PUCRS
Barbara Knowlton, UCLA
Jill Leutgeb, UCSD
Stefan Leutgeb, UCSD
Kelsey Martin, UCLA
Aaron Mattfeld, FIU
Andrew Maurer, Univ of Florida
Mark Mayford, Scripps
Richard Morris, Univ Edinburgh
John O'Doherty, Caltech
Barry Setlow, Univ of Florida
Alcino Silva, UCLA
Ivan Soltesz, Stanford
Larry Squire, UCSD
Wendy Suzuki, NYU
Brian Wiltgen, UC Davis

Director's Message

Dear Colleagues and Friends,

As we approach the Holidays, I would like to take a moment to reflect with you on a brilliant 2018.

This year, we celebrated our 35th anniversary with a landmark 5-day scientific conference that attracted over 1,000 attendees from more than 35 countries. We launched UCI Brain, a brand new campus-wide initiative on interdisciplinary brain science. Our CNLM Ambassadors trained two cohorts of the Brain Explorer Academy, our flagship community educational program for school-age children. We heard from renowned speakers at our Distinguished Lecture Series, including a lecture by UCI Founding Faculty Dr. James McGaugh, held in front of a capacity audience at the Barclay Theatre.

On the research front, our Fellows launched new campus research centers on sleep and circadian neuroscience as well as the study of cannabis. Collectively, the Fellows received over $30 million in new federal funding to conduct transformative brain research and published more than 100 research reports in high impact journals including *Nature*, *Neuron*, and *PNAS*. Our work continues to make headline news in venues such as *The New York Times*.

I am delighted to announce that Dr. Sunil Gandhi has accepted my invitation to serve as Associate Director of the CNLM. Dr. Gandhi leads a vibrant research group that is focused on understanding how certain brain cells control its ability to rewire connections and reorganize its functions. I look forward to working with Dr. Gandhi to serve the CNLM in the coming years.

While I am honored to work alongside such renowned, productive and brilliant faculty, we all recognize that we cannot do it alone. We are proud of our partnerships and are extremely grateful to have the support of our Friends and the generosity of the Orange County philanthropic community. The role of private philanthropy in moving the needle on high-risk, high-reward science is more important now than ever. Read more inside about the highly anticipated launch of the CNLM High Impact Research Program, or what we like to call "Shark Tank for Brain Science." We are very serious about meaningful partnership and are excited to share our most innovative ideas with you.

We are on the verge of the next transformative discovery. I hope you will seize this opportunity and join hands with us. It is an exciting time for the brain!

Michael A. Yassa, Ph.D.
Professor and CNLM Director

Brain Initiative

A Bold Vision for the Future

Unlocking the mysteries of the brain is humanity's final frontier.

The impact of such a feat will transform every facet of our lives. It will empower a new generation of innovative technology and transform how we educate our youth by unlocking the formidable potential of the human mind. It will allow us to eradicate brain disease and promote brain health. It will have countless legal implications from understanding criminal behavior and recidivism and assessing offender risk, to novel therapies for drug addiction. It will impact economic growth and development as we understand the basis of human decision making. It will elucidate the basis of emotion, social behavior, and artistic expression. It will fundamentally transform our understanding of cruelty and conflict, potentially helping us usher in a new era of generosity and peace. Such a feat can only be realized with an army of brilliant minds working together to crack the brain's code.

The Brain Research through Advancing Innovative Neurotechnologies® (BRAIN) Initiative was launched in 2013 to "accelerate the development and application of new technologies that will enable researchers to produce dynamic pictures of the brain that show how individual brain cells and complex neural circuits interact at the speed of thought."

Long desired by researchers seeking new ways to treat and prevent brain disorders, this picture will fill gaps in our knowledge and provide unprecedented opportunities for exploring how the brain enables us to record, process, store, and utilize massive amounts of information.

In December 2017, representatives from the world's major brain projects made a formal declaration to establish the International Brain Initiative. By coordinating their efforts globally, neuroscientists can speed up progress on 'cracking the brain's code.'

Investments in Brain Initiatives are now expanding at breakneck speed, creating a tremendous opportunity for UCI, a trailblazer in brain science, to have global impact. The first roots of systematic brain science began here at UCI in 1964 with Founding Faculty James McGaugh establishing the world's first neuroscience department.

Since then, UCI has been at the forefront of discovery in the neurosciences. Today, the neuroscience community at UCI spans across more than 60 departments and research units with over 100 scientists studying the brain at every level, from genes to intelligent machines. UCI was born to advance the audacious goal of improving society through globally preeminent research, life-enhancing discoveries and a world-class education for the most talented students, regardless of background.

The UCI Brain Initiative (UCI Brain) was launched in July of 2018 by the CNLM with support from the Office of the Provost with an equally audacious goal: to achieve a comprehensive understanding of the brain through collaborative, cutting-edge research, and to provide exceptional training to the next generation of leaders in brain science.

Neuroscientists at UCI will work in teams to pursue transformative research organized under four major themes: (1) The Healthy Brain, (2) The Computational Brain, (3) The Social Brain, and (4) The Artistic Brain. They will also access a global network of collaborators through the International Brain Initiative. The future is full of possibilities.

UCI Brain honors our legacy and re-imagines our future.

Visit us online
brain.uci.edu

Like us on Facebook
fb.me/ucibrain

Follow us on Twitter
@uci_brain

UCI Brain

An army of brilliant minds working together to crack the brain's code

UCI Brain includes a team of over **100 leading neuroscientists** on campus and connects to a global network of collaborators through the **International Brain Initiative**.

brain.uci.edu

April 2016

Over 75 stakeholders assembled to discuss “grand challenges” in neuroscience research at the Global Brain Workshop at The Johns Hopkins University.

September 2016

The concept of an international collaboration amongst large-scale government-sponsored neuroscience initiatives is introduced at the Rockefeller Meeting.

February 2017

Key players in the imminent creation of the International Brain Initiative met at the UN Headquarters to prioritize common challenges across global brain initiatives.

December 2017

During the “Brains at the Dome” Workshop, the Declaration of Intent for the IBI was announced, marking a historical day for neuroscience.

May 2018

At the first official meeting of the IBI in Daegu, Korea, attendees solidified the IBI’s mission by drafting the Vision and Aspirational Goals.

July 2018

Presentation of the final IBI Vision and Aspirational Goals occurs in Geneva. NSF workshop of the Inventory Working Group at the National Academy of Sciences.

October 2018

The UCI Brain Initiative and The Kavli Foundation co-host the Systems Implementation Workshop of the IBI Inventory Working Group in Irvine, CA.

November 2018

The initial IBI stakeholders gather in La Jolla, California to confirm the organization’s structure and discuss the 2019 outlook.

2019 and Beyond

Having established an organizing structure, the IBI will continue their support of global brain initiatives and the neuroscience community at large.

IBI INTERNATIONAL BRAIN INITIATIVE

internationalbraininitiative.org

UCI Hosts International Brain Initiative Workshop on Systems Implementation

By: Anna Smith

The UCI Brain Initiative and The Kavli Foundation jointly sponsored and hosted a workshop of the International Brain Initiative (IBI) on October 22-23, 2018 with the purpose of developing guidelines for implementation of a global inventory of brain projects.

Many governments around the world are investing heavily in neuroscience research. While new discoveries in brain science have the potential to help millions of people around the world, it is the belief of the IBI that by international collaboration and knowledge sharing we can accelerate discovery and maximize global neuroscience efforts.

The Declaration of Intent to establish the International Brain Initiative was announced on December 8th, 2017 at a meeting of representatives from some of the world's major brain research projects, supported by The Kavli Foundation and hosted by the Australian Academy of Science in Canberra.

The first project agreed upon by the international community is a **Global Inventory of Brain Initiatives**. To assist in the development of the Inventory, the National Science Foundation recently funded a Workshop to Develop a Global Inventory of Brain Initiatives that took place in Washington D.C. on July 23-24, 2018. Led by organizers Melina Hale and Patrick Hof, NSF Workshop participants contributed their 'blue-sky' ideas for Inventory features and use-cases, as well as advised on potential risks associated with inventory development and how to mitigate them.

The second workshop, held in October, was led by Michael Yassa (UC Irvine), Satrajit Ghosh (MIT), and Stephanie Albin (The Kavli Foundation). It sought to immediately build upon the enthusiasm and momentum generated at the NSF workshop by exploring more practically what the minimum set of requirements for the Inventory should be, and how to make the Inventory accessible and useful to the global neuroscience community.

Major outcomes from the workshop include identification of major categories of users, in order to focus the inventory on their particular use-cases, as well as providing guidelines for implementation of systems that allow scientists to identify potential collaborators across the globe, find and fill gaps in research, demonstrate productivity and impact, and create a community discourse platform. . Such a platform, viewed as a high priority item, would include information on funded projects, publications, and patents. A major publication to delineate these guidelines is now underway.

Feature Story

UCI Organizes Landmark International Conference on Learning and Memory

By: Cathy Lawhon Feldman

In April of 2018, UC Irvine's Center for the Neurobiology of Learning and Memory organized a wide-ranging conference that spanned everything from Aristotle to artificial intelligence and celebrated the work of neuroscientists around the world. It was a fitting tribute to the center, established 35 years ago by UC Regents as the first research unit of its kind, and it set the stage for an even more brilliant future.

"The CNLM is a remarkable place to work every day with incredible people," says Michael Yassa, Chancellor's Fellow and Professor of Neurobiology and Behavior, Center Director and the conference's host and program chair. "The biggest challenge in neuroscience today is to understand how the brain functions, how memory works, and how we acquire knowledge. We're taking the lead on that challenge at UCI."

The five-day International Conference on Learning and Memory was held April 18-22 at the Waterfront Beach Resort in Huntington Beach and attended by more than 1,000 professors, post-doctoral researchers and graduate students from 35 countries. Participants heard a keynote lecture from a Nobel laureate and sixteen plenary session speakers, and had opportunities to attend more than 50 symposia, panels, and lightning talks as well as more than 250 poster presentations. The atmosphere brimmed with the curiosity and excitement that comes with being part of a historical event. Neuroscience luminaries mingled with future stars, demonstrating the kind of collaboration many say is a crucial element to solving the mysteries of the brain and curing its ailments.

"One-third of all diseases are brain-related," Yassa says, "and yet globally we have failed dramatically in clinical trials because we have not yet deconstructed the brain to find out how it works. We also haven't adequately shared data. This is what we're doing at UCI – recruiting the best researchers to find out how the brain works and strengthening what has always been a culture of collaboration and team science."

UCI's Influence

James McGaugh, Distinguished Professor Emeritus in Neurobiology and Behavior, could accurately be called the patriarch of the effort. Along with the late Norman Weinberger and Gary Lynch, professor of psychiatry and human behavior, McGaugh proposed the Center for Neurobiology of Learning and Memory, drawing on his passion for the subject. He served as its founding director.

"If you think about it, our lives are only one second or less long," McGaugh said at the conference's opening presentation. "By the time we think about our next move, the moment is over. The glue in the process of our lives is the formation of memory. Without memory, there would be no science. Memory is amazing."

McGaugh's recent studies on people who remember in detail almost every autobiographical event of their lives has been presented at numerous scientific conferences and featured in mainstream media, such as 60 Minutes. His subtler but equally important influence has been his mentorship of high-level researchers now working at UCI and in labs across the globe, many of whom attended the conference.

Take Carol Barnes, former president of the Society for Neuroscience and a plenary session speaker. She studies aging and memory at the University of Arizona. Specifically, she looks at the loss of function in brain synapses and corresponding memory dysfunction. McGaugh and Lynch were on her doctoral review committee and she attended the first international conference on learning and memory that they helped organize in 1982.

"We've come a long way since then regarding knowledge of cognitive outcomes and the development of methods to possibly treat brain dysfunction," she says. "It's been possible, in part, because of these wonderfully interdisciplinary meetings."

Much of Barnes' research has been facilitated in part by John Guzowski, UCI Associate Professor of Neurobiology and Behavior, whose career path illustrates interdisciplinary relationships and influence. He earned his doctorate in molecular biology from UCI in McGaugh's lab then moved on to a post-doctoral position at Johns Hopkins University and a stint at a private biotech company before settling in Barnes' lab in Tucson with a National Institutes of Health grant. There, he perfected a procedure he'd been working on called catFISH (cellular Compartment Analysis of Temporal Fluorescence in Situ Hybridization). The single-cell imaging technique allows him, Barnes and others to look into the brain and identify neurons tagged by the Arc gene, indicating that they have been activated in a recent behavior.

"It was a case of chance favoring the prepared mind," says Guzowski of his discovery. He returned to UCI in 2005 and he's using the catFISH technology today to study inflammatory response to psychological distress and how it causes dysregulation in neural circuits, affecting behavior.

"Because I was trained as a molecular biologist instead of a memory researcher, I looked at results that others might have seen as an artifact or background problem and applied them to something useful," he says of the catFISH technique.

"This process of attacking problems from different angles and disciplines is what McGaugh, Weinberger and Lynch had in mind back in 1983. That's one reason CNLM has had the impact that it has."

Multi-pronged Approach

The conference highlighted other successes in UCI's team science approach to learning and memory research. Sessions were led by Elizabeth Loftus, Distinguished Professor of Psychological Science, who has done groundbreaking work on manipulation of memory, and Susanne Jaeggi, Associate Professor of Education, who studies working memory, or the amount of information one can hold, and how interventions can improve learning skills. Claudia Kawas, Professor of Neurology, shared her findings on cognition in people 90 and older while Gary Lynch, Professor of Psychiatry and Human Behavior, talked about synaptic plasticity and its implications in constructing complex memories.

James McGaugh and Carol Barnes

Memory is everywhere and everything. It is hard to imagine a more important facet of life than the glue that binds one moment to the next.

The CNLM routinely fosters connections between neuroscience and obvious partners such as engineering, biology, medicine and education, but also less traditional partners such as the arts, says Yassa.

A recent collaboration with UCI's Claire Trevor School for the Arts on the science of acting exposed drama students to the campus's top researchers in behavior, learning and memory, psychology and more, providing the opportunity to take findings from those fields and apply them to acting.

"Memory is everywhere and everything. It is hard to imagine a more important facet of life than the glue that binds one moment to the next. It is only natural that figuring out how we learn and remember can help an actor to simulate reality or help a musician master a new piece. We are simply formalizing this and taking a scientific approach to understanding it."

Looking for Big Ideas

Edvard Moser, 2014 Nobel laureate in physiology and medicine, traveled to the conference from the Norwegian University of Science and Technology in Trondheim, Norway to give the conference's keynote address. Moser's relaxed demeanor disguises a precise yet creative intellect that in 2005 recognized what other neuroscientists had missed. Dressed in jeans and a hoodie and armed with an easy smile, the globally renowned scientist described to a packed house how he and his research team discovered grid cells, brain cells that allow us to orient to and understand our position in space.

In an evening fireside chat with Yassa and other conference leaders and members of the public following his keynote lecture, Moser shared insights about research, winning a Nobel Prize, where neuroscience is going in the future, and walking on volcanoes.

"There is still much to do," he explained. "I could go on forever. That's the fun of science. The mark of a scientist is to be forever dissatisfied."

Moser too champions the concept of interdisciplinary teamwork.

"We knew this was an important breakthrough," he said of his discovery, "and it was appreciated by people in many different fields. Especially in neuroscience, we need to reach many levels beyond what one person can do, so more teamwork is very important."

"And," he added, "While teamwork is very important, we still need individuals who have ideas. Ideas are lacking most of all. For that, we need to promote creativity."

Future of Neuroscience

McGaugh looks around the packed conference venue at hundreds of young researchers and agrees with Moser. "We need ideas now," he says, "not to codify what was, but new people with new ideas. When we started CNLM in 1983, the Regents approved it, making it official in a very strong sense. It was the first of its kind in the nation."

"I did my part. Now, all these new scientists with fresh energy need to continue to study how systems work together to give rise to behavior."

In a session aptly named The Future of Neuroscience, experts in the field laid out some of the issues. Tools that allow scientists to re-engineer lab animals – to alter their brains in order to better understand how they work – will grow more and more sophisticated in the future

Elizabeth Buffalo, Professor of Physiology and Biophysics at the University of Washington, reminded conference attendees: "With all this talk of new tools and techniques and

We still need individuals who have ideas. Ideas are lacking most of all. For that we need to promote creativity.

data, I don't want us to lose track of the importance of behavior. We need to distinguish between learning and performance. So much of this data is dependent on how an animal

is trained. And invasive tools affect behavior."

What invasive tools? Talk to Sumner Norman, post-doctoral research scholar at Caltech and UCI alumnus, about brain-computer interfaces (BCI). "Simply put," he said, "these technologies decode brain signals into the control of an external device and then provide feedback to the brain." Current BCI imaging modalities include micro-electrode array, electrocorticography and electroencephalography, all with varying degrees of invasiveness.

In a video presentation, Norman showed that a quadriplegic man with micro-electrode array implantation buried in his brain could control a mechanical arm with brain signals, directing it to pick up a glass of beer and hold it to his lips so he could swallow. Norman predicts giant leaps in BCI due to booming interest both in academia and biotech industries. "We still can't begin to approximate the brain, since we have 80-100 billion neurons in the brain and more than 100 trillion synapses" he said.

Sunil Gandhi, UCI Associate Professor of Neurobiology and Behavior and CNLM's recently appointed Associate Director is studying the brain's capacity to rewire its connections and reorganize its function in by introducing immature cells rather than asking an injured adult brain to produce them. Testing the theory in mice, he has proven that an adult mouse brain deprived of vision can recover with implantation of inhibitory stem cells. He has also been able to image and reconstruct cells that were activated. Future questions include: what mechanism regulates the plasticity of connections in the young brain? How might we manipulate neural circuits to reactivate this plasticity?

Where does neuroscience go from here? Roger Bingham, affiliated with the Salk Institute for Biological Studies in La Jolla, asked the assembled scientists. With his focus on science communication, he co-founded the Science Network and created PBS station KCET's Science and Society Unit. He says neuroscience is at "a huge transitional moment.

In Alice in Wonderland," he said, "when Alice meets the Cheshire Cat after eating this and drinking that and growing and shrinking, he asks her: 'Who are you?' And she's not quite sure. So this is the same question I ask you: What size do you want to be? Who do you want to be? The notion of humans flourishing means we have to have a sense of who we are. Neuroscience is at the absolute forefront of supplying what we need. Will our inventions usurp us? Will we produce artificial intelligence that knows us better than we know ourselves? When you talk about the future of neuroscience, you're talking about the future of humanity."

Left to Right: Michael Yassa, Kei Igarashi, Edvard Moser, and Lynn Nadel

The Future at UCI

With nothing less than the future of humanity at stake, Yassa is excited about the CNLM's role, including its 35-year history, its present and its future.

"The CNLM is an incredible intellectual atmosphere – a great place to be a scientist," he says. "We're continuing to demonstrate leadership in the world. We're attracting faculty who are well-established in their careers and others who are rising stars. There's a great deal of creativity, teamwork and ideas here. A conference like this one serves to highlight some of it, but the hard work that goes into understanding the brain goes on every day. We're always looking forward to what we'll be able to discover and share with the world in the future."

Yassa and the CNLM team are planning to hold the next large international meeting in 2021. "It's OK to wait this long, because we hold our regular annual meeting for the CNLM Fellows and their labs. There will never be a shortage of venues to exchange ideas and collaborate," he says. "Every three years, we can open it up to the our colleagues worldwide."

If this conference is any indication, the world will be waiting in anticipation.

Cathy Lawhon Feldman is a freelance writer and retired senior director of media relations at UCI's Office of Strategic Communications.

Visit Learnmem2018
learnmem2018.org

Follow on Twitter
@learnmem

1134 attendees **35** countries **5** days **32** sponsors





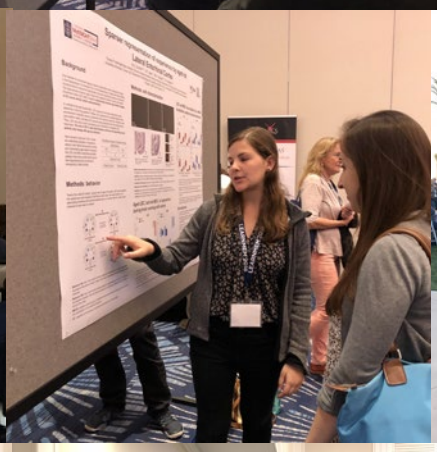


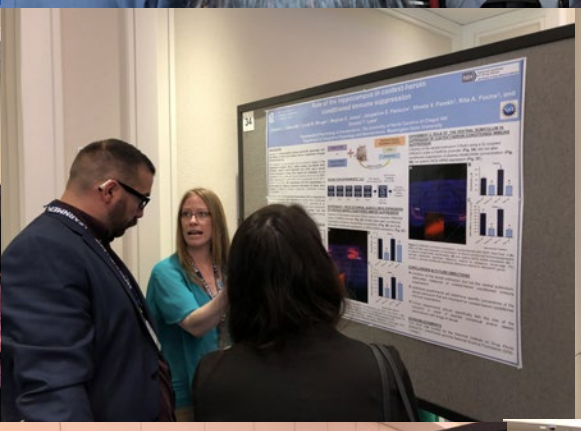

The International Conference on Learning and Memory was held in celebration of the 35th Anniversary of the UCI Center for the Neurobiology of Learning and Memory at the Waterfront Beach Resort in Huntington Beach, California on April 18-22, 2018.

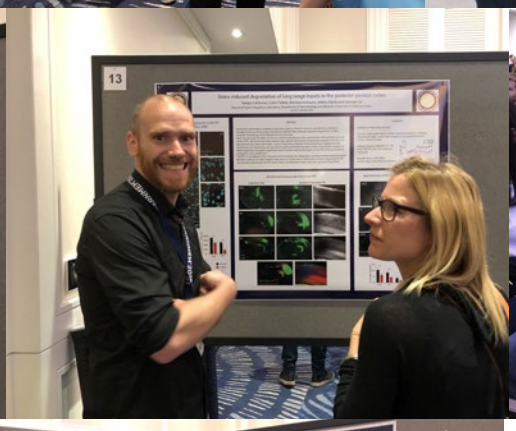


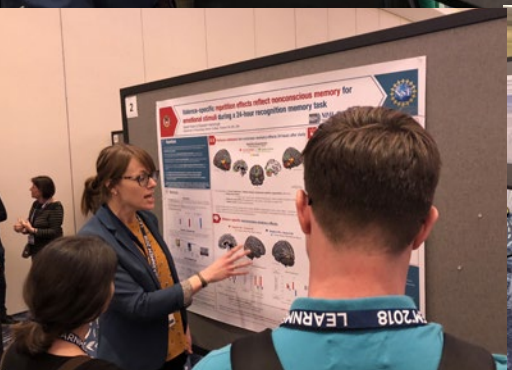


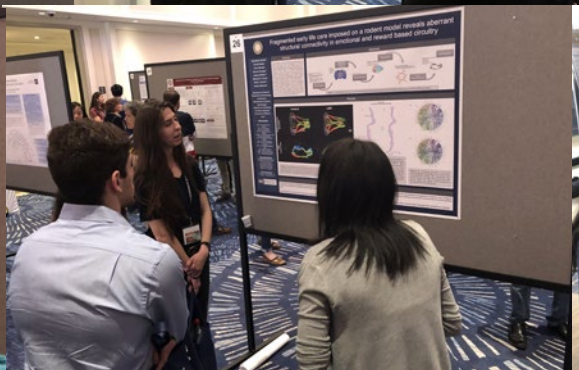

35 symposia **240** talks **16** plenaries **280** posters











Feature Story

UCI's Brain Explorer Academy Reviews Scientists' Papers ... Live!

By: Cathy Lawhon Feldman

Neuroscientists are accustomed to defining problems, developing experiments, testing hypotheses and analyzing and defending their findings. But the three research teams who appeared recently before a review board from the Brain Explorer Academy (BEA) were shaking in their lab coats. Penetrating questions and thoughtful critiques were thrown at them by a panel of 8- to 14-year-olds, and it was clear these future scientists had done their homework.

The Brain Festival and Live Review was a feature of the LEARNMEM™2018 conference, which celebrated the 35th anniversary of UCI's Center for the Neurobiology of Learning and Memory. More than 1,000 professors, researchers, postdoctoral fellows and graduate students from around the world attended the five-day event, which provided a forum for presenting research breakthroughs and assessing the future of the field. If the Brain Explorer Academy kids are any indication, the future of neuroscience is in good shape.

"These students met every Saturday morning for 8 weeks to learn about the brain," says Manuella Yassa, CNLM director of outreach and education and founder of the innovative program. "They have studied brain structure, animal models, ethics, evolution,

comparative anatomy and learned about careers in science. They have worked with graduate students, post docs and staff who act as mentors. It's been very rewarding to see the growing relationships between the science mentors and the children." The program is putting a face to science and it is hoped that it will lead to broader community engagement with science.

At the conference, it appeared to be working. Accomplished neuroscientists mingled with parents and their children as the young brain explorers aided them in handling sheep brains and human brains (with the requisite latex gloves) and participating in a brain-twisting mirror drawing exercise.

Following the open house, students – most from Irvine and Orange County schools – were asked to get to work, evaluating presentations for possible publication in Frontiers for Young Minds while the audience listened in. Robert Knight, UC Berkeley psychology/ neuroscience professor is partner and editor-in-chief of the open-access, non-profit journal for youths ages 8-14. He explained that all articles must be peer-reviewed and can be aimed at the under-12 or over-12 audience. It's a useful exercise for scientists, Knight says, because, "You have to truly understand your research in order to write about it in a way a 5th grader will grasp it."

Jessica Lin and Vlad Senatorov from UC Berkeley presented their paper, Stress: As We Age, the Shield that Protects the Brain Gets Leaky. Their findings showed that the blood-brain barrier becomes inefficient with age, allowing a protein called albumin to escape and incorrectly bind with receptors in the brain. This causes neurons to misfire and results in cognitive decline. A drug that inhibits that interaction could help, they said. The panel got it, but had a few suggestions.

"Would there be any side-effects to such a drug?" asked Arkhil, 12, who wants to be a rocket scientist. The panel also asked for a better

explanatory graphic. In the end, the paper was recommended for publication with some revisions

Before the session began, Tejal, 10, and Shazneen, 9, said they were most looking forward to the UCI team of Jim McGaugh and Navid Ghaffari who were presenting on People Who Rarely Forget. They study individuals with highly superior autobiographical memory, or HSAM, who remember almost every detail of their lives.

"My knees are trembling," said the veteran McGaugh, taking the podium after another team had endured a particularly grueling review calling for major revision.

Ghaffari presented findings from 18 years of research, explaining that HSAMs have a widened pathway between two regions of the brain that seems to allow storage and recall of an unusually large bank of autobiographical memories. The panel was intrigued.

"Why is this important to study if so few people have it?" (The team has verified only 100 HSAM subjects.)

"Look at it this way," McGaugh said. "If your car breaks down, you can't fix it until you know how it works. HSAM is the key to solving how memory works."

How to get HSAM or are you born with it?

"We think people are born with it," said Ghaffari, "but most don't realize they have it until they're in their teens."

In the end, the paper was accepted with few revisions.

"Thank you for participating in this," McGaugh told the children. "And thank you to your families. This is a wonderful program to help children engage in science and it will mean a much better future for us all.

The program is supported fully by the Center for the Neurobiology of Learning and Memory and is free for children and families to participate. "Though we received over 100 applications, we were only able to accommodate 40 children in the first cohort. It's terrific to see such interest in the community, and we look forward to expanding the program," Yassa said. She additionally credits the success of this program to the Academy mentors, a group of bright, dedicated trainees who are passionate about giving back to the community.

For this group of brain explorers, the conference marked the grand finale of their academy training. Except for one last thing, said Tejal: "After this, we get a pizza party."

Read more at:
explorethebrain.org

Sunil Gandhi Designs Leading-Edge Neuroscience Laboratory Course

By: Michael Gomez

If you close your eyes, and recall the last time you embarked on something new -- a project, a dream, a sport, an activity, a new home, a new gadget -- you will activate your limbic system, filling your brain with feelings of novelty and innovation. You might smile effortlessly, and taste the excitement of possibility. This is what happened to me when I spoke with Dr. Gandhi about his newest passion project and how it changed his goals and aspirations as a scientist and as an educator.

We arrived at his office at the same time in the morning. He began describing his work with youthful excitement, while still unpacking his bag. At the forefront of his mind was the new laboratory course he was teaching and in front of him, the camera he was using to document his journey. The cutting-edge content of the new laboratory course combined with its novel teaching philosophy generated the giddiness, which was rapidly becoming infectious. "You see this?" Dr. Gandhi asked, showing me a photo of a tiny brain floating in a clear liquid. "This is a mouse brain." He advanced to the next photo "You see this?" he asked again, anticipating the puzzled look on my face. The test tube now appeared to be empty. "This is a transparent mouse brain," he said. I smiled quizzically, feeling like a spectator in a magic show. Dr. Gandhi went on to describe the novel cutting-edge technique known as brain clearing. The method, a highly advanced variant of the technology first pioneered by Stanford's Karl Deisseroth in 2013, makes brain tissue transparent using hydrogels that maintain tissue structure. Combined with antibody or gene-based labeling, it enables highly detailed pictures of the protein and nucleic acid structure of organs, especially the brain. Dr. Gandhi's lab has developed some of the most innovative techniques to clear the brain and produce very high-resolution images of its structure using Light Sheet Microscopy.

Building on his lab's science and methods, and largely driven by his MD/PhD student Ricardo Azevedo, Dr. Gandhi designed a first-of-its-kind, interactive laboratory course that immerses students into the excitement of today's most cutting edge neuroscience.

With mentorship from graduate students, the undergraduates learn brain clearing, programming, imaging, data analysis and, most importantly, how to work together to collect real experimental data. They learn both conceptual and practical skills, and, unlike other lab courses, generate legitimate data that can be used to write grants and papers.

"The mentors play an essential role in this class," he told me. "With their participation, learning is faster and much more efficient." Mentored active learning is a win-win. Both mentors and mentees learn and edify each other. Both engage in deeper critical thinking as a result of the process. The mentors learn by teaching and gain valuable experience that is rarely found in other courses. The mentees are open to ideas and are willing to accept help - an experience that can leave a lasting impact that eventually turns the mentee into a mentor. Both duties are challenging, though at times uncertain, but the outcomes are among the most rewarding of human experiences.

Combining advanced neuroscience techniques with interactive mentorship has the potential to have significant positive and lasting impact on the way we train future leaders in neuroscience. This is exactly what Dr. Gandhi is envisioning. He raved about the success of his undergraduate students and the leaps that have taken to overcome the steep learning curves, as well as the thrill among the graduate mentors who are eager to mold these young minds.

I could practically smell the excitement and enthusiasm in the air during the class. "Their faces!" he said. "They are so eager to learn and they're enjoying it. I am too!"

His focus during the class is on teaching students critical thinking, guiding them through current research, and ensuring that they have a strong conceptual foundation in the basic sciences. He also creates


50mL
100µL

the necessary conditions that enable students to conduct innovative experimentation.

Unsurprisingly, shortly after setting off this "undergraduate nursery", he noticed how quickly the students adapted and learned to use the high-level techniques they were being taught. He successfully challenged them and they rose to the occasion, suggesting a new model for undergraduate teaching is indeed possible. "Our brains are wired for this type of challenging but exciting learning experience," he said.

The success of the students in this course has exceeded all expectations. Data obtained from their work has been used for two grant submissions to the National Institutes of Health. "We want to change the teaching lab culture to plug into what we know already works. That is the scientific way."

How has this experience changed him as a scientist and as an educator? It's "as if someone has hijacked my mind," he laughed. It has transformed the way he thinks about education and blurred the lines between research and teaching. He is now preparing a grant proposal to support the expansion of this new course. I asked him for examples of lessons he learned about teaching in this new structure.

"I think what we need more is innovation and entrepreneurship," he explained. Teaching these principles is quite rare in biological sciences, but is far more prevalent in engineering. Why is this important? An entrepreneurial mindset equips students with a success skill set that is necessary to thrive in today's job market. Entrepreneurs and innovators think differently and embrace their differences. They do not fear change. Instead, they seek it. They have limitless energy and a strong desire to create and to improve on the status quo.

What we need more is innovation and entrepreneurship.

Can these skills be taught? "Absolutely!" says Dr. Gandhi. Renowned psychologist Robert Sternberg writes that if we were to teach creativity to students, we must first teach them to decide for creativity. There is no better way to teach students to make this decision than by exposing them to the possibilities and excitement of today's modern neuroscience.

Armed with killer methods and a fiery passion for teaching students to be tomorrow's innovators, Dr. Gandhi is shaking up the pedagogical model. The results so far have been nothing short of extraordinary!

Read more at:
cnlm.uci.edu/gandhi/

Navid Ghaffari ’18 is Ready for the Next Chapter

Spend five minutes with him and you will see unbridled curiosity, infectious excitement, and an endless supply of ideas. Navid Ghaffari, B.S. ’18 is a phenom in every way. Having attained numerous distinctions and earning close to every award that he qualified for as an undergraduate, Ghaffari was one of the most successful and prolific undergraduates on UCI’s campus in recent history. While he gazes into his future as a medical student (he is currently deciding among several of the top medical schools in the country), let us take a glimpse at the remarkable journey that got him here.

In his sophomore year, Ghaffari became intrigued with the pioneering work of UCI Founding Faculty Dr. James McGaugh, and met with him to ask for a research assistantship. Though McGaugh is retired and no longer runs a research program, Ghaffari would not take ‘no’ for an answer. He insisted on working with McGaugh but additionally sought co-mentorship from CNLM Director, Dr. Michael Yassa. McGaugh and Yassa had recently begun collaborating on a project involving individuals with highly superior autobiographical memory (HSAM), and Ghaffari’s energy, dedication and curiosity were a perfect fit for this exciting project.

It was clear from the very beginning that Ghaffari was extraordinary. “He could very well be one of the smartest people I have ever met,” McGaugh says of his former student, whom he had come to know very well after nearly three years of mentorship. Ghaffari met with his mentors frequently, and worked with them to develop his ideas.

Working with the two scientists, Ghaffari developed a new test to assess HSAM that does not require expertise or command over certain knowledge categories such as sports or public events. He worked diligently to understand the literature and spent week after week testing participants from around the world. His hard work paid off, and he presented his findings at several conferences. In addition, he recently published a paper with McGaugh in the journal *Frontiers for Young Minds*, participating in the Live Review at the International Conference on Learning and Memory (see pp. 16). Additionally, Ghaffari was chosen as an undergraduate research ambassador of the University of California, and presented his research at an event hosted by the University of California Office of the President.

A talented tennis player and piano virtuoso, Ghaffari understands the value of living a balanced life. He is well traveled and soaks up new experiences with intensity and fervor. Before heading to medical school, he is spending seven months training with one of McGaugh’s most accomplished alumni, Dominique de Quervain, at the University of Basel, Switzerland. Known for his pioneering research on the use of cortisol in the treatment of PTSD and phobias, de Quervain’s work demonstrates how fundamental science can inform translation.

“I am grateful for the incredible education I received at UCI and for the research training and mentorship I experienced at the CNLM. The McGaugh alumni family is very special and has welcomed me with open arms.” Ghaffari is the most recent of a long line of scholars who trained under McGaugh. This opportunity is an indication of the strength of the network’s tight knit bond as well as a testament to Ghaffari’s promise and aptitude.

Ghaffari is a terrific example of what a student can do with a UCI education. Arriving as a freshman with an open mind, he embraced the numerous opportunities that were available to him, and worked persistently to accomplish his dreams. Through it all, he constantly looked for ways to give back to the community and to the campus. While the past has been bright, the future is brilliant for this proud Anteater!

New Facility

UCI Opens State-of-the-Art Sleep Laboratory for Clinical Research and Patient Care

Ruth Benca, M.D., Ph.D. delivering the Distinguished Lecture on Brain, Learning and Memory at the Irvine Barclay Theatre

Sleep is crucial for memory and for brain health. Understanding its mechanisms and developing means by which sleep loss can be reversed will transform healthcare as well as our understanding of how memories are stored.

UCI's new, state-of-the-art sleep laboratory and clinic, located at 20350 Birch Street, a short drive from the main UCI campus, is now open for patient care and clinical research.

Led by Dr. Ruth Benca, Chair of Psychiatry and Human Behavior at UCI's School of Medicine, Fellow of the Center for the Neurobiology of Learning and Memory, and renowned sleep specialist, the new 6,500 square foot sleep lab and clinic is a major addition to UCI's growing lineup of new clinical services and clinical research facilities.

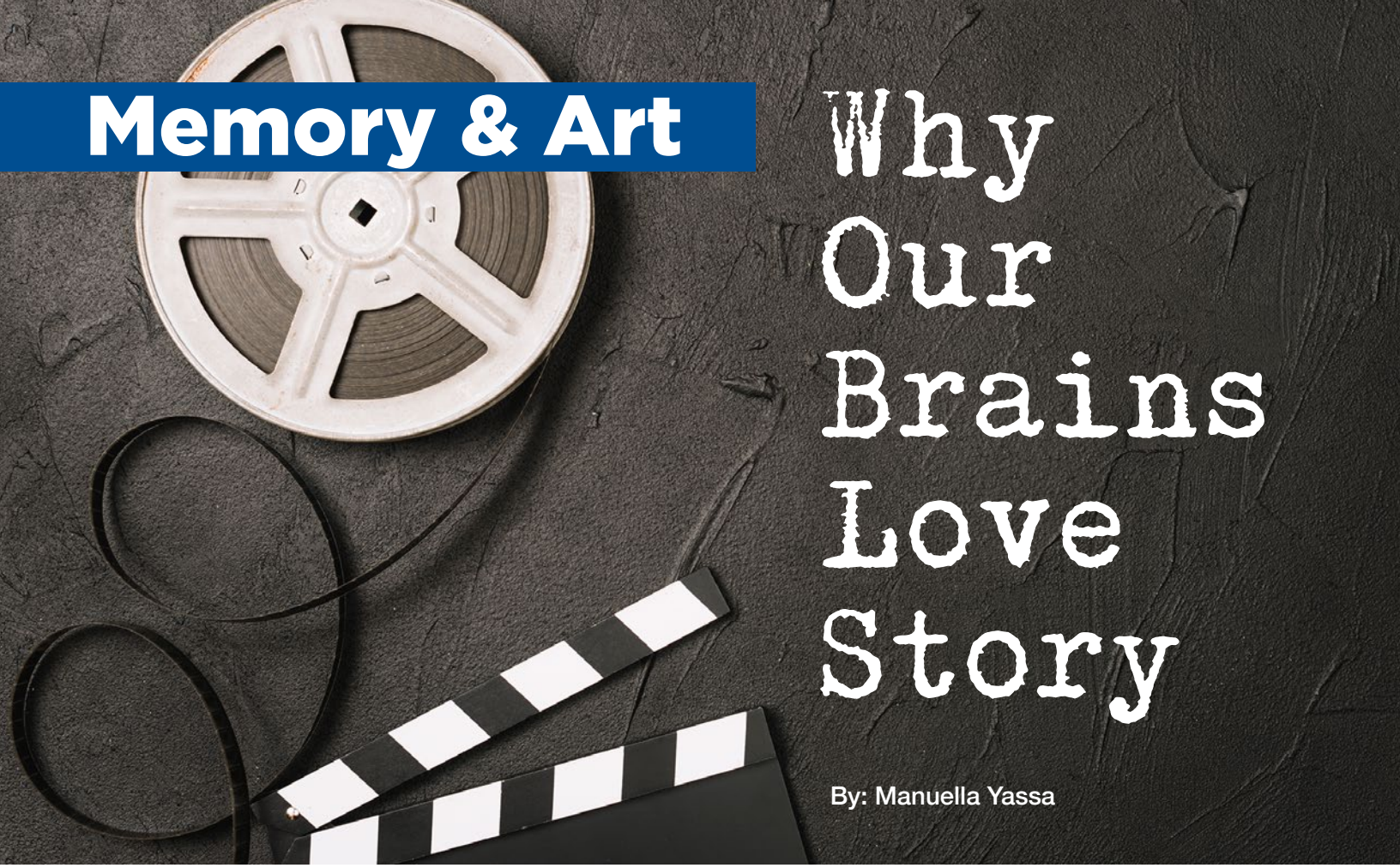
Dr. Benca was recruited to UCI from the University of Wisconsin, Madison in 2016 with a vision to transform both psychiatry research and care as well as sleep medicine at UCI. Now, almost two years later, it's clear that the new sleep lab is well suited to accomplish this vision. The large and welcoming space includes 8 bedrooms with private bathrooms, several clinic rooms for daytime use, and a sleep laboratory control room to monitor patients/research subjects and analyze recorded data.

Overnight sleep recording equipment includes capability of recording up to 256 channels of EEG (photo on the right is of a research participant preparing for overnight sleep study - Photo credit: Anna Smith) and transcutaneous CO_2 monitoring. Each bedroom is electromagnetically shielded, has an extra-long double bed, satellite television and is outfitted to resemble a comfortable hotel room. Equipment for home sleep testing and actigraphy is also available.

It is hoped that the new sleep lab will enable numerous research studies at UCI and increase extramural funding in the area of sleep research. Earlier this year, the Sleep and Circadian Neuroscience (SCN) Center, which is funded by the UCI Office of Research and co-directed by Benca and CNLM director Michael Yassa, organized two symposia on sleep and brain disease with the purpose of developing collaborative center-scale federally funded projects.

The SCN awarded pilot grants to four scientists at UCI: Bryce Mander (Psychiatry and Human Behavior), Mark Mapstone (Neurology), Kim Green (Neurobiology and Behavior), and Norbert Fortin (Neurobiology and Behavior). The team is now working together to develop a strong program of research on links between sleep disruption, neuroinflammation, and cognitive decline. Sleep is UCI's newest areas of integrative health research and it is anticipated that this area will see considerable growth over the coming years.

To learn how you can support sleep research at UCI contact Ms. Valerie Amador at vgamador@uci.edu



Memory & Art

Why Our Brains Love Story

By: Manuella Yassa

We all love to sit down with a good book or a movie and feel transported to an alternate reality. What makes a story so captivating? How does the brain construct a narrative and why does it seek logic and structure in any story? Can neuroscience offer insights into the art of storytelling?

Acting instructor David Ihrig and neuroscientist Michael Yassa believe storytelling comes naturally to humans and our brains are wired for it. With funding from UCI Illuminations, the Chancellor's Arts and Culture Initiative, as well as support from the Center for the Neurobiology of Learning and Memory and the Claire Trevor School of the Arts, they designed a two-part interactive series to take a deep dive into the brain basis for storytelling.

Part I of this series took place at the Herklotz Conference Facility on November 13, 2018. The concept for this session titled "Scientific Story Shaping" was to create a story with help from the audience and deconstruct its components in terms of neuroscientific principles. This crowd-sourced story outline will serve as the starting point for Part II, The Performance, a minimalist production based on the art and (neuro)science of storytelling.

In addition to Yassa and Ihrig, two more panelists took the stage and worked with the audience to shape the story elements. The first panelist was Adam Leipzig, CEO

Lisa Cron

Our brains are wired for story. It's a survival mechanism.

of Entertainment Media Partners and a former Disney Executive. He supervised such films as *Dead Poets Society* (1989), *Honey, I Shrunk the Kids* (1989), and *The Way Back* (2010). While president of National Geographic Films, he acquired the international rights to March of the Penguins and created the US version. He is a faculty member at UC Berkeley Haas School of Business, and Senior Creative Advisor for CreativeFuture.

Leipzig kicked off the panel discussion by describing the process by which the story was created for *A Plastic Ocean* (2016). It began with a loud thud - boxes of uncut tapes landing in a production warehouse containing thousands of hours of footage. But there was no story. The challenge was to take this raw material and craft from it characters, narrative, and a compelling storyline. Of course, the film went on to win awards at film festivals all around the world and was an eye-opening experience for its viewers.

The second panelist was Lisa Cron, story consultant, author, speaker, and instructor at UCLA Extension Writers' Program. She has written two books that utilize brain science in story creation; *Wired for Story* & *Story Genius*. Lisa has worked in publishing at W.W. Norton, as a producer on shows for Showtime and CourtTV, and as a story consultant for Warner Brothers.

Cron walked the audience through the tenets of storytelling and why our brains are wired for story. In her words, "A story is about how what happens affects someone who is in pursuit of a deceptively difficult goal and how that person changes internally as a result." Emphasizing complex characters with a history and back story was a recurring theme throughout the evening.

"My story is one about survival," said Yassa. The brain is wired to encode memories in terms of narrative as it is the basis for building causal chains. "If A happens, then B happens, then C happens, and I can remember that narrative, my brain can predict the future. After all, that is exactly what memory is good for. It cares very little about our past. It only cares about making future decisions that benefit our survival." Putting storytelling in the context of the brain's survival instinct clicked with Cron who writes about the same themes in her books.

Ihrig was last to take the podium. The last time he successfully bridged neuroscience and the arts was during his innovative interdisciplinary course, the "Science of Acting." The highly acclaimed course was by all measures a successful experiment that will likely transform how acting is taught in the classroom.

"I want you all to close your eyes and think for a minute about the one thing you would like to get out of today's session," he said. Ihrig's passion for teaching shows clearly as he guides the audience through this exercise.

"Now you're ready. You're primed. You each have a sense of purpose and a goal. A back story. That's the most important element of building a narrative," he beamed.

Over the next hour, the four panelists solicited feedback from the audience to create and shape a story together. Elements began to flow and Leipzig took to the white board to take down the barrage of ideas. A few minutes into this exercise, however, he stopped. The audience were hitting a roadblock. Leipzig called them out and told them to dig deeper and come up with something real and emotional. After a little hesitation, ideas began to flow again, but this time with refreshed vigor and realism that was more compelling than any stereotypical Hollywood story.

Slowly but surely, the ideas started to take shape and follow an interesting and non-typical narrative. A shoe store, a mother's relationship with her daughter, and a cliché about people always being out for themselves became the basis for a crowd-sourced original story. Working with these elements, students in UCI's Drama department will work with Ihrig as well as Jane Page, Head of Directing and faculty member in Drama to create a minimalist production that takes into consideration neuroscientific principles of storytelling. Part II will be early in 2019 and will bring back the audience for a live performance and reflection.

Parting words of advice to the audience of impromptu writers from Adam? "Make it funny!"

Adam Leipzig

New Research

Ten Minutes of Light Exercise Enhances Memory

Irvine, Calif., Sept. 24, 2018
People who include a little yoga or tai chi in their day may be more likely to remember where they put their keys. Researchers at the University of California, Irvine and Japan's University of Tsukuba found that even very light workouts can increase the connectivity between parts of the brain responsible for memory formation and storage.

"Even short walking breaks throughout the day may have considerable effects on improving memory and cognition," says study co-leader Michael Yassa, UCI professor and Chancellor's Fellow of neurobiology & behavior.

In a study of 36 healthy young adults, the researchers discovered that a single 10-minute period of mild exertion can yield considerable cognitive benefits. Using high-resolution functional magnetic resonance imaging, the team examined subjects' brains shortly after exercise sessions and saw better connectivity between the hippocampal dentate gyrus and cortical areas linked to detailed memory processing.

Their results were published today in *Proceedings of the National Academy of Sciences*.

"The hippocampus is critical for the creation of new memories; it's one of the first regions of the brain to deteriorate as we get older – and much more severely in Alzheimer's disease," said Yassa. "Improving the function of the hippocampus holds much promise for improving memory in everyday settings."

The neuroscientists found that the level of heightened connectivity predicted the degree of recall enhancement.

Yassa, director of UCI's Center for the Neurobiology of Learning and Memory and the recently launched UCI Brain Initiative, said that while prior research has centered on the way exercise promotes the generation of new brain cells in memory regions, this new study demonstrates a more immediate impact: strengthened communication between memory-focused parts of the brain.

"We don't discount the possibility that new cells are being born, but that's a process that takes a bit longer to unfold," he said. "What we observed is that these 10-minute periods of exercise showed results immediately afterward."

A little bit of physical activity can go a long way, Yassa stressed. "It's encouraging to see more people keeping track of their exercise habits – by monitoring the number of steps they're taking, for example," he said. "Even short walking breaks throughout the day may have considerable effects on improving memory and cognition."

Yassa and his colleagues at UCI and at the University of Tsukuba are extending this avenue of research by testing older adults who are at greater risk of age-related mental impairment and by conducting long-term interventions to see if regular, brief, light exercise done daily for several weeks or months can have a positive impact on the brain's structure and function in these subjects.

"Clearly, there is tremendous value to understanding the exercise prescription that best works in the elderly so that we can make recommendations for staving off cognitive decline," he said.

Read more about Dr. Yassa's work at yassalab.org

Scientists Uncover How Rare Gene Mutation Affects Brain Development and Memory

Irvine, Calif. – Oct. 18, 2018 Researchers from the University of California, Irvine School of Medicine, have found that a rare gene mutation alters brain development in mice, impairing memory and disrupting the communication between nerve cells. They also show memory problems could be improved by transplanting a specific type of nerve cell into the brain. The findings were published today in *Neuron*.

"Mutations in hundreds of genes have been linked to neurodevelopmental disorders, many of which have devastating behavioral consequences that cannot be managed with available treatment options," explained Robert Hunt, PhD, assistant professor of Anatomy & Neurobiology, who led the study with Young Kim, PhD, a postdoctoral fellow. "Now, a major challenge in the field is to identify the underlying cause for each of these rare genetic disorders so that new, disease-specific therapies can be developed."

The UCI team focused on the gene CHD2, which scientists believe modifies the structure of chromatin — the coiled complex of DNA and proteins — and controls expression of hundreds of other genes. Normally, humans have two copies of the CHD2 gene. However, in some cases, one copy is lost, which can lead to developmental disorders such as intellectual disability, epilepsy or autism.

To mimic the human disorder and better understand how CHD2 is involved in brain development, Hunt and his colleagues created mice that possess only one functioning copy of the CHD2 gene. Remarkably, the mice had severe memory problems and an increase in electrical oscillations in the brain, features similar to the condition in people.

A closer look at the animals' brains revealed an abnormal development of brain circuitry, including changes in the way neurons communicate with each other, and fewer inhibitory interneurons, which control the activity of brain circuits. The mouse neurons also showed differences in the expression of more than 100 other genes associated with neurodevelopmental disorders. In the embryo, many of the altered genes are involved in critical biological processes like neurogenesis, but in adult animals, genes associated with neuronal activity and synapse function were changed. That insight indicated CHD2 may play different roles in early brain development and adulthood.

The findings prompted Hunt's team to transplant embryonic progenitor cells capable of generating inhibitory interneurons into the brains of the mutant mice. They targeted the hippocampus, a brain region critical for learning and memory, for cell transplantation.

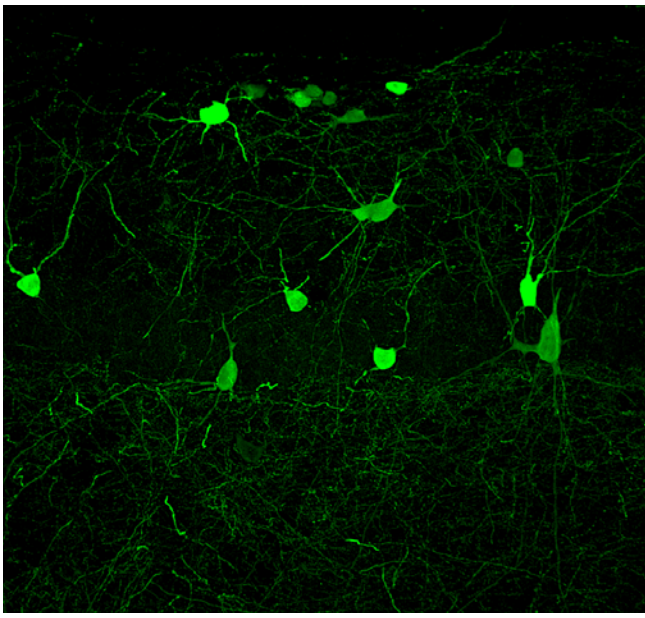
"Inhibitory neurons regulate oscillatory rhythms that are required for memory functions," Hunt said. "We've been developing a similar interneuron cell therapy for epilepsy, so we naturally thought of trying this approach in mice with CHD2 mutation."

In the UCI study, the transplanted inhibitory cells migrated throughout the hippocampus and generated new interneurons, in effect replacing the brain cells that were missing in the mutant mice. In addition to having more inhibitory nerve cells, the treated mice showed a dramatic improvement in hippocampus-dependent memory.

"At least in principle, it should be possible to develop targeted therapies for genetic disorders like CHD2 mutation," Hunt said. "That would be great, because in many cases, the medications that are currently available offer no therapeutic value."

While the new research offers an important step toward understanding the role of CHD2 in brain development and function, further studies are necessary before interneuron progenitors can be used for cell therapy in the clinic. Hunt's lab next aims to evaluate brain wiring in the mouse model more closely and to explore how CHD2 mutations affect different pathways.

Read more about Dr. Hunt's work at roberthuntlab.org



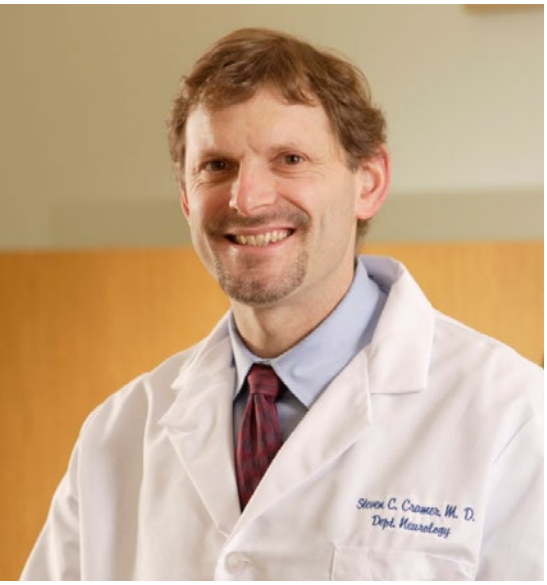
Transplanted inhibitory interneurons (green) integrated into recipient mouse hippocampus
Photo credit: Robert Hunt, PhD

New Research

UCI Study Shows In-Home Therapy Effective for Stroke Rehabilitation

Irvine, Calif., May 24, 2018
In-home rehabilitation, using a telehealth system and supervised by licensed occupational/physical therapists, is an effective means of improving arm motor status in stroke survivors, according to findings presented by University of California, Irvine neurologist Dr. Steven C. Cramer at the recent *2018 European Stroke Organization Conference* in Gothenburg, Sweden.

"Motor deficits are a major contributor to post-stroke disability, and we know that occupational and physical therapy improve patient outcomes in a supervised rehabilitation program," said Cramer, a professor of neurology in the UCI School of Medicine and Fellow of the Center for the Neurobiology of Learning and Memory. "Since many patients receive suboptimal therapy for reasons that include cost, availability and difficulty with travel, we wanted to determine whether a comprehensive in-home telehealth therapy program could be as effective as in-clinic rehabilitation."



Steve Cramer, Ph.D.

In a study conducted at 11 U.S. sites, 124 stroke survivors underwent six weeks of intensive arm motor therapy, with half receiving traditional supervised in-clinic therapy and half undergoing an in-home rehabilitation program supervised via a video-conferenced telemedicine system.

Subjects were on average 61 years old, 4.5 months post-stroke, and had moderate arm motor deficits at study entry. When examined 30 days after the end of therapy, subjects in the in-clinic group improved by 8.4 points on the Fugl-Meyer scale, which measures arm motor status and ranges from 0 to 66, with higher numbers being better. Subjects in the telerehab group improved by 7.9 points, a difference that was not statistically significant.

"The current findings support the utility of a computer-based system in the home, used under the supervision of a licensed therapist, to provide clinically meaningful rehab therapy," Cramer said. "Future applications might examine longer-term treatment, pair home-based telerehab with long-term dosing of a restorative drug, treat other neurological domains affected by stroke (such as language, memory, or gait), or expand the home treatment system to build out a smart home for stroke recovery."

He said that the demand for rehabilitation services will likely increase, due to an aging population and increased stroke survival as a result of better access to advanced acute care. Telehealth, defined as the delivery of health-related services and information via telecommunication technologies, can potentially address this growing unmet need.

"We reasoned that telerehabilitation is ideally suited to efficiently provide a large dose of useful rehab therapy after stroke," said Cramer, whose team is part of the NIH StrokeNet consortium.

This research builds on the findings of a pilot study of 12 patients with late subacute stroke and arm-motor deficits who were provided 28 days of home-based telerehab program. The results, published in Nov 2017 in the journal *Neurorehabilitation and Neural Repair*, found that patient compliance was excellent (97.9 percent) and participants experienced significant arm-motor gains (Fugl-Meyer scale increase of 4.8 points). The study also found that patients did not need any additional computer skills training due to the design of the telerehab system. "Greater gains are associated with therapy that is challenging, motivating, accompanied by appropriate feedback, interesting and relevant." he said. "It is adjusts to individual needs, is easy to use – and is fun!"

More at http://faculty.sites.uci.edu/neuralrepairlab/

UCI Cracks Code to Restoring Memory Creation in Older or Damaged Brains

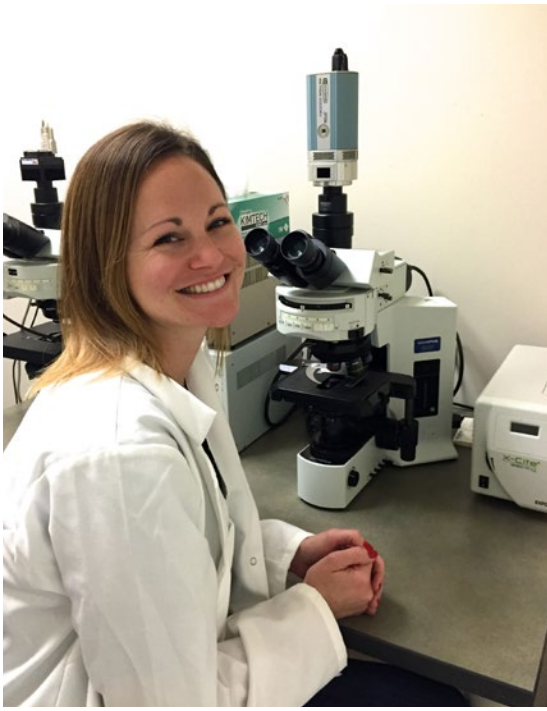
Memory linked to circadian clock gene regulation

Irvine, Calif., Feb. 16, 2018
Aging or impaired brains can once again form lasting memories if an enzyme that applies the brakes too hard on a key gene is lifted, according to University of California, Irvine neurobiologists.
"What we've discovered is that if we free up that DNA again, now the aging brain can form long-term memories normally," said senior author Marcelo Wood, UCI's Chair in Neurobiology & Behavior and Fellow of the Center for the Neurobiology of Learning and Memory, who will present the findings at the American Association for the Advancement of Science's annual meeting, in Austin, Texas.

"In order to form a long-term memory, you have to turn specific genes on. In most young brains, that happens easily, but as we get older and our brain gets older, we have trouble with that."

That's because the 6 feet of DNA spooled tightly into every cell in our bodies has a harder time releasing itself as needed, he explained. Like many body parts, "it's no longer as flexible as it used to be." The stiffness in this case is due to a molecular brake pad called histone deacetylase 3, or HDAC3, that has become "overeager" in the aged brain and is compacting the material too hard, blocking the release of a gene called Period1 (Per1). Removing HDAC3 restores flexibility and allows internal cell machinery to access Per1 to begin forming new memories.

Researchers had previously theorized that the loss of transcription and encoding functions in older brains was due to deteriorating core circadian clocks. But Wood and his team, notably postdoctoral fellow Janine Kwapis, found that the ability to create lasting memories was linked to a different process – the overly aggressive enzyme blocking the release of Per1 – in the same hippocampus region of the brain



Janine Kwapis, Ph.D.

That's potentially good news for developing treatments. "New drugs targeting HDAC3 could provide an exciting avenue to allow older people to improve memory formation," Wood said.

Update - August 20, 2018
Results from this work were published in Kwapis et al. Epigenetic regulation of the circadian gene Per1 contributes to age-related changes in hippocampal memory. *Nature Communications* 9:3323 (2018).

More at mwoodlab.bio.uci.edu

New Research

Brain Imaging Provides Clues About Memory loss in Older Adults

Irvine, Calif., March 7, 2018
As we get older, it's not uncommon to experience "senior moments," in which we forget where we parked our car or call our children by the wrong names. And we may wonder: Are these memory lapses a normal part of aging, or do they signal the early stages of a severe disorder such as Alzheimer's disease? Currently, there's no good way to tell.

University of California, Irvine-led researchers, however, have found that high-resolution functional magnetic resonance imaging of the brain can be used to show some of the underlying causes of differences in memory proficiency between older and younger adults.

The study, which appears today in the journal *Neuron*, involved 20 young adults (ages 18 to 31) and 20 cognitively healthy older adults (ages 64 to 89). The participants were asked to perform two kinds of tasks while undergoing fMRI scanning – an object memory task and a location memory task. Because fMRI looks at the dynamics of blood flow in the brain, investigators were able to determine which parts of the brain the subjects were using for each activity

In the first task, participants viewed pictures of everyday objects and were then asked to distinguish them from new pictures. "Some of the images were identical to ones they'd seen before, some were brand-new and others were similar to ones they'd seen earlier – we may have changed the color or the size," said Michael Yassa, director of UCI's Center for the Neurobiology of Learning and Memory and the study's senior author. "We call these tricky items the 'lures.' And we found that older adults struggle with them. They're much more likely than younger adults to think they've seen those lures before."

The second task was nearly the same but required subjects to determine whether the location of objects had been altered. Here, older adults fared quite a bit better than in the prior task.

"This suggests that not all memory changes equally with aging," said lead author Zachariah Reagh, who participated in the study as a graduate student at UCI and is now a postdoctoral fellow at UC Davis. "Object memory is far more vulnerable than spatial, or location, memory – at least in the early stages." Other research has shown that problems with spatial memory and navigation do manifest as individuals progress toward Alzheimer's disease.

Importantly, by scanning the subjects' brains while they underwent these tests, the scientists were able to establish a cerebral mechanism for that deficit in object memory.

They found that it was linked to a loss of signaling in a part of the brain called the anterolateral entorhinal cortex. This area is already known to mediate communication between the hippocampus, where information is first encoded, and the rest of the neocortex, which plays a role in long-term storage. It's also an area severely affected in people with Alzheimer's disease.

"The loss of fMRI signal means there is less blood flow to the region, but we believe the underlying basis for this loss has to do with the fact that the structural integrity of that part of the brain is changing," Yassa said. "One of the things we know about Alzheimer's disease is that this region of the brain is one of the very first to exhibit a key hallmark of the disease, deposition of neurofibrillary tangles."

In contrast, the researchers did not find age-related differences in

another area of the brain connected to memory, the posteromedial entorhinal cortex. They demonstrated that this region plays a role in spatial memory, which was not significantly impaired in the older subjects.

"This suggests that the brain aging process is selective," Yassa said. "Our findings are not a reflection of general brain aging but rather of specific neural changes that are linked to specific problems in object but not spatial memory."

To determine whether this type of fMRI scan could eventually be used as a tool for early diagnosis, the researchers plan to expand their work to a sample of 150 older adults who will be followed over time. They will also be conducting positron emission tomography, or PET, scans to look for amyloid and tau pathology in their brains as they age.

"We hope this comprehensive imaging and cognitive testing will enable us to figure out whether the deficits we saw in this study are indicative of what is later to come in some individuals," Yassa said.

"Our results, as well as similar results from other labs, point to a need for carefully designed tasks and paradigms that can reveal different functions in key areas of the brain and different vulnerabilities to the aging process," Reagh added.

Read more about Dr. Yassa's work at yassalab.org

Related News

New Funding to Identify Preclinical Biomarkers for Alzheimer's Disease

Irvine, Calif. July. 2018

With support totaling $6.8 million from the National Institute on Aging, Professor Michael Yassa and his team are working to identify the earliest indicators of dementia in older adults as disease-related brain plaques and tangles accumulate but before symptoms can be observed.

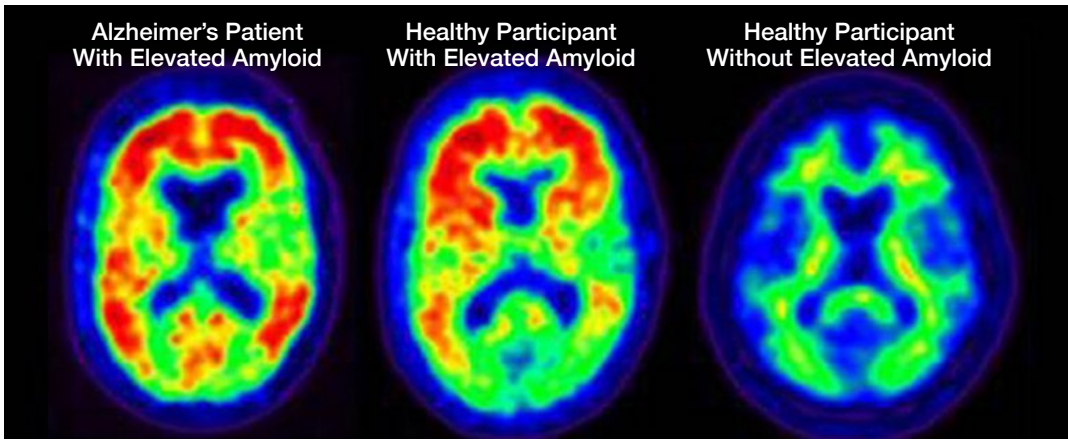
The researchers are developing sophisticated methods using brain imaging technology to understand the mechanisms of Alzheimer's disease and predict its onset before any outward manifestations. If successful, their work will pave the way for effective preventive treatments that will substantially increase quality of life for patients and reduce the burden on families and the healthcare system.

"Cognitive decline is a significant public health concern as the population over the age of 60 continues to grow sharply," said Yassa. "We will be faced with $50 trillion in Medicare costs as baby boomers age, making this effort to determine biomarkers for Alzheimer's disease all the more significant."

He added that the study aims to pinpoint factors leading to cognitive decline in the presence and absence of beta-amyloid proteins, the hallmark brain plaques associated with Alzheimer's disease. Not everyone with amyloid will develop the disease. Yassa will lead a team in testing and monitoring 150 adults between the ages of 60 and 85 who have no symptoms of dementia but may have a family history of it.

Ultrahigh-resolution MRI scans will be used to gauge brain structure and function, and florbetapir PET scans will measure amyloid plaques, while highly sensitive cognitive examinations will detect subtle memory deficits. The most recent addition to the study involved PET scans to detect tau tangle pathology using an experimental tracer known as MK-6240 (Merck).

Participants' cognitive health will be followed for several years to determine whether the test results can reliably predict outcomes. It is hoped that this research will shed light on the mechanisms of Alzheimer's disease during the pre-symptomatic phase. Successful completion will allow Yassa and his colleagues to provide guidelines for designing future clinical trials to prevent or delay the onset of Alzheimer's.



New Research

Environmental Enrichment Facilitates Successful Brain Aging

By: Michael Leon and Cynthia Woo

You have no doubt heard this story before. Keeping your brain engaged will help stave off dementia. Sounds simple, right?

One way to heed this advice is to sign up for 'brain gym memberships' so you can train your brain on a regular basis by playing complex games and trying to increase mental fitness. Indeed, that *may* work.

But what if enrichment could be far simpler?

We asked veteran CNLM Fellow Michael Leon and his long time collaborator Cindy Woo to tell us everything we need to know about environmental enrichment. We were also curious about their new research study and simple intervention that may be just what the doctor ordered.

Cognitive Loss in Aging

The aging human brain requires a great deal of stimulation to maintain its cognitive efficacy. However, many older adults seek ineffective forms of stimulation, such as nutritional supplements, in an effort to maintain their memory. For example, GNC stores list 484 products for brain improvement, none of which have shown to improve cognitive function.

Other older adults play computer games to improve their cognition, but these too don't really work. Indeed, the general rule is that playing a specific computer game makes you play that game better, but does not improve your general intelligence. Nevertheless, there are about 85 million people who have been playing Lumosity's computer games, a company that has been fined $50 million by the Federal Trade Commission for falsely claiming to improve general memory ability, while only improving performance on the games that have been played.

On the other hand, there are effective ways to maintain your memory as you get older. We have recently reviewed the literature on this topic (Leon and Woo, 2018) and found that maintenance of your sensory systems can have a dramatic effect on your ability to remember things. The first two systems that we will describe probably won't be surprising to you, but the second two systems we'll bet will be a surprise.

Vision

The ability to see deteriorates with age. Older adults with good visual ability have a 63% decreased risk for developing dementia, while older adults with poor visual ability are 5 times more likely to experience cognitive loss than are older adults with good vision. In addition, older adults with age-related cataracts have a 1.4 times the likelihood of developing Alzheimer's disease.

It is also the case that older adults with poor vision engage in fewer activities that involve their cognitive ability than those with normal vision, suggesting a likely mechanism for cognitive deterioration with failing vision. At the same time, the use of reading glasses or cataract surgery in older adults improves both vision and cognition.

Hearing

Age-related hearing loss is common in older adults, with almost two-thirds of those over 70 years old having poor hearing, and about a third of older adults experiencing serious hearing loss. The odds of having a hearing loss are 5.5-fold higher in men than in women (we don't know why). Hearing impairment in older adults increases the risk of cognitive problems by 57%. Older adults with mild to severe hearing impairment also have a 2-5-fold increase in their risk of developing dementia

compared to older adults with normal hearing. It is quite possible that the loss of hearing prevents stimulating social and intellectual pursuits that negatively affect the cognitive brain.

Many studies have shown that hearing aids both improve cognitive abilities and decrease depression in older adults with hearing loss. Unfortunately, hearing aids can cost thousands of dollars and these devices are typically not covered by medical insurance in the United States. In addition, many people refuse to wear them because they are afraid that it labels them as being "old". Consequently, only 3-4% of those with mild-moderate hearing loss are wearing hearing aids.

Mastication

While the loss and restoration of vision and hearing have somewhat predictable effects on cognition, most people would not predict the same relationship between dental health and cognition. Tooth loss and chewing ability are correlated with cognitive loss, but it's quite possible that there is no causal relationship between these two factors.

On the other hand, when rats and mice have some teeth removed, or are given only powdered or liquid food, their cognitive ability also declines. Interestingly, switching mice from powdered food to hard pellet food reverses the cognitive deficit.

Similarly, humans who have lost teeth and were subsequently given dentures or dental implants had improved cognitive performance. Finally, increased chewing has been shown to increase activity in the brain's cognitive areas and improve cognition in humans.

Olfaction

Normal human aging is accompanied by a loss of olfactory abilities, with 46% of those over 80 years old having very poor olfactory capabilities. Surprisingly, the olfactory system is the only sensory system that has direct projections to brain's cognitive and memory regions and the loss of olfactory function results in both diminution of these brain areas as well as cognitive loss.

Indeed, olfactory loss precedes the early symptoms of cognitive disorders such as Alzheimer's disease and a poor olfactory ability predicts both an elevated risk of mild cognitive impairment, as well as predicting which individuals with that condition will develop Alzheimer's.

Olfactory Stimulation?

We and others have recently shown that increasing olfactory stimulation in a specific way reverses the olfactory loss that older adults have experienced, as well as improves their cognitive function.

Michael Leon, Ph.D.

This intervention improved their performance on tests of verbal fluency and memory. It also improved depressive symptoms and led to an improved sense of wellbeing. These results were quite remarkable because the effects are far larger than what is typically observed in cognitive training interventions. Not to mention, it was a passive intervention that required very little work on part of the participants.

We have recently partnered with industry giant Procter and Gamble to manufacture a custom device that can provide olfactory enrichment in a home setting. We are now recruiting participants to enroll in a clinical trial to extend our prior findings and additionally conduct brain imaging studies to determine the basis for cognitive improvement.

While it is unlikely that an intervention like olfactory enrichment will prevent dementia, it can perhaps allow us to stave it off for 5-10 years. If we do so successfully, most older adults will not die of Alzheimer's disease, and we are that much closer to addressing this global challenge.

For **more information about this ongoing study**, contact Dr. Leon
Email: mleon@uci.edu
Tel: 949-237-3026

To **read more about environmental enrichment**, see Leon and Woo (2018). Environmental Enrichment and Successful Aging. *Frontiers in Behavioral Neuroscience* 12:155.

New Awards

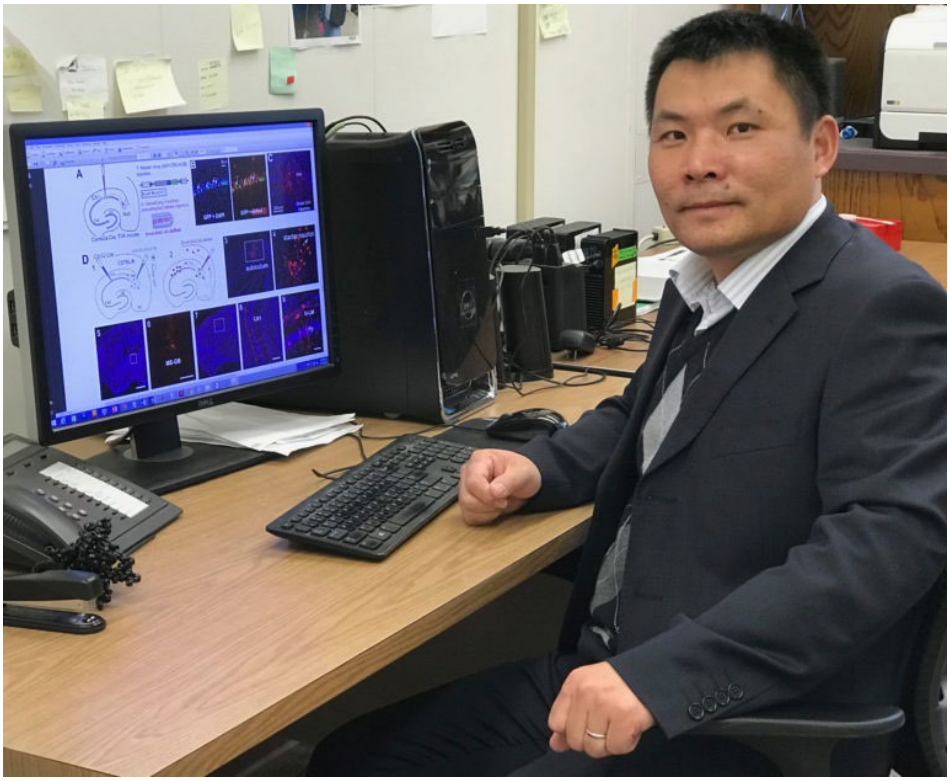
CNLM Fellows Receive Prestigious New Grants to Support Brain Research

Dr. Xiangmin Xu receives BRAIN Initiative Grant to study newly discovered neural pathways in the hippocampus

Irvine, Calif., April 2, 2018
The National Institutes of Health has awarded Xiangmin Xu, UCI associate professor of anatomy & neurobiology and Fellow of the Center for the Neurobiology of Learning and Memory, a five-year, $2.5 million grant to study new neural circuit pathways in a region of the brain associated with learning and memory and epilepsy. He shares the grant with Douglas Nitz of UC San Diego.

The proposed research is part of the **Brain Research Through Advancing Innovative Neurotechnologies (BRAIN)** Initiative. Using recent technological advancements, the team will focus on newly discovered neural pathways in the hippocampal formation. This brain structure plays essential roles in learning and memory and spatial navigation, and it's implicated in many neurological diseases, including Alzheimer's and temporal lobe epilepsy. The research will address mechanisms of circuit function in the context of specific neural systems and shed light on circuits of the central nervous system by systematically controlling stimuli and behavior.

For more information about Dr. Xu's work visit his website at http://xulab.anat.uci.edu



Xiangmin Xu, Ph.D. says the research could lead to new therapeutic interventions for Alzheimer's and temporal lobe epilepsy.

$30 million in new extramural funding secured by CNLM Fellows in 2018

Dr. Ruth Benca wins the Strategic Research Award from the American Academy of Sleep Medicine to study link between obstructive sleep apnea and Alzheimer's disease pathology

Irvine, Calif., Oct 31, 2018
Ruth Benca, M.D., Ph.D., Chair of Psychiatry and Human Behavior and Fellow of the Center for the Neurobiology of Learning and Memory was recently awarded the AASM Foundation 2018 Strategic Research Award to pursue a study the mechanisms linking obstructive sleep apnea to Alzheimer's Disease biomarkers and cognitive decline and determine the impact of positive airway pressure (PAP) treatment adherence on longitudinal AD biomarker and cognitive decline over a period of two years. The project leverages the recently opened sleep center (see pp 22-23).

For more information about Dr. Benca's work visit http://cnlm.uci.edu/benca/

Ruth Benca, M.D., Ph.D. says changes in our brains that result in mid-life from sleep disturbances, such as obstructive sleep apnea, or pauses in breathing during sleep, could be powerful early-warning indicators of cognitive decline.

Dr. Jack Lin and collaborators at the University of Washington and UC Berkeley awarded a U19 grant from NINDS to study the brain mechanisms underlying rapid learning

Irvine, Calif., Sept 15, 2018
The National Institute of Neurological Disorders and Stroke (NINDS) awarded a cooperative grant (U19) to investigators at the University of Washington, UC Berkeley and UC Irvine to study computational and neural mechanisms underlying rapid learning. Dr. Jack Lin, Professor of Neurology and Biomedical Engineering and CNLM Fellow, serves as UC Irvine site principal investigator and director of the human physiology component program.

Learning rapidly is one of the defining features of human cognition. Despite its importance, the circuit mechanism that governs rapid learning in humans is unknown. This new project will bridge systems neuroscience across primate species and address these questions.

Lin directs UCI's Comprehensive Epilepsy Unit where the pre-surgical evaluation of patients with epilepsy provides a unique and potent opportunity to study these brain networks directly. Specially, large-scale high-density intracranial electrodes will be used to record neural signals from the brain while patients perform various learning tasks. These studies will be combined with similar work in nonhuman primates conducted by U19 collaborators at the University of Washington.

Understanding the mechanisms of rapid learning will provide a framework to develop interventions in people with disordered memory, including those with Alzheimer's disease, autism, major depression, and epilepsy.

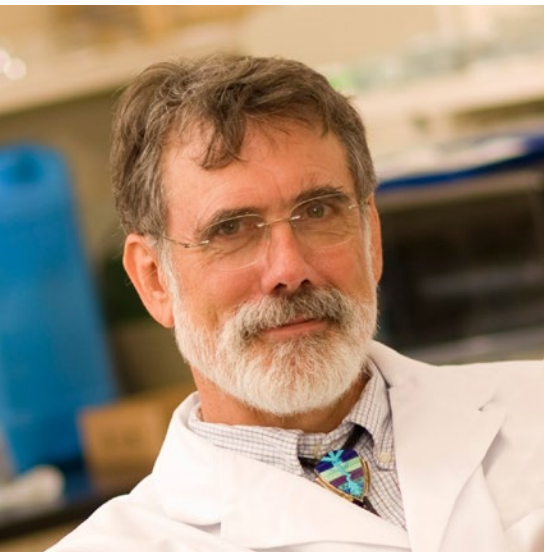
Jack Lin, M.D.

For more information about Dr. Lin's work visit http://faculty.sites.uci.edu/linlab/

New Awards

Bruce McNaughton Awarded DARPA L2M Project to Build New Learning Machines

The project will combine empirical studies with biophysical and computational modeling to develop new Lifelong Learning Machines (L2M) that adapt continually to new circumstances without forgetting previous learning.



Bruce McNaughton, Ph.D.

Irvine, Calif., Feb 8, 2018
Machine learning (ML) and artificial intelligence (AI) systems have significantly advanced in recent years. However, they are currently limited to executing only those tasks they are specifically designed to perform and are unable to adapt when encountering situations outside their programming or training. DARPA's Lifelong Learning Machines (L2M) program, drawing inspiration from biological systems, seeks to develop fundamentally new ML approaches that allow systems to adapt continually to new circumstances without forgetting previous learning.

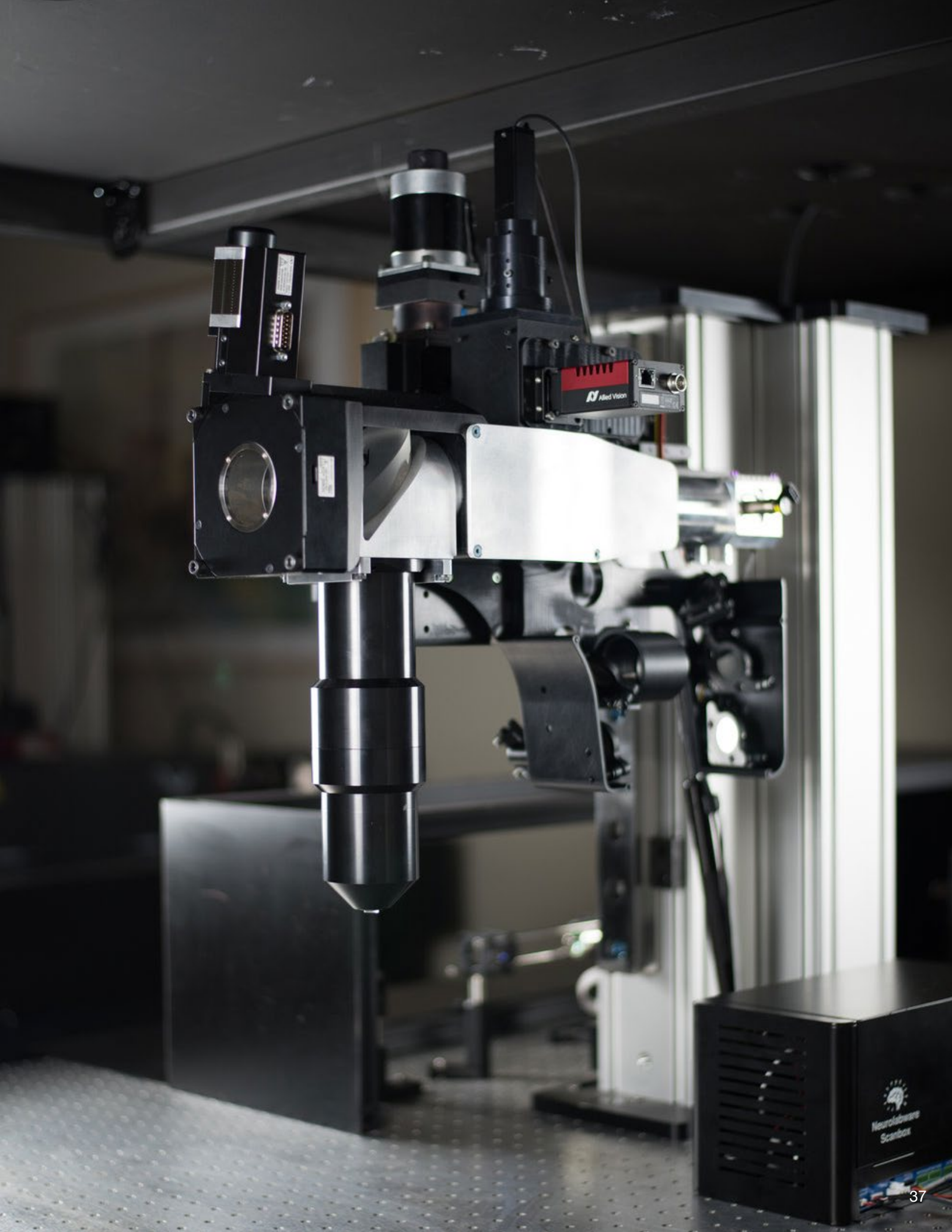
DARPA's L2M program awarded Bruce McNaughton, Distinguished Professor of Neurobiology and Fellow of the Center for the Neurobiology of Learning and Memory, and his research team $5.2M in funding to study the dual memory architecture of the hippocampus and cortex and create a powerful new biologically-inspired ML system that can adapt and learn while retaining previous memories.

"With the L2M program, we are not looking for incremental improvements in state-of-the-art AI and neural networks, but rather paradigm-changing approaches to machine learning that will enable systems to continuously improve based on experience," said Dr. Hava Siegelmann, the program manager leading L2M. "Teams selected to take on this novel research are comprised of a cross-section of some of the world's top researchers in a variety of scientific disciplines, and their approaches are equally diverse."

The project has already enabled a major advance for UCI. Earlier this year, McNaughton and colleagues purchased and installed a wide field two-photon mesoscope (right). The team plans to modify the instrument further to make it the most advanced multi-photon mesoscope in the world. This technique allows for live imaging of the activity of hundreds or thousands, of cells simultaneously by directly visualizing their calcium signaling.

Using these remarkably advanced techniques, McNaughton and his team will attempt to understand how the brain's storage system has developed the means to refresh its own knowledge base whilst merging new data gracefully and without overwriting older memories. The team will specifically examine offline periods such as quiet rest and sleep, during which the brain retrains itself to replay recent episodes of experience, interleaved with reactivating aspects of prior knowledge that are related to those experiences. Developing a working model of how the brain accomplishes this incredible feat will transform ML approaches and profoundly alter our understanding of how memory works.

For more information about Dr. McNaughton's work visit sites.uci.edu/mcnaughtonlab/


Allied Vision
Neurolabware
Scanbox

Junior Scholar Awards

CNLM Trainees Receive Awards for Distinction in Research and Service

A record-setting ten named fellowships were awarded to exceptional CNLM students and postdoctoral fellows to support their research and conference travel.

The CNLM is fortunate to have strong support from a dedicated philanthropic community who have endowed several awards in perpetuity to support student research and travel to scientific conferences.

Applications are highly competitive and a special faculty committee is appointed by the Director to review the applications and select the winners. This year, we were thrilled to be able to support the largest number of fellowships we have ever awarded.

Ten brilliant students and postdoctoral fellows received the 2018 awards. The award recipients presented their work in brief Elevator Pitch format to the UCI community and the public at the annual CNLM Awards Ceremony.

Keshav Suresh
Carol and James McGaugh Award

Established in Biological Sciences in memory of Mrs. Carol Becker McGaugh and to honor Dr. James McGaugh, this award recognizes a student with strong moral character, integrity and potential for making a difference in neuroscience. The award winner was Keshav Suresh, an undergraduate student working with Dr. Tallie Z. Baram. His talk was titled "Astrocytes as a Potential Player in Stress-Induced Brain Plasticity."

Caden Henningfield
Friends of the CNLM Award

Supported by generous annual contributions from the Friends of the CNLM, the award goes to a student who demonstrates excellence in laboratory research as well as academic scholarship. The award winner was Caden Henningfield, an undergraduate (now graduate) student working with Dr. Craig Stark. He is also a CNLM Ambassador. His talk was titled "Exploration of a Virtual Environment Improves Hippocampal Cognition."

Jude Banihani
Carol Becker McGaugh Award

This award was established in Biological Sciences in 2013 by Mrs. Carol (Becky) and Dr. James L. McGaugh to recognize an exceptional undergraduate student who excels in neurobiology scholarship and research. The award winner was Jude Banihani, an undergraduate student working with Dr. Marcelo Wood and postdoctoral fellow Dr. Thekla Helmstedt. Her talk was titled "The role of CREST in the Regulation of Memory-Associated Genes."

Alana Porat
James Tait Goodrich Award

Established in Biological Sciences this year by Dr. James and Mrs. Judy Goodrich to honor Dr. McGaugh, this award goes to a student who demonstrates excellence in neurobiology research. The winner was Alana Porat, an undergraduate student working with Dr. Karina Cramer. Alana majors in human biology with a minor in medical humanities. Her talk was titled "The Impact of Microglia Upon Synaptic Pruning in the Auditory Brainstem."

From Left to Right: Caden Henningfield, Alberto Lopez, Jude Banihani, Caitlin Suire, Maria Montchal, Mitchell Farrell, Eva Morozko, Freddie Marquez, Keshav Suresh, and Alana Porat.

Mitchell Farrell
John Haycock Memorial Award

Established by the Haycock family and friends, the award goes to outstanding graduate students to support travel to the annual Society for Neuroscience conference to present research. The first award winner is Mitchell Farrell, a graduate student working with Dr. Stephen Mahler. Mitch is a CNLM Ambassador and Brain Explorer Academy Mentor. His talk was titled "Risky rewards: Brain mechanisms of risky decision making."

Alberto Lopez
Roger W. Russell Award

Established by his family and friends, the award recognizes individuals who demonstrate Roger's values of dedication to exacting scholarship, integrity, collegiality, and service. The second award goes to Alberto Lopez, a graduate student with Dr. Marcelo Wood. Alberto received one of the nation's first K99/R00 NIH awards paving his path to independence. His talk was titled "Insights into the circuitry regulating cocaine relapse."

Freddie Marquez
Jared Roberts Memorial Award

Established in memory of Jared Roberts, this award supports an outstanding graduate student to travel to the Winter Neurobiology of Learning and Memory conference in Park City, UT. The award winner is Freddie Marquez, a graduate student working with Dr. Michael Yassa. Freddie is a also a CNLM Ambassador. His talk was titled "Toward understanding the early mechanisms that contribute to Alzheimer's disease."

Caitlin Suire
John Haycock Memorial Award

Established by the John Haycock family and friends, the award goes to outstanding graduate students to support travel to the annual Society for Neuroscience conference to present research. The second award goes to Caitlin Suire, a graduate student working with Dr. Frank LaFerla. She is co-chair of the CNLM Professional Development Committee. Her talk was titled "Alzheimer's disease: It's all about balance."

Maria Montchal
Roger W. Russell Award

Established by Roger Russell's family and friends, the award recognizes individuals who demonstrate dedication to exacting scholarship, integrity, collegiality, and service. The first award goes to Maria Montchal, a graduate student working with Dr. Michael Yassa. Maria is also the Chair of the Communications Committee of the CNLM Ambassadors. Her talk was titled "Studying memory for real life-like events in the laboratory."

Eva Morozko
Renee Harwick Award

Established by Dr. Renee Harwick, this award supports an exceptional advanced graduate student complete his or her thesis research. The award winner was Eva Morozko, a graduate student with Dr. Leslie Thompson, an ARCS Foundation Scholar, and a NSF graduate research fellow. She is co-chair of the CNLM Professional Development Committee. Her talk was titled "Protein Balance in Huntington's Disease."

CNLM Ambassadors Set New Standard for Outreach and Community Education

The group designed and implemented more than 25 outreach and education activities in 2018, serving more than 4,000 community members.

The CNLM Ambassador Program, formally established in 2017, aims to advance public understanding of brain science through outreach and educational activities. The engine of the program is the group of more than 60 UCI undergraduate students, graduate students and postdoctoral fellows who design, execute and evaluate educational programs on campus and in the local and regional community.

The Ambassador program provides meaningful leadership opportunities for UCI junior brain scientists as well as professional development training in scientific communication, educational program outcome design and evaluation.

The program is the brainchild of Manuella Yassa, the CNLM's Director of Outreach and Education and is organized and run by students, postdocs, and volunteers.

One of the organization's chief activities is the design and implementation of the UCI Brain Explorer Academy, the CNLM's flagship educational neuroscience program for school-age children. The program is the first in the world to combine neuroscience research, scientific communication and critical thinking skills training for tomorrow's brilliant minds.

The UCI Brain Explorer Academy science mentors are members of the CNLM Ambassadors who gain valuable experience in teaching and scientific communication. In 2018, the Academy trained two cohorts, each composed of 40 elementary and middle school children. Each cohort was directly mentored by 12 Ambassadors who receive training by Yassa, the program's founder and executive director.

In 2018, the CNLM Ambassadors designed and implemented more than 25 outreach and education programs, not including the Brain Explorer Academy. This includes several campus tours for high schoolers, several visits to local and regional high schools, including schools in Santa Ana and Anaheim, booths at health fairs, visits to senior centers, and other community venues. The group led a SFN-sponsored live, public webinar on memory and the brain and taught Girl Scouts about habits for a healthy brain.

The Ambassadors hosted the Brain Festival at LEARNMEM™2018 and led the brain exhibit at UCI's Homecoming 2018. They also designed and implemented their own professional development activities including a CNLM workshop by Bri McWhorter (*Activate to Captivate*℠) on public speaking and communication.

The group has grown in size and now has a formal leadership structure with two student co-chairs (Jessica Noche and Rachon Sweiss), and appointed committtes on K-12 Programs (chair: Natalie DiProspero), Adult Programs (co-chairs: Myra Larson and Elena Dominguez), Communications (chair: Maria Montchal), Outcomes Assessment (chair: Angie Quagletti), and Professional Development (co-chairs: Eva Morozko and Caitlin Suire). Lena Nguyen serves as the group's historian.

The CNLM Ambassadors is a volunteer-based organization that does not receive campus financial support. For a complete listing of the CNLM Ambassadors please visit cnlm.uci.edu/ambassadors.

To inquire about opportunities to support the CNLM Ambassadors and their activities, please contact:

manuella.yassa@uci.edu

(949) 824-5193

cnlm.uci.edu/ambassadors
explorethebrain.org


Jeff

Brains and Mind Benders at UCI's Homecoming in Aldrich Park

By: Manuella Yassa

Returning Anteaters held real human brains, while CNLM Ambassadors offered lessons in anatomy and taught them "mirror drawing"!

Irvine, Calif., Sat. Mar 3, 2018 The CNLM Ambassadors, joined by CNLM's Director, staff, and a number of Faculty Fellows spent most of the day on Saturday mingling with returning Anteaters and members of the UCI Community at Homecoming in Aldrich Park. Visitors had a chance to hold a real human brain and learn about its anatomy. Eva Morozko (left), co-chair of the Ambassadors' professional development committee could be seen pointing out different parts of the brain to a visitor.

"I didn't expect it to be so heavy", said one of the visitors. "It's densely packed. This convoluted structure makes it possible to pack 100 billion brain cells into the small space that is your cranium," said Michael Yassa, CNLM Director and anatomist-in-chief. Sporting a pair of purple gloves and an Anteater baseball cap, he gave short lessons in brain anatomy to groups of visitors.

On the other side of the exhibit, along with several Ambassadors I walked visitors through the procedure of mirror drawing. The task became famous in memory research for its use to demonstrate intact procedural memory in Patient H.M., a famous amnesic patient who had his hippocampus and surrounding regions surgically resected.

Mirror drawing is a true mind bender and can lead to hilarity, followed by a healthy appreciation for the intricacies of how certain functions are wired in the brain, and how new plasticity is needed to practice and improve on the task.

While they waited, Anteaters made their own artistic renderings of neurons out of colored pipe cleaners.

For their participation, Anteaters got to go home with a 'got brain?' goodie - either a t-shirt or a memory stick. The two commodities were among the most desired items at the festival and supplies quickly ran out!

As the event began to wind down, celebratory fireworks in sight, we all took a second to appreciate the joy of Homecoming activities and to feel the Anteater pride with the UCI community. We can't wait till Homecoming 2019. Zot Zot Zot!

Nicolelis Delivers the 24th Distinguished Lecture on Brain, Learning and Memory

Miguel Nicolelis, the world's most influential neuroscientist, made the audience at the Irvine Barclay Theatre laugh, cry, and think about what the future of neuroscience holds.

Irvine, Calif. Feb 27, 2018
The Distinguished Lecture Series on Brain, Learning and Memory was founded by James L. McGaugh in 1995 as a flagship public education program and has since become UCI's most well-recognized and highly acclaimed community lecture. It is jointly sponsored by the CNLM as well as the School of Biological Sciences and the UC Institute for Memory Impairments and Neurological Disorders (UCI MIND).

Nicolelis after his lecture, pictured with high schoolers who traveled, some for more than two hours, to see him.

This year, the 24th Annual Lecture was delivered by Dr. Miguel Nicolelis, Distinguished Professor of Neuroscience and Professor of Neurobiology, Biomedical Engineering, Psychology and Neuroscience at Duke University. Nicolelis is the author of several books including *Beyond Boundaries: The New Neuroscience of Connecting Brains with Machines – and How it will Change Our Lives*. His transformative research has been published in *Nature* and *Science* and has been reported in Newsweek, Time and Discover magazines. His committment to public education is visible through his work in his native Brazil, where he spends half his time.

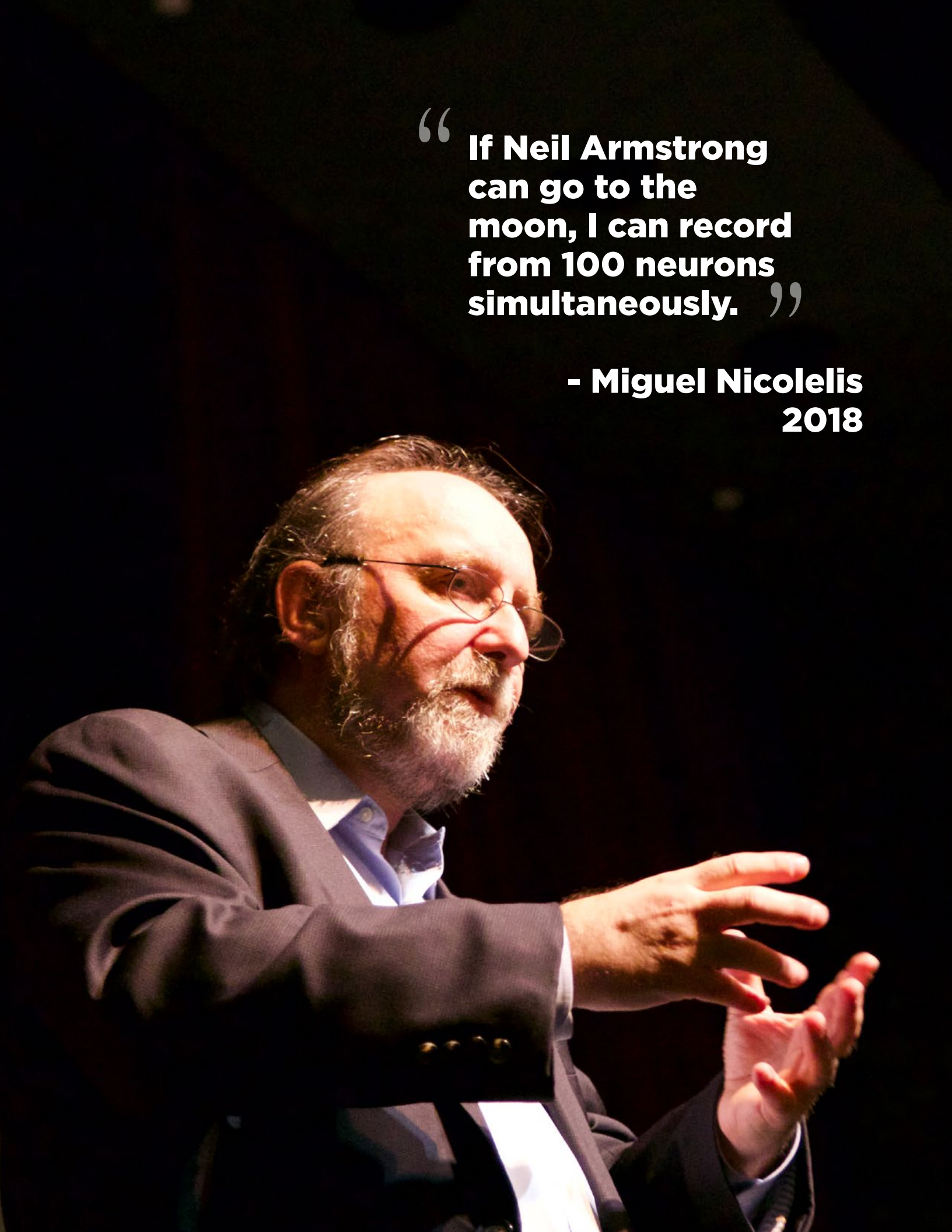
As the world's most influential neuroscientist alive today, Nicolelis has pioneered the field of Brain-Computer Interfaces (BCI), and his discoveries have created a world in which paraplegics have a chance of walking again. He has also developed an integrative approach to studying neurological and psychiatric disorders that will allow for a more complete understanding of neurological illness.

As soon as he took the stage in front of a large audience at the Irvine Barclay Theatre, Nicolelis took the audience on a beautiful journey through his career. He described the challenges he encountered and the perservence he needed to accomplish what seemed like the impossible - to record from more than just a handful of brain cells at the same time.

"I thought that if Neil Armstrong can go to the moon, I can record from 100 neurons simultaneously," he declared with determination. At the time, this was an astonishing accomplishment but it paved the way to the future of BCI. When he finally took things to the clinic, the results were nothing short of astonishing. A young man who had been paralyzed for more than 9 years could finally walk again, thanks to the hard work of Nicolelis and his team of more than 100 colleagues from all around the world. Advances in brain-machine interfaces, pioneered by Nicolelis and his colleagues, are now helping individuals like him walk again.

Nicolelis believes in building a strong foundation in fundamental neuroscience - the engine of discovery and creativity - before moving to clinical translation. Nicolelis' work is a great example of how dedication to fundamental science pays off!

For more information about the CNLM's public lectures see cnlm.uci.edu/barclay


“If Neil Armstrong can go to the moon, I can record from 100 neurons simultaneously.”
- Miguel Nicolelis
2018

Founder James McGaugh Delivers the Inaugural McGaugh-Gerard Lecture

UCI's sixth Chancellor, Howard Gillman introduces his colleague as a trailblazer and neuroscience giant.

Chancellor Howard Gillman

Irvine, Calif., Oct. 8, 2018
Very few people alive today can say they were there at the dedication of UC Irvine's campus in 1964. Recruited from the University of Oregon by the first dean of Biological Sciences at UCI, Edward Steinhaus, to be the Founding Chair of the world's first neuroscience department (then named psychobiology), on a UC campus that was yet to exist aside from a few trailers and an abundance of bison, James L. McGaugh is a trailblazer and a pioneer in every meaning of the word.

As Founding Director of the CNLM and the Founding Chair of the Department of Neurobiology and Behavior, McGaugh has made seminal contributions to the field of neuroscience and to the University. During his 54 years at UC Irvine, he has served as Dean of Biological Sciences, Vice Chancellor for Academic Affairs and Executive Vice Chancellor/Provost. McGaugh is internationally recognized for his studies of drug and hormone influences on memory as well as his more recent work on Highly Superior Autobiographical Memory. He has been featured on 60 Minutes, PBS Nova, and Scientific American, has authored several notable books, and published well over 500 peer-reviewed publications.

McGaugh was introduced by UCI's sixth Chancellor, Dr. Howard Gillman, who began by quoting Sir Isaac Newton "If I have seen further it is by standing on the shoulders of giants. In the field of memory creation, retention, and recall, James McGaugh is a giant," he said.

McGaugh took the stage and immediately quipped, "I thought it was going to be a handful of people - family and friends in the first couple of rows," he said with a broad smile to a capacity audience of 800 at the Irvine Barclay Theatre. The evening indeed was emotional, not only for McGaugh's family and friends, but for an audience that was taken on a journey through UCI's past, present

Distinguished Professor Emeritus James L. McGaugh

It is difficult to imagine what UCI would be like today if Jim McGaugh had decided back in 1964 to stay at the University of Oregon.

and future. "Memory is not about the past. It's about the future," he said.

Listening to McGaugh interlace the description of his pioneering work on memory and arousal with his own reflections of the campus was a unique and captivating experience.

As McGaugh ended the lecture, he looked out onto the audience - now standing and applauding vigorously. The emotion in the crowd was clear - deep gratitude to a giant who has given so much to the campus as well as pride to be affiliated with UCI. Chancellor Gillman said it best, "It is difficult to imagine what UCI would be like today if Jim McGaugh had decided back in 1964 to stay at the University of Oregon."

The McGaugh-Gerard Lectures

The McGaugh-Gerard Lecture series is a brand new public lecture series hosted by the CNLM aiming to engage the public in dialogue about findings from brain science. The lectures are made possible by the McGaugh-Gerard Endowment that was established by Dr. James L. McGaugh and the family trust of the late Dr. Ralph W. Gerard.

Dr. Gerard arrived at UC Irvine in 1964 and helped founding Chancellor Daniel G. Aldrich, Jr. organize the new campus. He was appointed the first Dean of the Graduate Division. Dr. McGaugh also arrived at UCI in 1964 and was interviewed by Dr. Gerard for the position of founding chair of Psychobiology, which is now known as the Department of Neurobiology and Behavior.

Of Gerard, Dr. McGaugh remarks "I felt privileged to know him, as he had a highly distinguished career in physiology and was one of the founders of the Society for Neuroscience. After he retired he invited me to meet with him in his home on Friday afternoons for many interesting discussions of science, campus activities and other matters." It is a fitting tribute to Gerard's memory and the two scholars' friendship that this lecture bear their names together.

For more information about the CNLM's public lectures see cnlm.uci.edu/barclay

Gifts and Giving

Introducing the Norman Weinberger Graduate Award

We are delighted to announce that with the generosity of the friends and family of the late Dr. Norman M. Weinberger (1935-2016) as well as the support of the School of Biological Sciences and the Department of Neurobiology and Behavior, the $25,000 endowment supporting an annual graduate student award in Dr. Weinberger's name has been fulfilled in 2018. Thank you to all of those who contributed to this important award, which recognizes the immense contributions of Dr. Weinberger to the UCI campus.

We are also delighted to announce that UCI's Dean of the Graduate Division has partnered with us and pledged to match the endowment income dollar for dollar, doubling the award's value.

Dr. Weinberger began his university career on January 1, 1965. He was a founding member of the CNLM, and led the planning of much of its activities including the construction of its buildings and conference facilities. His legacy lives on in his trainees who have become influential leaders in the field of neuroscience. The named award will memorialize Norm's contributions and reward the most exceptional students at the CNLM.

Norman M. Weinberger (1935-2016)

Shark Tank for Research

At the CNLM, we strongly believe in supporting innovative high-risk, high-reward research, the kind of research that has the potential to accelerate transformational, rather than incremental discovery. This research is too risky to be supported by traditional funding routes including the federal and state governments. We rely on private funding to support our scientists in the initial stages of discovery when it is most critical. Investment in these programs can be leveraged for large-scale federal funding that can yield more than 1000% return.

In 2018, we launched the *Shark Tank for Research* - an innovative way to create partnerships between scientists and community members. Program finalists will pitch their best ideas to philanthropists who play the role of the "Sharks" and will ultimately make the funding decisions. The program is led by Mr. David Ruhm, a valued CNLM community supporter. Initial seed investment of $25,000 was made by long-time CNLM supporters Drs. Igal and Diane Silber (right). With this generous gift, we are more than halfway towards our 2019 goal.

Igal and Diane Silber pictured with their with dog Tasha

To learn how you can join the Shark Tank for Research contact Manuella Yassa at (949) 824-5193 or manuella.yassa@uci.edu.

Supporting the CNLM

The CNLM would not exist if it were not for the dedicated community of supporters who share our vision. We have a long history of scientific discovery and a global reputation for advancing the field. More discoveries are just around the corner. But we cannot do it withour your support!

Memorial & Honorary Gifts

All donations are fully tax-deductible. You can make a donation in any amount in someone's honor or memory. No amount is ever too small. Gifts can be made online at **http://cnlm.uci.edu/gifts**

Memory Lane Dedications

Create a memory that will last forever. The CNLM courtyard is home to cherished memories inscribed on the bricks of our courtyard's Memory Lane and on the benches in our Memorial garden. With donations ranging from $500 to $2500 you can memorialize a loved one, honor a friend or colleague, celebrate a special occasion, or champion a cause.

Friends of the CNLM

Friends of the CNLM are community patrons who generously support and sustain the CNLM and its research, education, and service programs through commitments to annual giving. Friends receive access to our newsletter and are invited to join us for special events including our Evenings to Remember lecture series, the annual Distinguished Lectures in Brain, Learning, and Memory, as well as other special interdisciplinary scientific symposia and community lectures. Opportunities to invite CNLM Fellows to give lectures or salons at Friends' homes are also available.

CNLM Legacy Society

The Legacy Society honors supporters who designate the CNLM as a beneficiary of a planned gift. Legacy Society members receive invitations to all of our events and seminars including the annual Barclay lectures and our Evenings to Remember series, an invitation to an annual luncheon at the Chancellor's home, as well as exclusive Legacy Society mailings. Gifts include charitable bequests, charitable lead trusts and remainder trusts, charitable gift annuities, as well as retirement accounts. If you wish you could do more for our mission and cause, please consider naming the CNLM in your will. Your bequest will go a long way to supporting our work. For more information on legacy gifts please contact Roland Ho at 949-824-6454 or roland.ho@uci.edu.

Help Spread the Word!

One of the best ways to support the CNLM's activities is by spreading the word about our research mission and our outreach activities. By being an advocate for the CNLM, you can multiply our efforts and educate others passionate about brain science.

Please contact Manuella Yassa at (949) 824-5193 or manuella.yassa@uci.edu to discuss opportunities to support the CNLM's mission.

cnlm.uci.edu/gifts

Annual Giving

Friends of the CNLM

Friends of the CNLM are community patrons who generously support and sustain the CNLM and its research, education, and service programs through commitments to annual giving. Below are the giving levels for 2019. Contributions and renewals made before the end of the year will activate or retain membership in the Friends group for 2019.

NeuroSilver $500

Patrons at this level are acknowledged at all public lectures and events, receive access to our quarterly newsletter, invitations to our annual Distinguished Lecture in Brain, Learning and Memory at the Irvine Barclay Theater including backstage passes, reserved seating, and an exclusive opportunity to meet the distinguished speakers.

NeuroGold $1000

Patrons at this level receive all of the benefits of NeuroSilver PLUS invitations to our exclusive Evenings to Remember lecture series.

NeuroPlatinum $2000

Patrons at this level receive all of the benefits of NeuroGold PLUS a choice between a personal meeting with one of our CNLM scientists or an exclusive guided tour of one of the CNLM labs.

NeuroDiamond $5000

Patrons at this level receive all of the benefits of NeuroPlatinum PLUS invite one of our CNLM scientists to give a lecture at a salon or party at a location of your choosing (subject to Fellow's availability). In addition, if your annual giving is at this level or above, we would love for you to invite up to two guests at any of our exclusive events and gatherings.

If you would like to explore the possibility of joining the Friends of the CNLM but you are not sure about the structure or the benefits, please let us know and we can provide opportunities to explore what the CNLM has to offer.

Refer a Friend

In 2016, we launched our referral program. If you refer a friend or colleague to the Friends of the CNLM and they join the annual giving program, your membership for the following year will automatically be upgraded to the next level, with all of the associated benefits.

For more information, please contact Manuella Yassa at (949) 824-5193 or manuella.yassa@uci.edu.

Gifts Received 2017-2018

We are privileged to have the support of a community of philanthropists who believe in the CNLM's mission and the work that our faculty and students are doing every day to create and disseminate knowledge and develop innovative solutions to solve the global challenges of brain illness. Thank you for your support.

Richard and Michele Africano
James and Elaine Alexiou
The Allergan Foundation
Anonymous
Diane and Dennis Baker
Craig Boardman
D'Arcy Bolton
The BrightFocus Foundation
John and Peggy Bunnell
Valerie Beth Cantwell
Dr. Virginia Carson
Tom Casey
Kenneth & Shari Charlton
Patricia and Larry Colando
Nancy and Matthew Collett
Communication Disorders Res Fdn
Frank and Patricia Conner
Dr. Leo Cummins
Carla Dalmaz and Jorge Quilfeldt
Elsevier Publishing
Fidelity Charitable Gift Fund
Joanne M. France
Armida Fournell
Phillip and Kathryn Friedel
John and Carolyn Garrett
Edith Gibson
Sharlene and Lawrence Goodman
Dr. James Goodrich
Glenn and Marcia Griffith
Dr. Renée S. Harwick
Dr. Tamera Hatfield
Adeleh Hashemi
John C. Herklotz
Franz Hock
The Kavli Foundation
Deborah Kessler
Christine Meister
Karin and Michael Mesches
Richard Nelson
Marise and Louis Parent
Andrea Tenner and Tom Poulos
Shirley Pruitt
Ralph and Leona Gerard Family Trust
Clifford and Carol Ranney
A. Kimball and Romaine Romney
Audrey Schneiderman
Sempra Energy Foundation
SciTechEdit International
Drs. Diane and Igal Silber
Dr. Robert Elliott Simon
Betty Solloway
Craig and Shauna Stark
Joan Stratton
Thomas and Marilyn Sutton
Marsha Swartz
Sandi Teitsworth
Judith Thompson
Charles and Suzanne Turner
Vanguard Charitable Trust
Jim and Natalie Vogt
Lynne Wahlquist
Joyce Weatherford
Jacquie Weiberger
Jay and Sandra Wilbur
Michael and Manuella Yassa
Rosalind & Gary Ziccardi

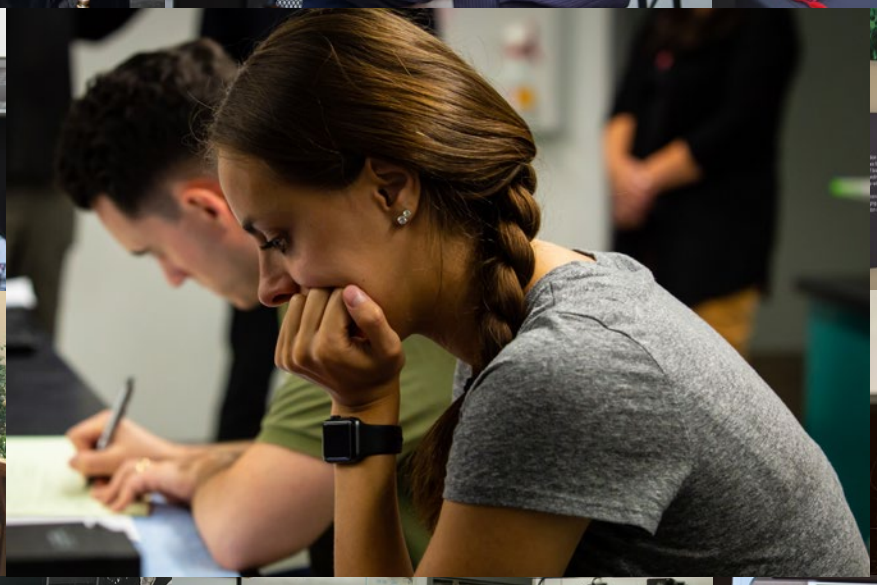
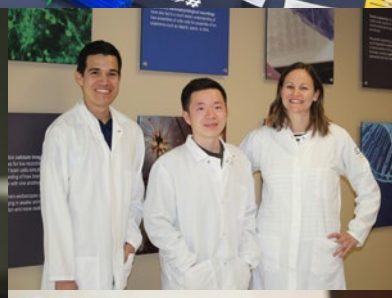
In memory of John Haycock
Jane Woods

In memory of Norman Weinberger
A-M Systems Inc
Dennis Baker
Candice Chavez
Marta Collett
Cheryl Diane Conrad
Jason Duko
Robert Garb
Drew Headley
Lisa Hinshelwood
Thomas Jacob Imig
Patricia Jackson-Colando
Jewish Communty Foundation of OC
Kristi Maharrey
Leanore C. Mesches
Lori Metherate
Amy Weinberger Randall
Tamara Lynne Weinberger
Ernest Wright
Michael and Manuella Yassa

In memory of Jared Roberts
Timothy Allen
Max Eugene Anderson
Ann Baerny
Megan Baerny
Michael Baerny
Morgan Barense
Darren J. Baum
Emily Bawden
Andrew Budson
Stacie Bullough
Kyeongho Byun
Allen Chang
Conor Cox
Gay Crist
Fishlock, David
Tim Dearing
Michelle Thuy Vi Doan
Keith Dye
Howard Eichenbaum
Builder's FirstSource
Norbert Fortin
Karole Holland Hagino
Daniel Hardy
Sam Hashizu
Holly Haueter
Carolyn Hopkins
Elsa Ingersoll
Grace Yukiko Izuhara
Wendy and Rob Jensen
Rex K. Jolley
Geoffrey M. Jones
K&S Furs, Inc.
Dwayne Kantaris
Robert Katzenbach
Bobi Keenan
Raymond Kesner
Edwin Kimoto
Brock and Maren Kirwan
James Knierim and Geeta Rao
Adithia S. Kurniawati
Catherine Lake
Stephanie Leal
Catherine Lee Spruance
Rita E. Loiotile
Zheng Ma
Cheryl Mattson
Sarah McCutcheon
Brad Anderson and Taylor McKinnon
Maria Elizabeth Montchal
Erik O. Nyholm
Erik Kyle Phillips
Tiffany Pusatello
William R. Rausch
Michael C. Riley
Tammy Riley
Brittany Roberts
James and Patricia Roberts
Reg Sauceda
Jim Sheltmire
Michael Smith
Mark Stanton
Craig and Shauna Stark
Eve Stark
Rebecca Stevenson
Summit Pet Care Services, Inc.
Stacy Sutton
Tanaka Farms LLC
Erin Walter
Dee Ann Webb
Doug Westwood
Shane W. Worthen
Steven D. Woodland
Stephanie Cherie Wu
Michael and Manuella Yassa



got brain?



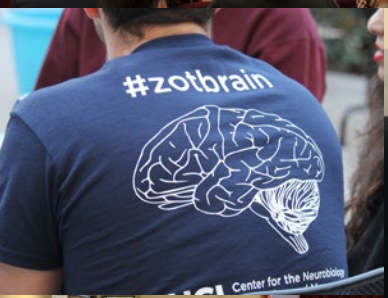




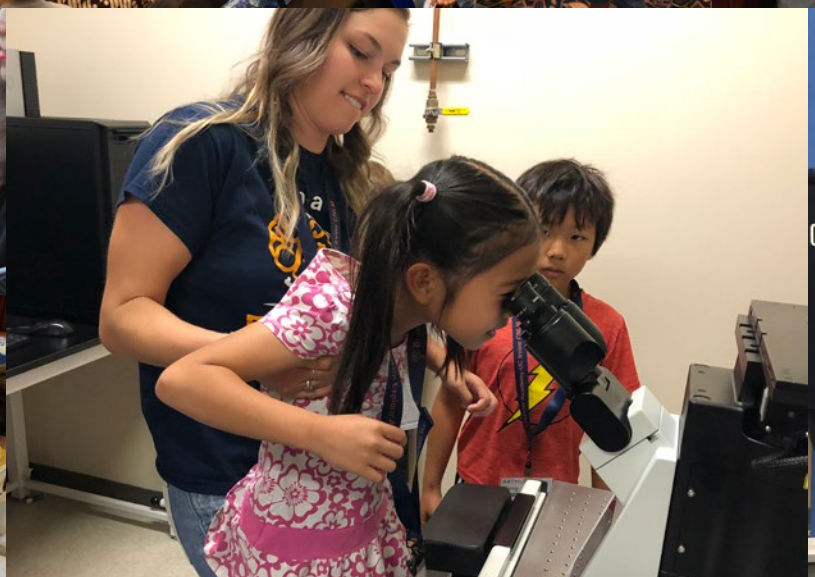

Awarded
KESHAN SUBESH
In recognition of your outstanding achievement
potential for making a difference in medicine
2018

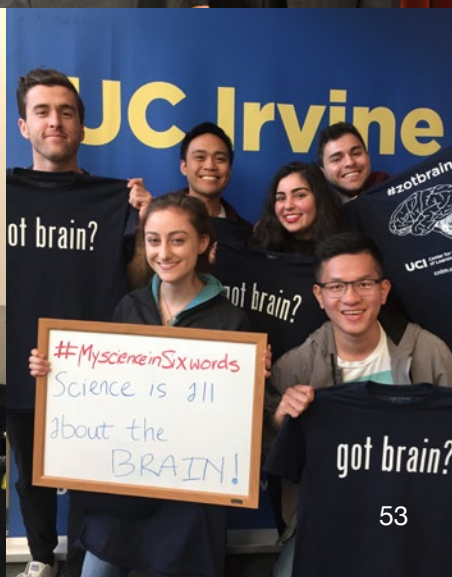

got brain?

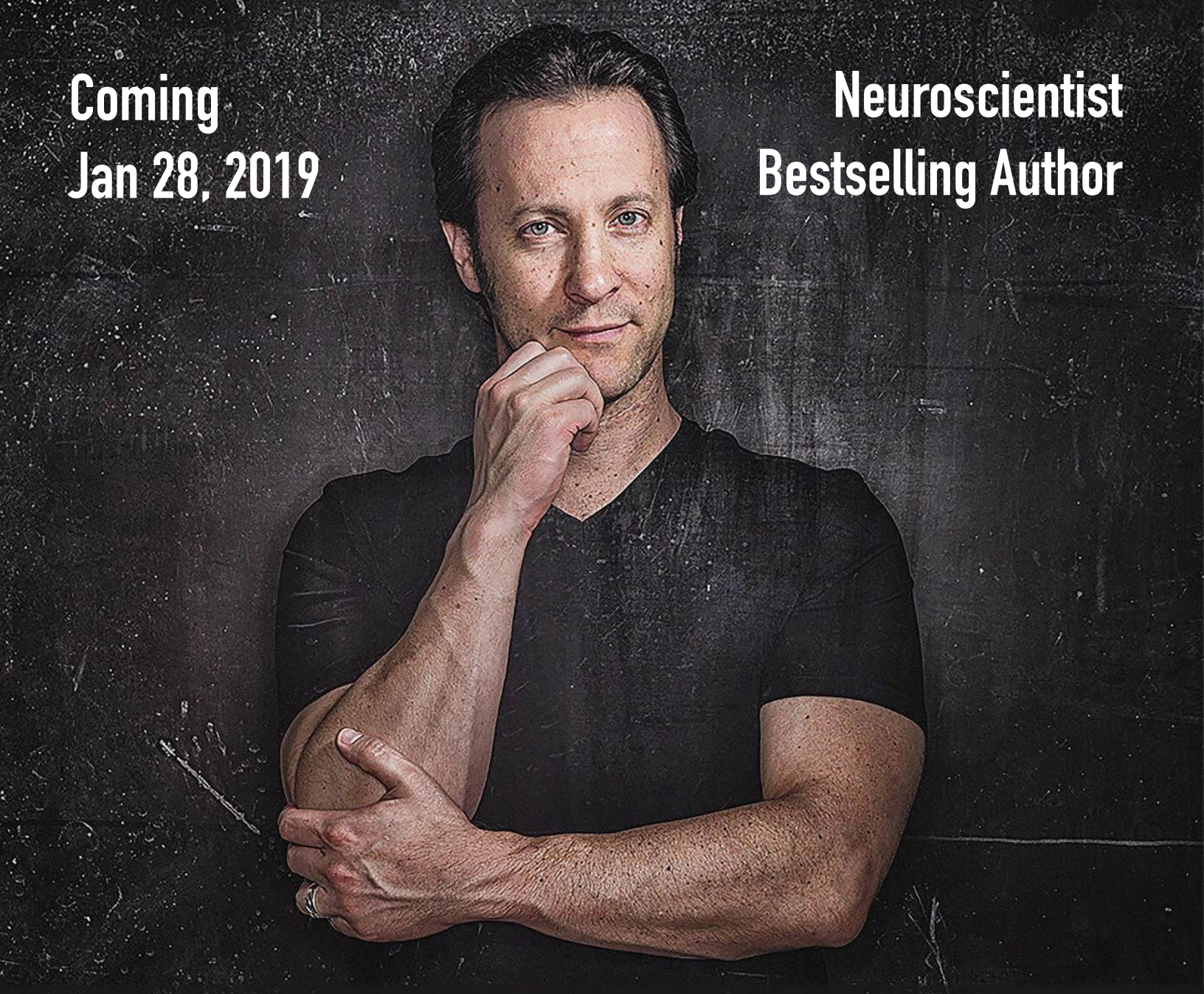

Carol Becker McGaugh Award
JUDE BANIHANI
The Role of CREST in the Regulation of Memory-Associated Genes


#zotbrain
Center for the Neurobiology


got brain?




UC Irvine
got brain?
got brain?
#MyscienceinSixwords
Science is all about the BRAIN!
got brain?



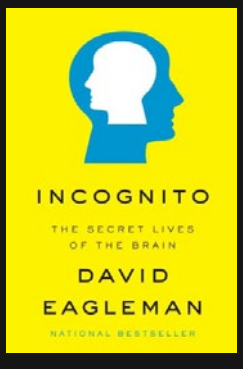
Coming
Jan 28, 2019

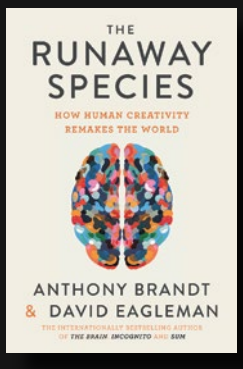
Neuroscientist
Bestselling Author

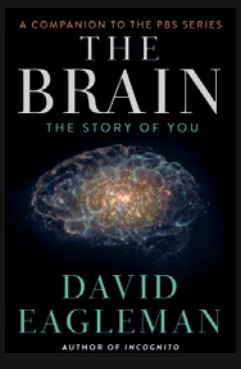
DAVID EAGLEMAN, PH.D.

CAN WE CREATE NEW SENSES FOR HUMANS?

THE 25TH DISTINGUISHED LECTURE ON
BRAIN, LEARNING AND MEMORY







RSVP online cnlm.uci.edu/eagleman


University of California, Irvine

University of California, Irvine