THE PUBLICATION OF THE NEUROSCIENCES INSTITUTE

BrainMatters

Fall/Winter 2011

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Delving Deeply into Animal Cognition to Unlock the Mysteries of the Human Brain...page 3

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Note from the Director

Some sciences are exciting because of their generality and some because of their predictive power. A very special value of yet other sciences is that they provoke unusual ideas, some of which are applicable to other fields of study. One example that comes to mind arises in the biological sciences of genetics, immunology, and neuroscience. Among other concepts, a study of these fields prompts an idea called degeneracy. Degeneracy refers to the fact that the action of different structures (e.g., molecules, cells, or organs) can give rise to the same result or output. This is strikingly true of how the brain is organized, from the finest levels to whole networks of brain components. One consequence of degeneracy is robustness—if one area or brain region is inoperative, another structure can often be called upon to carry out a function that would otherwise be lost. We know that degeneracy is necessary during evolution to counteract the loss of critical elements and to buffer the effects of mutation.

Degeneracy is only one of the many concepts employed by our Fellows when designing their experiments and analyzing their research results. The articles within contain updates about several of our scientific projects. I hope you will enjoy learning about their progress.

Dr. Gerald M. Edelman
Director

THE NEUROSCIENCES INSTITUTE

Delving Deeply into Animal Cognition to Unlock the Mysteries of the Human Brain

Deep in the ocean, an octopus relies on a surprisingly sophisticated neural network to learn the most efficient way to catch a crab. In a barn, a rat applies its own form of brainpower to carry out a decision-making process weighing the risk-reward of a leap needed to reach a sack of grain. On "YouTube," a cockatoo listens to a Backstreet Boys song and instantly launches into a high-stepping dance that perfectly matches the rhythmic beat.

For most of recorded history, science has been unable to observe, let alone understand, exactly what happens in animal brains that allows them to engage in cognitive activities like these—many of which parallel those previously thought to be uniquely human and which require much higher brain function than the simple rote tricks we teach our pets.

However, in the past quarter century and particularly in recent years, the study of animal cognition has expanded rapidly, driven by technological advances in neuro-physiology that allow researchers to actually observe and measure brain activity as it occurs, and in the process, demonstrate that much higher order activity is going on in those brains than ever thought possible. Scientists at The Neurosciences Institute are among those leading the quest to unravel the mysteries of animal cognition—loosely defined as the mental processes involved in acquiring, retaining, and applying knowledge. In recent years, this area of inquiry has evolved into an Institute-wide focus, propelling its scientists into conducting some of the most exciting and groundbreaking cognitive research in the world.

In one lab, for example, neurophysiologist Stephen Cowen, Ph.D., has developed innovative micro-techniques for measuring real-time neuronal activity in rats to determine how two different areas of the brain may work together in reward-based decision-making. In the Institute's new Octopus Lab (see story page 6), David Edelman, Ph.D., analyzes the brain of the invertebrate to understand how a nervous system that evolved so differently from mammals may still conform to many of the same neural principles. Meanwhile, Drs. Aniruddh Patel and John Iversen are studying how the rhythmic moves of Internet sensation "Snowball," the dancing cockatoo, may help explain certain complex brain processes, including those that may underlie language and movement.

Understanding these processes in animals has created a critical foundation for helping the Institute's researchers achieve their ultimate goal: understanding how the much more complicated human brain works, according to Gerald M. Edelman, M.D., Ph.D., Institute Founder, Director, and author of the theory of Neural Darwinism.

"What happens in our brain when we smell a fragrant rose, marvel at a sublime Monet landscape, or revel in a Brahms symphony?" Edelman asks. "What mental processes are in play when we walk from one room to another, recall an event from years ago, or simply decide which TV show to watch tonight?

"All are outwardly simple activities that seemingly require little or no thought," Edelman adds. "Yet inside our brains, a massive storm of neural activity involving millions of cells interacting with each other on a molecular level—often in multiple parts of the brain—occurs each and every time we engage in one of these acts of perception, motor activity, or memory."

And while it's true that important advances in electronic brain monitoring, such as magneto-encephalography (MEG) and functional magnetic resonance imaging (fMRI), have become extremely valuable tools by providing spectacular pictures and time frames of exactly where in the brain these processes occur, understanding how they work is quite another matter.

Says Edelman, "The remarkable mechanism by which our nervous system coordinates these complex and nearly instantaneous interactions stands as one of the most unique—and largely still unexplainable—mysteries of the human brain. Solving it is a vast challenge that will require years of dedicated, basic investigation and patience. However, by studying similar and simpler mechanisms in animal brains, in tandem with our studies on human cognition, the Institute is already beginning to gain insight into how the brain coordinates all of these processes into a dynamic representation of the world."

Thanks to his own groundbreaking research over the past two decades, Edelman has provided Institute scientists with a strong foundation for their inquiry into animal cognition. Among the key Edelman principles guiding his colleagues:

• Brains, whether human or animal, cannot be understood separately from the bodies they inhabit. In turn, how the brain and the body combine to relate and interact with the world determines how nervous systems and neural structures develop from the embryonic stage and continue to change and evolve throughout an organism's entire life span.

"We believe that components of this behavioral trinity—the brain, the body, and the environment—are constantly working together to form complex neural circuits that allow and mold functions such as perception, motor coordination, learning, memory, and ultimately consciousness," Edelman says.

• Nervous systems and the brains that control them are not wired like electronic devices, nor can the cognitive and behavioral activities they generate be explained simply by examining each individual's genome, two trends of scientific thought increasingly expounded as computers and artificial intelligence become more sophisticated and the successful mapping of the human genome spawns a seemingly endless array of new theories.

"We're confident in our core belief that nothing that happens in the brain is pre-destined or pre-ordained," Edelman says. "Brain circuitry is not "hard-wired" like a computer, with software-like instructions that govern all nervous systems in all organisms. It's why every individual organism on the planet is different from every other, including identical twins.

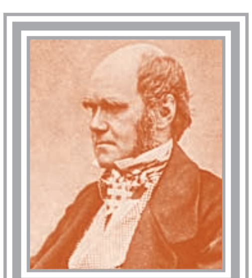
"Our research shows that cognition in animals is a dynamic, integrated mental process occurring in multiple sub-regions in the forebrain. We believe the structures and mechanisms underlying cognition were selected during evolution because they allowed animals to plan and prepare for future action in a complex environment, such as tracking prey or migrating long distances to find food and water, while staying alert to avoid being eaten."

The Institute's research also counters strictly genetics-based theories of brain function. In essence, such theories argue that how the brain works, from underlying biological processes to the cognitive and behavioral activities they produce, can be explained by analyzing and cataloging the genetic structure of each organism.

"Genetics unquestionably plays a crucial role in the biological development but makes no significant contribution to how the higher level brain processes operate," Edelman says. "There's no gene that explains the genius of Shakespeare, the power of Newton's mind, or the virtuosity of Jascha Heifetz. Instead, brains and nervous systems develop their unique characteristics thanks to the complexity, ambiguity, and unpredictability of signals received from encounters with the world. Sampling and integrating that complexity requires highly flexible brain mechanisms that can deal with endless and unforeseen novelty and organize it into a coherent view of the environment."

Scientists at the Institute are often asked why understanding brain function is important, how the investment of significant amounts of time and resources can be justified, and ultimately, what are the benefits of the research.

The answer, Edelman says, must be explained on two levels. First, the Institute prides itself on conducting fundamental research that may seem unglamorous but which allows researchers to solve basic questions "from the bottom up," creating a solid foundation on which to

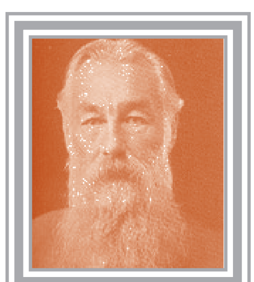


1871

Charles Darwin
Suggests the possible continuity of cognitive processes among different species.

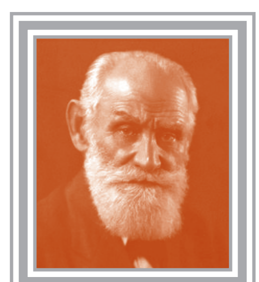
1887

George Romanes
Systematically investigated the comparative psychology of intelligence using an anecdotal method.



1894

C. L. Morgan
Cautioned researchers to avoid the tendency to anthropomorphize animals.



1901

Ivan Pavlov
Discovered the conditioned response using dogs.

1911

Edward Thorndike
First empirical and theoretical analyses of animal learning by observation or imitation.

EARLY PIONEERS IN THE STUDY

build more complicated inquiry.

Stephen Cowen's work offers an excellent example of the kind of research conducted throughout the Institute. Cowen created a device that enables him to attach electrodes thinner than human hairs to the pre-frontal cortices in rats and measure in real time—in two areas simultaneously—how and when single neurons and neuronal groups are active as the animal tries to solve risk-reward problems that require true decision making.

"All Stephen is doing is attempting to understand at the simplest level the dynamics of how these neurons interact to produce specific behaviors in the rat, such as deciding whether to climb a difficult barrier for more reward versus choosing an easier path for less reward," Edelman says. "No one's been able to do that before, and the huge database of brain activity measurements he's collecting will be critical for future stages of research."

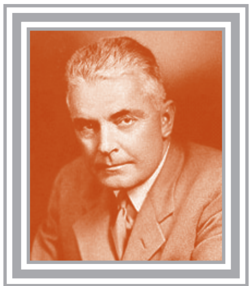
On the second level, it is those future stages of research that the ultimate justification for the Institute's work lies. Returning to Cowen, once his research reveals exactly how the underlying mechanism works, he'll be able to study what happens to the rat's decision-making system when it's altered in early development, disrupted by drugs, disease, or injury, or slowed by aging.

"The potential benefits of this research range from understanding why and how organisms make poor decisions, how addictions and obsessive-compulsive disorders develop, what breaks down in these two areas of the brain when they're damaged by Alzheimer's, dementia, and other degenerative diseases, and what types of treatments and therapies might mitigate these disorders.

"With certain aspects of brain research on humans largely not being possible for ethical or practical reasons, we're fortunate at the Institute that our scientists can look to the animal kingdom to provide us with insights into the functioning of the healthy brain. This promises to shed light on dysfunctions that lead to disease and disorders that are devastating to individuals and families and so costly to society," Edelman says.

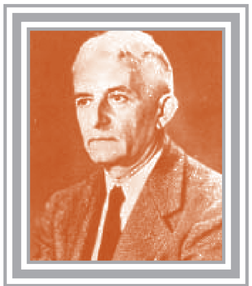
UPDATE ON SNOWBALL PROJECT

Cockatoos, like humans, are social creatures and Snowball is no exception. While he dances on his own with music, he dances even more vigorously when he has a partner (in this picture his owner, Irena Schulz of Bird Lovers Only). Are the visual, social cues as important as sound? To answer this question Institute scientists devised the "two-tempo" experiment in which Snowball's dancing partner listens over headphones to the same music as Snowball, but at a different tempo. With his partner dancing at one tempo and the music at another tempo, does Snowball simply ignore the sound and follow his partner, or does he try to integrate the conflicting cues? Preliminary results suggest he was not at all happy with the situation, often turning his back on his owner so he could move to the beat of the music. The answer gives important clues about the mechanisms Snowball uses to dance and further supports the idea that the complexity of bird behavior in dancing to music is similar to that of humans.



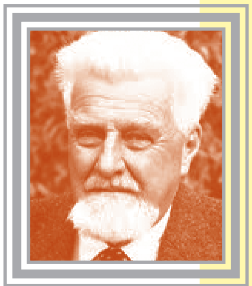
1913

John B. Watson
Founded the American School of Behaviorism after studying animals.



1917

Wolfgang Kohler
Developed the first cognitive analysis of learning in animals observing their ability to solve problems.



1930

Konrad Lorenz
Played a key role in the development of the ethological study of animal behavior.

1930

Karl Von Frisch
Investigated the sensory perceptions of the honey bee and was the first to translate the meaning of how they communicate through "dance".

1931

B.F. Skinner
Originated important ideas about behaviorism and operant conditioning, still in use today.

OF ANIMAL COGNITION

Dr. David Edelman holds Octopus bimaculoides, commonly called the two-spotted octopus.

The Octopus Lab

Octopus Brain, Behavior Intrigue Institute Scientist

Despite anecdotal evidence suggesting conscious states in a variety of non-human animals, no systematic neuroscientific investigation of animal consciousness has yet been undertaken.

David B. Edelman and Anil K. Seth
Animal consciousness: a synthetic approach.
Trends in Neurosciences 2009;32(9):476-84.

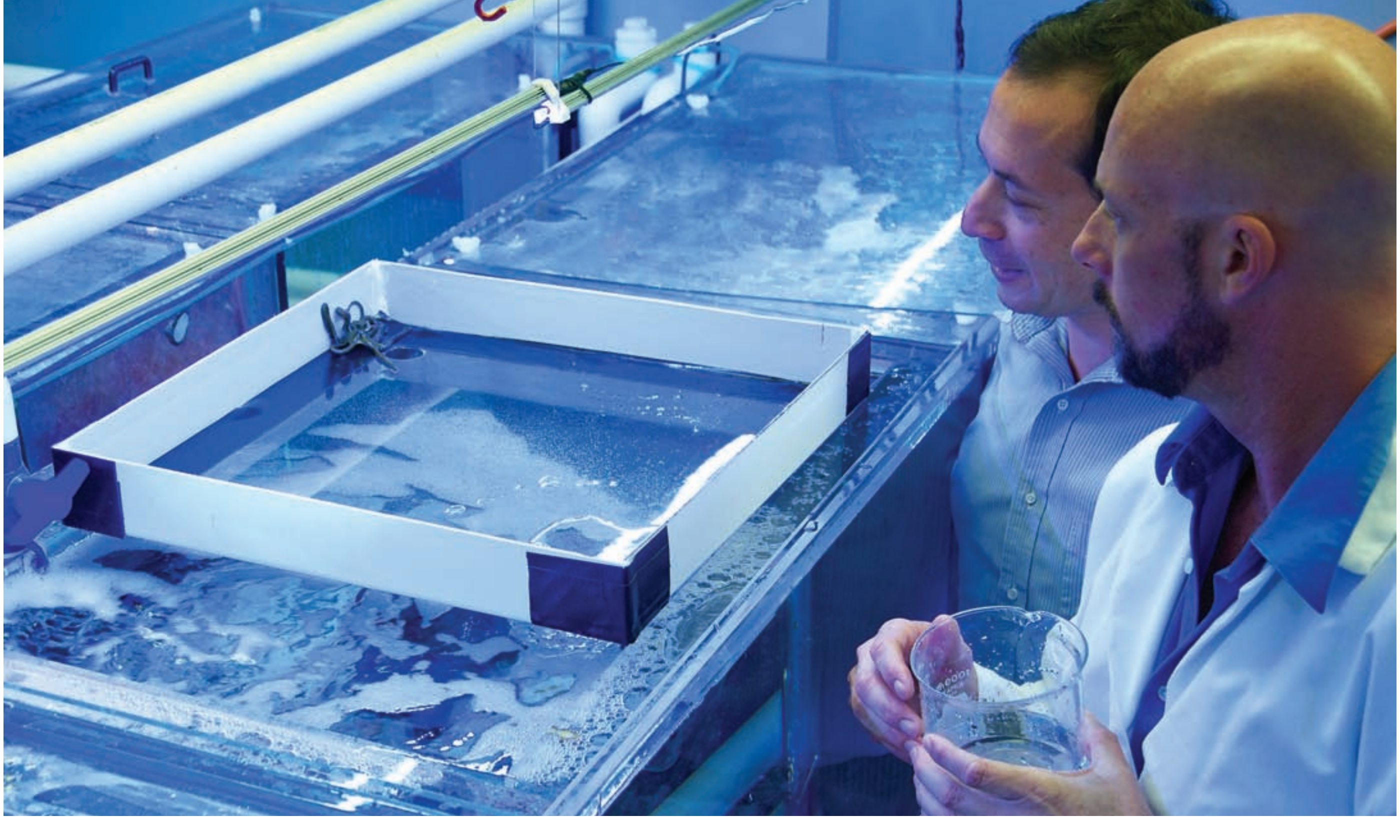
The octopus has always been among the most interesting of creatures, but new research reveals that this invertebrate is far more fascinating than previously thought, thanks to an evolutionarily divergent brain, a remarkably complex nervous system, and learning and memory capabilities that rival those of some mammals.

The sophistication of the octopus' brain and behavior is precisely why this cephalopod has become The Neurosciences Institute's latest animal cognition research subject, under the direction of Associate Fellow David Edelman, Ph.D., in the Institute's new Octopus Lab. Edelman's fascination with octopuses was sparked over the past few years, first by his review of the cephalopod literature, and then more recently by studies in which he participated at the Stazione Zoologica Anton Dohrn in Naples, Italy, one of the world's premier marine research institutions.

"It isn't widely known, but the octopus is among the most intelligent and behaviorally flexible of all invertebrates," Edelman says. "With more than half of its neurons not even residing in its brain, but rather in its eight arms, a nervous system that is strikingly different structurally from that of mammals, and an evolutionary history so different from our own, the octopus raises a host of intriguing scientific questions."

Edelman and his team plan to significantly expand the octopus knowledge base by studying how the animal's primary sense, vision, is linked to underlying mechanisms in the nervous system that control learning, the acquisition of short-term and long-term memories, problem-solving skills, and other faculties that might otherwise be associated with so-called higher brain function if the object of study were a mammal.

"The challenge is that the octopus nervous system evolved almost completely independently from those of mammals," Edelman says. "Despite these differences, octopus brains have lobes, nuclei, and in some cases, regions that, in their architecture and function, seem strangely reminiscent of human learning and memory areas, such as the hippocampus. But while the general structural anatomy of the octopus brain is fairly well characterized, the relationship between that brain and the animal's behavior remains largely unexplored.



Dr. David Edelman and Senior Research Technician Thomas Moller put the Indonesian octopus through the maze.

"Our goal is to examine this connection to see if there are implications for how evolution builds nervous systems and how uniquely different nervous systems can solve challenging problems," Edelman adds. "As we get deeper into the exploration of the octopus nervous system and its underlying physiology, we hope to achieve a platform-independent understanding of how the brain gives rise to higher level processes.

"What's exciting is that if we can show that two very different neural architectures can both support advanced forms of cognition, it should help us identify the fundamental neurophysiological requirements for intelligent behavior," Edelman says.

The Indonesian octopus greets the hand that feeds her.

Thomas Moller trains the two-spotted octopus to associate food with a target–in this case, a white ball.

The Indonesian octopus explores her realm.

View from the water feature across the courtyard to the auditorium at The Neurosciences Institute.

The Institute Recognized in the Community

In September, an on-line story ran locally that captured the essence of what makes The Neurosciences Institute such a special and unique place. The story included the following especially moving comment by Dr. Lawrence Kline, a donor and member of the Board of Trustees.

"I am a supporter of The Neurosciences Institute because it is the quintessential example of an uncontaminated system of scientific investigation that isn't controlled by industry and not polluted by government grant timetable reports and bureaucracy. Instead, it can focus on scientific creativity and innovation. Fresh creative thinking is essential to good science but often is hard to find. The Institute values ideas and produces new science more efficiently than many other large academic centers in the world. It is a rare gift to the scientific world and is truly a place with powerful potential that delivers quality science that can have a huge impact on us all. It's an honor to be able to support such greatness."

An Exciting New Study Partnership

Institute scientists are involved in a developing study to explore the impact of musical and symphonic training on cognitive and brain development in children. The study involves a new partnership between The Neurosciences Institute, represented by Aniruddh Patel and John Iversen; San Diego Youth Symphony, led by Dalouge Smith; and UC San Diego's Temporal Dynamics of Learning Center. The team is interested in how musical training impacts the development of language, attention, and executive function and of the brain networks that support these abilities. Pilot studies have begun in two Chula Vista elementary schools, with children primarily learning stringed instruments (e.g., violin). The team plans to use behavioral cognitive tests and structural brain imaging to assess the results.

Grant to Help Retrofit The Neurosciences Institute Auditorium

We are pleased to announce that the Institute has received a $50,000 grant toward retrofitting the auditorium through the San Diego County Neighborhood Redevelopment Program. Special thanks go to Pam Slater-Price for her recommendation to the County Board of Supervisors. The auditorium is loaned to many local non-profit arts and educational organizations free of charge through the Performing Arts at The Neurosciences Institute Program. Since its inception in 1996, this program is estimated to have saved those organizations over $2.8 million in costs associated with their performances and lectures. The grant funds will allow us to complete some much-needed improvements and refurbishments.

Drumming up Funding for the Performing Arts Program

Mission of the Performing Arts at The Neurosciences Institute Program

The Performing Arts at The Neurosciences Institute Program was founded in 1996 to enhance the vibrancy of San Diego's Arts community by offering premier performance space to local non-profit performing arts and educational organizations at no charge. The program focuses on instrumental, vocal, dance, and theatrical performances, as well as lectures aimed at a broad audience.

By offering use of the space, the Institute encourages organizations to provide high-quality events at lower ticket prices, allowing more San Diegans access to these enriching experiences. To this end, tickets for the events approved as part of the Institute's program must be priced at a maximum of $50, and many are less.

This program also serves to increase public awareness of the Institute's world-class scientific research activities that are directed toward developing a comprehensive understanding of how the brain works for the benefit of mankind. They include pioneering studies on how rhythm, music, and language are perceived and produced.

Minding the Arts – An Evening to Remember

Audrey Geisel and Alex Butterfield

Martin Wollesen, Joani Nelson (Event Chair), Dr. Gerald Edelman, Linda and Joe Satz, Esther Nahama

Gigi and Ed Cramer with members of San Diego Taiko

Anni Lipper, Dalouge Smith, Jeanette Stevens

Doreen Schonbrun, Jean-Marie Hamel, Reena Horowitz

Dr. Gerald Edelman with event emcee Ian Campbell

Arthur and Anni Lipper with Patti and Coop Cooprider

Sam Ersan and Lyndie Yagi with San Diego Symphony performers

The Neurosciences Institute's

Minding the Arts

www.mindingthearts.org

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The San Diego Foundation,
Dr. Seuss Fund

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Minding the Arts, presented by Audrey S. Geisel/Dr. Seuss Fund and chaired by Joani Nelson, raised over $100,000 for the Institute's Performing Arts Program! Thanks to the generous sponsors, caterers, performers, volunteers, and all who attended to help the Institute's auditorium continue to be available to local non-profit organizations free of charge!

Special thanks to the Institute's Performing Arts Ambassadors for their guidance and support:

Kathleen Charla	**Esther Paul**	**Linda Satz**	**Veryl Mortenson**
Jean-Marie Hamel	**Anni Lipper**	**Patti Cooprider**	**Toni Nickell**
Esther Nahama	**Joani Nelson**	**Reena Horowitz**	**Jeanette Stevens**

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Fall/Winter 2011

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Bennington President Shares Institute's Passion for Pursuit of Knowledge

Among the myriad intellectual realms that constantly occupy the mind of Bennington College President Elizabeth Coleman, Ph.D., few ignite her passion more than the groundbreaking exploration of the brain she's witnessed first-hand at The Neurosciences Institute.

What began as a simple visit to the Institute a decade ago at the invitation of Institute Trustee Susan Borden has developed into a remarkable personal and professional partnership in which the college and the Institute have both benefitted from a rich interplay of ideas at the highest levels of education and science.

Elizabeth Coleman

Coleman, who has presided over the Vermont-based liberal arts college since 1987, has developed a strong relationship with the Institute. In addition to serving on the Board of Trustees, she supports research through personal donations, has served as a Visiting Fellow, and presented at the Library Roundtable lecture series on how the "Neural Darwinism" theories of Institute Founder and Director Dr. Gerald M. Edelman, "provide a framework for transforming and reinvigorating undergraduate education."

"My admiration for The Neurosciences Institute begins with the respect I have for Dr. Edelman as one of the most profound thinkers I've ever encountered. His brilliant concept that scientific advances are most likely to emerge in a collaborative environment rooted in free inquiry, creativity, and innovation isn't just beneficial to the work of his researchers, it has profound applicability well beyond neuroscience into many other areas of human aspiration."

Over the years, Bennington faculty members have visited the Institute and Institute scientists have made similar journeys to the college, cultivating a fertile cross-pollination of ideas that have enhanced the intellectual life of both institutions.

Says Coleman, "I'm extremely proud to say that both institutions have the ambition and courage to address what it means to be human: The Neurosciences Institute through its work toward a global theory of the human brain, and Bennington College through its unwavering commitment to expose its students to the whole of human experience. Above all, we are both deeply committed to pushing the boundaries of intellect and imagination in pursuit of scientific and human truth."

The Institute is deeply grateful for Dr. Coleman's significant contributions as an advisor and collaborator and for her generous financial support.