

## A MESSAGE FROM THE DIRECTOR

---

This is the inaugural issue of *Brain Matters*, the newsletter of The Neurosciences Institute. We created this new communication tool to share with you some of the pioneering research we are conducting at the Institute.

Our work centers on a human organ that weighs just 48 ounces, yet is the most complex object in the known universe. The network of connections between its neurons is so vast that counting the connections of the cerebral cortex alone at the rate of one per second would take 32 million years.

It is no surprise, then, that our knowledge of the brain is only in its infancy. Intense study by the Institute and other research organizations over the past two decades has laid down the fundamental principles governing how the brain works. It has also taught us how much we must learn about how the brain functions, how it develops and reacts to a complex and changing environment, how it affects consciousness and sleep, and how it lays the foundation for intelligence and creativity.

Finding answers to these questions is our challenge and despite its magnitude, we believe that conquering this “final frontier” is only a matter of time. It will represent one of the most spectacular breakthroughs in human history, transforming mankind’s quality of life and standard of living in ways never envisioned.

The impact on our lives cannot be underestimated. The medical costs alone of treating brain disorders exceed \$600 billion a year in the United States alone, far more than any other group of illnesses. The economic impact due to the loss of productivity is more than \$1 trillion each year. The emotional costs defy measurement.

We believe The Neurosciences Institute to be a unique research center in the world, one that is equipped with both the scientific skills and tremendous will required to meet this formidable scientific challenge.

In its ongoing issues, *Brain Matters* will chronicle our quest. We will delve into some of our groundbreaking research that is already unlocking some of the mysteries of the brain. We will tell you how that research ultimately will impact the lives of human beings across the globe. And we will give you a more personal “up close” look at some of individual members of our wonderful team of dedicated researchers.

We hope you enjoy *Brain Matters*, and we welcome your comments and suggestions.

**Gerald M. Edelman, M.D., Ph.D.**  
*Founder and Director*  
*The Neurosciences Institute*

## THE NEUROSCIENCES INSTITUTE

**A unique center devoted to completing the picture of how the brain makes us human**

From the time human beings became aware of the importance of the brain centuries ago, they have attempted to reveal the secrets that enshroud that remarkable organ.

Now, as we enter the 21st Century, The Neurosciences Institute – for the first time in human history – is taking our knowledge of the brain to levels that could not have been imagined, even a few years ago.

With a commitment to recruiting the most gifted and broadly educated brain scientists from around the world, the Institute uses an innovative, interdisciplinary approach to the study of brain function. The Institute is unique in its commitment to both theoretical and experimental approaches in carrying out research on the brain.

“Our mission is to understand the power and versatility of the human brain through fundamental scientific research,” says Nobel laureate Gerald M. Edelman, M.D., Ph.D., founder and director of The Neurosciences Institute. “The work of the Institute emphasizes the critical importance of understanding brain function as a basis for human individuality and creativity.”

Edelman adds, “We have created an environment that encourages exceptional scientists to develop unique perspectives on how our nervous system functions. The goal is to provide an understanding of sensation, perception, memory,

*continued on page 4.*



## INSTITUTE RESEARCHERS DISCOVER FRUIT FLIES SLEEP

### Finding could provide key to understanding one of the great mysteries of life

Fruit flies sleep.

The statement is simple, yet the considerable research effort that led to that dramatic discovery at The Neurosciences Institute earlier this year was anything but simple. What's more, the implications of this finding for the future health and well-being of the human race are potentially profound.

The average person might find this somewhat hard to believe. After all, what is so exciting that both *Science* magazine and *Time* magazine would print a feature story on this news?

Dr. Paul Shaw, one of the Institute's lead researchers on the project, has in fact heard just that type of response from those outside the scientific world. He fully understands when people shrug their shoulders and say, "Why would anyone care if fruit flies sleep?"

But Shaw has a powerful response that instantly puts the Institute's research in perspective.

"Do you remember the tragedy at Chernobyl and the scare we had at Three Mile Island?" he asks. "Do you remember the disaster at Bopal in India and the Exxon Valdez Alaska oil spill nightmare? We all do. Well, we believe the research we're doing on sleeping fruit flies will someday help us prevent those kind of disasters, which it so happens may well have been the result of sleep deprivation related to late-shifts."

And that is just one of the many areas in which the Institute's discovery will have an impact, Shaw and his fellow researchers believe.

The study reported that the common fruit fly, *Drosophila melanogaster*, seems to undergo biochemical changes similar to those observed among mammals. Like humans, a fly's "beauty rest" can be altered by caffeine or antihistamines and sleep deprivation prompts it to over-compensate by "catching a few winks."

According to the study, a fruit fly's night-time rest period meets all of the essential criteria for sleep – right down to the level of turning off many of the same genes during

sleep as mammals. And when the fly has a specific mutant gene, the ability to regulate sleep is disturbed.

The study was conducted as a collaboration between the labs of The Neurosciences Institute's Senior Fellows Giulio Tononi, a sleep expert; Ralph J. Greenspan, a fly expert; and their associates Shaw and Dr. Chiara Cirelli.

"In recent years," Greenspan says, "*Drosophila* has become a favorite organism for studying the influence of genes on all aspects of an animal's life, in part because its genes bear such a strong resemblance to our own, and in part because of the ease of studying how genes work in fruit flies. The demonstration of sleep in the fruit fly opens a way to unraveling the mystery of sleep."

Most importantly, Greenspan adds, the fruit fly seems to share several markers believed to modulate sleep and waking in mammals. Of particular note is an enzyme, *arylalkylamine N-acetyltransferase*, which is thought to aid sleep by regulating levels of neurotransmitters called monoamines.

"In humans, sleep may be more important for breaking down and lowering brain levels of monoamines, such as norepinephrine and serotonin," says Tononi. "Understanding these functions might ultimately prove helpful to people with insomnia or late-shift workers who must forego sleep on a regular basis."

When deprived of sleep, mammals become seriously impaired. Without it, they do not survive. Previous studies in Tononi's laboratory showed that certain genes in mammals are closely regulated by sleep: some are on only during sleep and others are only on during waking.

The Institute's findings constitute the first rigorous demonstration of a sleep-like state in an invertebrate at the behavioral and molecular levels, Shaw says.

"The finding of authentic sleep in the fruit fly shows that it shares a sophisticated brain function with humans," Greenspan says. "The significance lies in the power of the fruit fly's genetics to help us figure out the function of sleep and to develop safe new drugs for sleep as well as wakefulness." 



## Dr. Paul Shaw

### RESEARCHER'S LONG HOURS DON'T DIM PURE JOY OF SCIENTIFIC QUEST

Like many of his fellow researchers at The Neurosciences Institute, Dr. Paul Shaw puts in long and often draining hours in his search for answers to how the human brain works.

But the sleep researcher's intense schedule is offset by the fact that he loves what he does, and has fun doing it.

"The best thing about being a scientist doing the work we do is that every morning is like Christmas," the 36-year-old Shaw says with a boyish grin. "You never know what's going to be under the tree, but you know you're going to get to open a present."

The thrill of the scientific hunt has been with the Northern California native since the late 1980s when he was trying to figure out what to study in graduate school after getting his bachelor's in psychology and criminal justice from Niagara University in upstate New York.

He found the answer after traveling across the country to seek his masters degree at San Jose State University, where he happened to take a class in biological psychology.

"That course really caught my imagination," Shaw recalls. "I knew at that moment that I wanted to study the physiology of behavior, and more specifically, how the brain produces behavior and how behavior changes how the brain works."

Shaw went on to the University of Chicago where he obtained a Ph.D., studying with one of the world's leading sleep researchers. The network of scientists who conduct brain research led to an opportunity to join The Neurosciences Institute staff in 1996.

Shaw has thrived at the Institute, where he has become immersed in the project that earlier this year announced the discovery that fruit flies sleep (see previous article). The satisfaction of that discovery more than makes up for Shaw being too busy to actively pursue the one hobby he enjoys – surfing. And while research has its share of frustrations and frequent dead-ends, Shaw can't imagine doing anything else with his life. He extends his Christmas metaphor.

"Sure, sometimes the Grinch comes by and hands you a lump of coal," Shaw laughs. "But overwhelmingly, the chance to work alongside extremely bright colleagues in a great scientific environment, doing research that has the real potential to improve the human condition is incredibly exciting and rewarding." ☺

#### Brain teaser...

Dolphins and aquatic mammals that live in muddy waters sleep using one-half of their brain at a time so that they can swim continuously.

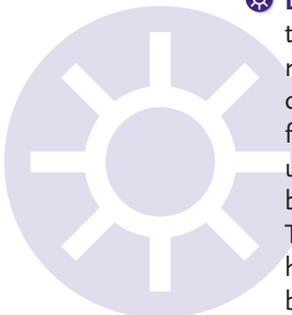
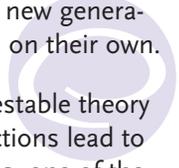


*"...the chance to work alongside extremely bright colleagues in a great scientific environment, doing research that has the real potential to improve the human condition is incredibly exciting and rewarding."*



emotion and consciousness as matters centrally important to all human concerns.

That commitment has paid off. The Institute's small but talented team of scientists has compiled a remarkable record of groundbreaking discoveries that are greatly influencing international thinking about how we view the brain and its role in the human equation. In the past five years, Institute researchers have:

-  **Discovered** fruit flies sleep, much as humans do, a discovery that could someday offer clues to sleep disorders that torment untold numbers of people (see related article).
-  **Discovered** a new technique for measuring the brain's response to complex patterns of pitch, such as musical melodies and speech intonation. The study suggests how different parts of the brain – particularly the left and right hemispheres – work together during the perception of sound sequences.
-  **Developed** several generations of the world's most sophisticated machines that outwardly resemble conventional robots, but which in fact are controlled by realistic simulations of the brain and are capable of learning through experience. These devices are used to explore how brain activity gives rise to behavior and learning processes. They are prototypes of machines representing a totally new generation that truly “think” on their own.
-  **Developed** the first testable theory about how brain functions lead to human consciousness, one of the most obvious yet least understood aspects of life.
-  **Demonstrated** for the first time that instinctive behavior can be transferred between one species of higher animals to another (chicken and quail) by transplanting early

brain regions. This work is helping identify the location of brain cells that control specific behaviors.

How did this remarkable institution come about? The Neurosciences Institute was founded in 1981 at the Rockefeller Institute in New York City to address the need for combining theoretical and practical problem-oriented approaches to fundamental research on the brain.

Relocated to San Diego in 1993, The Neurosciences Institute is world renowned for its efforts in developing and encouraging new lines of inquiry in brain research. The work of the Institute is supported by the Neurosciences Research Foundation, a non-profit research and educational organization.

The Neurosciences Institute holds firmly to the principle that creativity in science is best fostered in an environment with few pre-conceived research constraints and with unlimited opportunities for discovery and communication. Over the years, it has developed a unique and flexible program of scientific activities tailored to the requirements of each researcher, whether resident fellow or visitor.

Resident Fellows in theoretical and experimental neuroscience meet daily to exchange data and ideas. The Institute also brings to its campus outstanding visiting scientists in many different disciplines. It supports the individual creative work of these visiting scientists during their stay and encourages them to formulate new research to be carried out upon their return to their own universities and laboratories. More than 1,000 scientists from over 300 institutions and 24 countries have participated in Institute programs.

The Neurosciences Institute neither seeks nor accepts government funding. The Institute is entirely supported by private contributions to assure complete freedom of scientific exploration without strings attached, avoiding potential conflicts with the Institute's basic philosophy and values. 

## NEUROSCIENCES RESEARCH FOUNDATION, INC. GOVERNING BOARDS

### OFFICERS OF THE CORPORATION

William D. Walsh,  
*Chairman*

Lewis B. Cullman,  
*Vice Chairman*

Gerald M. Edelman, M.D., Ph.D.  
*President*

John R. Costantino,  
*Treasurer*

W. Einar Gall, Ph.D.  
*Clerk*

Henry G. Walter,  
*Chairman Emeritus*

### BOARD OF TRUSTEES

William O. Baker, Ph.D.  
*Retired Chairman of the Board and President  
Bell Telephone Laboratories, Inc.  
Murray Hill, New Jersey*

Susan P. Borden  
*Vice Chairman  
Bumper Development Corporation  
Calgary, Alberta, Canada*

Kay Delaney Bring  
*Retired Executive Vice President  
Turner Broadcasting  
New York, New York*

Esther J. Burnham  
*Former President and Life Director  
The San Diego Opera Association  
San Diego, California*

H. Michael Collins  
*Managing Director  
Van Kasper Advisers  
San Diego, California*

Erminio Costa, M.D.  
*Scientific Director of the Psychiatric Institute  
Professor of Biochemistry and Psychiatry  
University of Illinois at Chicago  
Chicago, Illinois*

John R. Costantino  
*Partner and Founder  
Walden Partners, Ltd.  
New York, New York*

Lewis B. Cullman  
*President and Chief Executive Officer  
Cullman Ventures, Inc.  
New York, New York*

Spencer Davidson  
*President and Chief Executive Officer  
General American Investors, Inc.  
New York, New York*

Gerald M. Edelman, M.D., Ph.D.  
*Director  
The Neurosciences Institute  
San Diego, California*

Peter K. Ellsworth  
*President  
The Legler Benbough Foundation  
San Diego, California*

Anthony M. Frank  
*Chairman  
Belvedere Capital Partners  
San Francisco, California*

William J. Gedale  
*President and Chief Executive Officer  
Mount Everest Advisors, LLC  
New York, New York*

Leon M. Jaroff  
*Writer and Retired Managing Editor  
Time Inc.'s "Discover" Magazine  
East Hampton, New York*

Harvey L. Karp  
*Chairman  
Mueller Industries, Inc.  
New York, New York*

Bryce W. Rhodes  
*Vice President  
Whittier Energy Company  
Del Mar, California*

Robert K. Shaye  
*Chairman and Chief Executive Officer  
New Line Cinema Corporation  
Los Angeles, California*

William R. Stensrud  
*General Partner  
Enterprise Partners  
La Jolla, California*

William H. Sweet, M.D.  
*Retired Neurosurgeon  
Harvard University  
Brookline, Massachusetts*

Charles R. Wall  
*Senior Vice President and General Counsel  
Philip Morris Companies, Inc.  
New York, New York*

William D. Walsh  
*Founder  
Sequoia Associates  
Menlo Park, California*

Henry G. Walter, Jr.  
*Retired Chairman and Chief Executive Officer  
International Flavors and Fragrances, Inc.  
New York, New York*

Ira J. Weinstein  
*President  
The Schnurmacher Foundations  
New York, New York*

M. Faye Wilson  
*Senior Vice President  
The Home Depot  
Atlanta, Georgia*

### HONORARY TRUSTEE

William T. Golden  
*Chairman Emeritus  
American Museum of Natural History  
New York, New York*

### MEMBERS OF THE CORPORATION

William O. Baker, Ph.D.  
*Retired Chairman of the Board and President  
Bell Telephone Laboratories, Inc.  
Murray Hill, New Jersey*

John R. Costantino  
*Partner and Founder  
Walden Partners, Ltd.  
New York, New York*

Spencer Davidson  
*President and Chief Executive Officer  
General American Investors, Inc.  
New York, New York*

Gerald M. Edelman, M.D., Ph.D.  
*Director  
The Neurosciences Institute  
San Diego, California*

William J. Gedale  
*President and Chief Executive Officer  
Mount Everest Advisors, LLC  
New York, New York*

Carl B. Hess  
*Founder and Controlling Partner  
AEA Investors, Inc.  
New York, New York*

Leon M. Jaroff  
*Writer and Retired Managing Editor  
Time Inc.'s "Discover" Magazine  
East Hampton, New York*

Harvey L. Karp  
*Chairman  
Mueller Industries, Inc.  
New York, New York*

Burton J. Manning  
*Chairman Emeritus  
J. Walter Thompson, Inc.  
New York, New York*

William H. Sweet, M.D.  
*Retired Neurosurgeon  
Harvard University  
Brookline, Massachusetts*

Dr. Alberto J. Vollmer  
*Ambassador  
Republic of Venezuela to the Holy See  
Caracas, Venezuela*

William D. Walsh  
*Founder  
Sequoia Associates  
Menlo Park, California*

Henry G. Walter, Jr.  
*Retired Chairman and Chief Executive Officer  
International Flavors and Fragrances, Inc.  
New York, New York*

Ira J. Weinstein  
*President  
The Schnurmacher Foundations  
New York, New York*

### GENERAL COUNSEL

Sander Lehrer, Esq.  
*Partner  
McDermott, Will & Emery  
New York, New York*

## NEW BOARD MEMBERS

The Neurosciences Institute welcomes the following new trustees:

**Esther J. Burnham**, San Diego, California, is life director and past president of The San Diego Opera Association, a former commissioner of the San Diego Arts and Cultural Commission, and a member of the UCSD Board of Overseers.

**H. Michael Collins**, San Diego, California, is managing director of Van Kasper Advisers, a director of the San Diego Hospital Association and Rancho Santa Fe Foundation, and former chairman of the Sharp

HealthCare Foundation and the San Diego Museum of Natural History.

**Peter K. Ellsworth**, San Diego, California, is president of The Legler Benbough Foundation. A former attorney in private practice, he is the former president and chief executive officer of the San Diego Hospital Association, parent corporation of the Sharp HealthCare system.

**Bryce W. Rhodes**, Del Mar, California, is vice president of Whittier Energy

Co., an oil and gas investment firm that is a subsidiary of the M.H. Whittier Corporation, chairman of the board of the Helen Woodward Animal Center, and director of The Whittier Institute for Diabetes.

**William R. Stensrud**, La Jolla, California, is general partner of the La Jolla-based venture capital firm of Enterprise Partners, director of several high technology companies, and incoming president of The San Diego Opera Association.



### NEXT ISSUE:

#### NOMAD: "It just keeps on thinking..."

It may look like a robot, but NOMAD is a far more sophisticated creation of The Neurosciences Institute. NOMAD has the ability to interact with its environment, actually shaping its behavior on what it learns. In the summer issue of *Brain Matters*, see how NOMAD is providing researchers a unique window into how the human brain may work.

### LEAVE IT TO A BRAIN SCIENTIST TO HELP DOUBLE YOUR MONEY!

Every resident of San Diego County who makes a first-time gift of \$100 or more to The Neurosciences Institute will trigger an additional gift of the same amount to the Institute.

The Legler Benbough Foundation has pledged up to \$50,000 as a challenge grant. To receive these matching funds, the Institute invites San Diegans to make a gift of \$100, \$500, \$1,000 or more. Our foundation benefactor will match all gifts from first-time donors, with a limit of \$1,000 per donor.

Use the return envelope provided to make your gift. And gifts of appreciated stock or other property also qualify for a match!

If you have any questions, please contact David Mitchell at (858) 626-2020 (phone), (858) 626-2013 (fax), [mitchell@nsi.edu](mailto:mitchell@nsi.edu) (e-mail), or visit our website at [www.nsi.edu](http://www.nsi.edu).

  
**THE  
NEUROSCIENCES  
INSTITUTE**  
 10640 John Jay Hopkins Drive  
 San Diego, California 92121

# BRAIN MATTERS

PRSRT STD  
 US Postage  
**PAID**  
 Permit No. 751  
 San Diego, CA

ADDRESS SERVICE REQUESTED