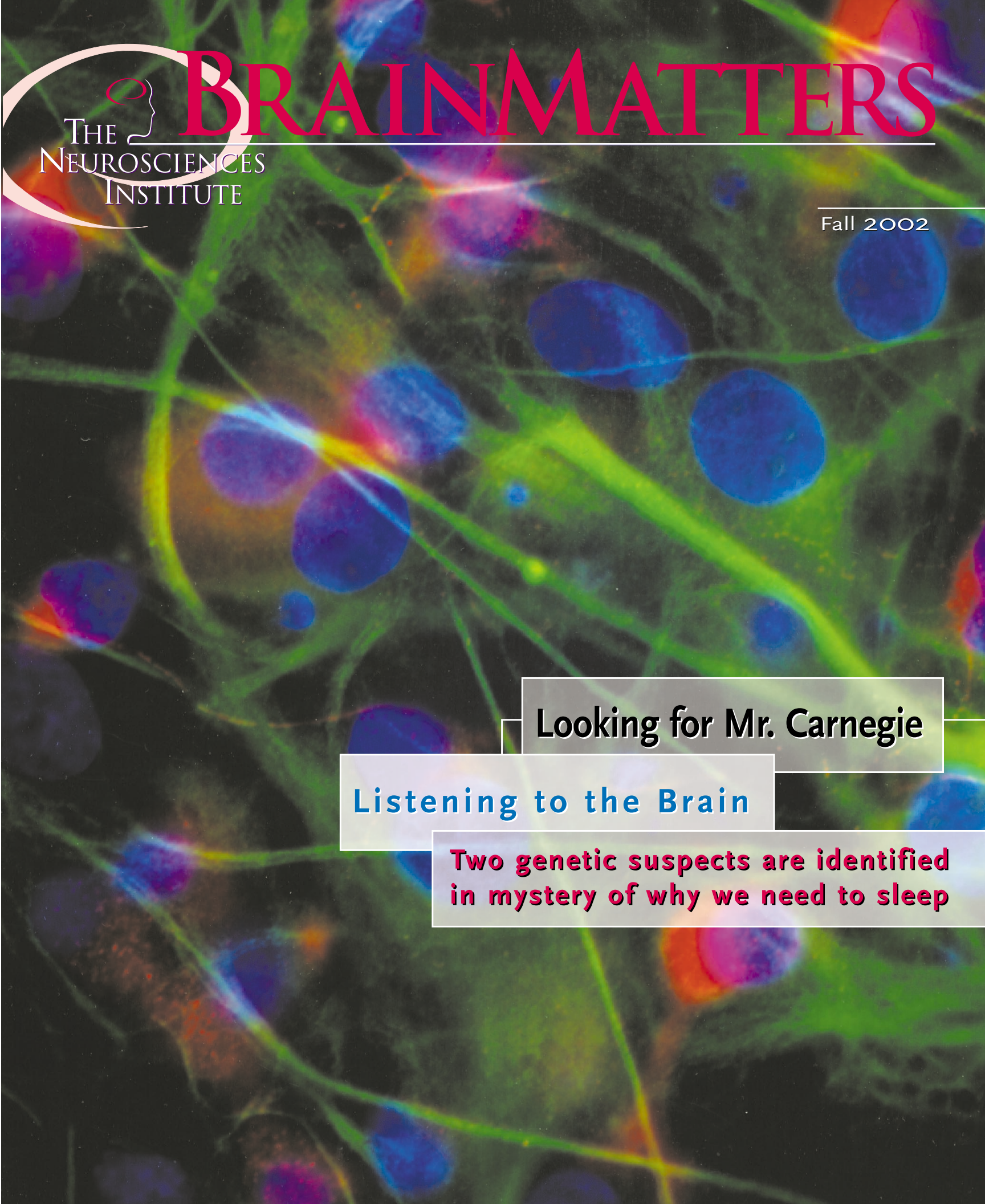
The Neurosciences Institute

BrainMatters

Fall 2002



Looking for Mr. Carnegie

Listening to the Brain

Two genetic suspects are identified in mystery of why we need to sleep

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THE NEUROSCIENCES INSTITUTE

A Message from the **Founder and Director**

One of the outstanding questions in neuroscience has been to determine how the structure of the brain is related to its specific functions such as seeing, hearing, touching, and moving.

Early studies in the 19th century by Broca and Wernicke showed that damage to particular regions of the cerebral cortex led to specific defects in speech known as aphasias. To the present day, there is increasing evidence that different parts of the brain carry out different specific functions.

In the visual system, for example, there are regions of the cortex that are functionally segregated – some for color, some for motion of objects, some for orientation. The same is true for regions of the brain responsible for initiating motion. The development of modern techniques for examining the microscopic anatomy of the brain and for measuring the activity of single nerve cells has fortified the conclusion that local brain regions have quite specific functions.

These observations have led to the view of the brain as a collection of functionally specialized modules. While not sharing the obviously false faculty psychology of Franz Joseph Gall, the 19th century founder of phrenology who assigned various higher order functions to regions and bumps in the skull, the idea of modularity or localization of function as a sufficient basis for how the brain works persists to this day.

Nonetheless, there remains another view which also arose in the 19th century – that of holism. The idea behind this view is that the brain operates as a whole. Perhaps the most trenchant example of this position is provided by Karl Lashley, whose attempts in 1917 to study the memory patterns of rats in mazes failed to provide evidence for localization. While he accepted some degree of localization, he argued for the notions of mass action and "equipotentiality" – the capacity of any intact part of a functional area to carry out functions lost by destruction of other areas or parts of the same area.

The argument between localizationalist and holist views of brain function has waxed and waned ever since the early days. Recently, however, new views championed at The Neurosciences Institute have revealed the entire question to be ill-posed. For example, much evidence has accumulated to support the notion that the brain is a selectional system which is highly plastic.

This view, called neural Darwinism, suggests that groups of neurons can compete for function to some degree while connecting to distant groups to allow integration of brain functions in both time and space. To some extent, damage to a functionally segregated area of the cortex can be compensated for. Yet there is no doubt that functional segregation is a feature of cortical and subcortical areas.

Out of this view has emerged the notion of the brain as a complex system. A complex system is one in which smaller parts form a heterogeneous set of components which are more or less independent. But as these parts connect with each other in larger and larger aggregates, their functions tend to become integrated, yielding new functions that depend on such higher order integration. This is, in fact, just what happens in the brain.

As has often been the case in other scientific controversies, adoption of a new view removes the occasion for argument between proponents of modularity and proponents of mass action. But it also sets the stage for a whole new set of questions. Which parts are integrated with other parts to yield a pattern of response or a complex behavior? And how can we see the action both of the parts and of the whole in time and space?

Much has been revealed concerning such questions by modern techniques that can image the living brain during performance of particular tasks. These techniques, including fMRI, which correlates neuronal activity and blood flow to localize active areas, and magnetoencephalography, which can measure the responses of neurons in very small intervals of time, have given support to the idea of the integration of functionally segregated neural regions.

Still, for ultimate precision, the tools of scientists known as systems neurophysiologists cannot be beaten. The measurement in exquisite detail of the activity of single neurons by implanted electrodes in a behaving animal is an essential tool in exploring brain function. In general, relatively few neurons in only a few areas of the brain can be recorded at the same time. Recently, however, improvements in technique and the new views of brain function have come together to allow a tour de force – the simultaneous recording of detailed neural activity of many neurons in multiple brain areas during an animal's learning and behavior.

This is the approach taken by the researchers at The Neurosciences Institute that is described in this issue. Success in their studies will further refine our ideas about how the brain works. In addition, their results will give us new ways to attack brain defects arising from trauma and disease. Such attacks will allow us to exploit the plasticity of the brain to compensate for or avoid the deficits that have so crippling an effect on patients with strokes, Parkinson's disease, and other disorders.

The ability of researchers at the Institute to form interactive groups across many specialties in a free and rapid fashion makes success in these exciting explorations highly likely. Indeed, in a certain way, their social interactions as specialists interacting closely resemble the neural interactions of the brains they are studying.

Gerald M. Edelman, M.D., Ph.D.

Listening to the brain

A multiple-region recording of neuronal activity provides a unique picture of brain function

"I think we may see a day in which a patient who has experienced a major loss in function in one part of his brain may be able to restore it by shifting that function to another region."

Douglas A. Nitz, Ph.D.
Associate Fellow in
Experimental Neurobiology

On the surface, it looks like the simplest of experiments: a white rat races through a maze and receives a food pellet for successfully completing the task.

Yet it takes only a few minutes observing and talking to the young scientist conducting the study to realize that what is occurring in this lab at The Neurosciences Institute is far from uncomplicated.

In fact, it is one of the more sophisticated studies ever conducted in brain research. The information gained from this investigation could significantly expand our knowledge of how humans learn and remember. It could also give us new tools to understand and potentially address Alzheimer's, Parkinson's, strokes, and other devastating brain disorders.

A closer look at the experiment itself reveals why this is such a unique endeavor. The lead researcher, Associate Fellow Douglas A. Nitz, Ph.D., has attached an array of electrodes to the rat that enables him to simultaneously record single neuron activity in three separate regions of the animal's brain as it learns to navigate through the maze.

Data pour in from the rat's cerebellum, the portion of the brain that helps coordinate movement and balance; from the frontal cortex, which is involved in planning and problem-solving; and from the hippocampus, which is involved in helping the rat remember what it has learned.

This investigation... could also give us new tools to understand and potentially address Alzheimer's, Parkinson's, strokes and other devastating brain disorders.

"This is one of the first times that anyone has attempted simultaneous, multiple-region recording in the brain," Nitz says. "It allows us to observe not only the specific contributions each brain region makes in the execution of a task, but also how various brain regions interact with and influence each other."

Recording when and where the brain cells discharge during the rat's trip through the maze is Nitz's key measurement.

"It turns out that the neurons from each of the regions fire rhythmically at slightly different rates," Nitz says. "One may fire every 30 milliseconds, another every 125 milliseconds, and another every 500."

Nitz can actually amplify the neuronal cell activity and play it through a speaker in the lab as he observes the rat.

"I listen to the brain keeping time, one or two cells at a time. Just by listening to the tones, I can often tell exactly where the rat is in the maze, which way its head is turned, and how fast it is going."

Nitz believes his research will show that patients with brain disorders such as Parkinson's have probably experienced a severe disruption in the mechanism that controls the timing of when their brain cells fire.

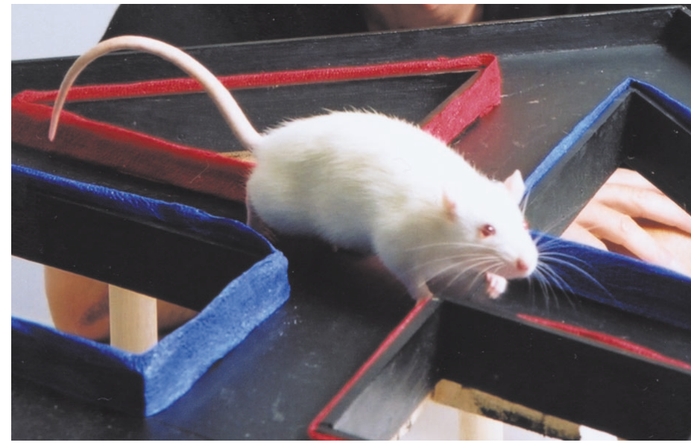
"This is also seen in people who have a lesion in their cerebellum. If they were to try to throw a ball, they might get the overall arm motion correct but release the ball too late or too early because their timing would be off."

Studying multiple regions at the same time has also revealed a phenomenon that might someday help people with other types of motor problems and possibly disorders associated with memory loss.

"One of the other exciting things we've learned is that there appears to be some overlap in function among the brain's regions," Nitz says. "As important as the overlap of function is the shared time base common to most, if not all, brain regions."

The application stage for Nitz's work is well into the future. For now, he is content with carrying out the task of methodically mapping a kind of brain activity that has up until now been uncharted territory.

"I think we may see a day in which a patient who has experienced a major loss in function in one part of his brain may be able to restore it by shifting that function to another region. Our main job right now is to make sure we understand the basic mechanisms of how the brain operates on a multiple-region level,"



Nitz says. "This basic research is crucial to any future applications. It's much easier to fix something that's broken once you know how it's supposed to work in the first place."

Douglas A. **Nitz**

Birthplace:
Grand Rapids, Michigan, 1965

Education:
B.A., University of Cincinnati, 1987
Ph.D., University of California, Los Angeles, 1995

Hobbies:
First and foremost, surfing. I especially enjoy it before sunrise when the waves are cleanest and it's still a little foggy. A morning golf run at Torrey Pines can be the same way sometimes. I manage to attend a rather wide variety of concerts and I very much enjoy watching the National Hockey League on television.

Why are you interested in studying the brain?

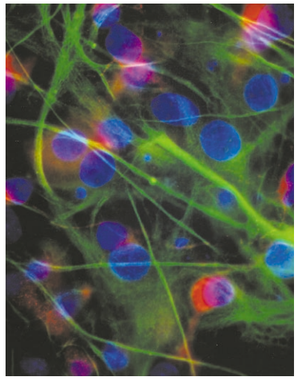
It's really hard to pinpoint, but my interest level shot up with my first exposure to neuroscience in an undergraduate physiological psychology course, and it hasn't flagged since. I enjoy the opportunity to delve into aspects of brain function that haven't yet been considered. My graduate school training in sleep research stoked my interest in understanding how different brain regions interact across time.

What are you researching at The Neurosciences Institute?

Systems neuroscience. We record single neuron activity in several brain regions as animals learn and perform various tasks such as navigation through a maze. Each task allows us to examine the contributions from different brain regions to execution of the task. We also seek to determine which changes to the structure of brain activity underlie learning. Specifically, we are interested in uncovering the time base(s) used to integrate neuronal activity within and across brain regions.

What do you hope to achieve at The Neurosciences Institute?

The timing of neuronal activity is remarkably precise over both short and long time scales. Despite this precision, the timing of neuronal activity can be regular (like the beat of a metronome) or irregular (like the beat of a jazz drummer) and often changes flexibly to meet task demands. Such time bases underlie coordination of our every act or experience. Their disruption is a feature of several neurological disorders. My hope is to understand the fundamental 'rules' of timing for neuronal activity.



On the cover

There is an elegant beauty to the microscopic photo of brain cells isolated from the hippocampus of embryonic rats. The cover photograph was taken by Postdoctoral Fellow Edward W. Keefer, Ph.D., (with a Leica inverted microscope) as part of a study demonstrating that a population of neural stem cells – with appropriate culture techniques – can be induced to form networks of neurons and glia that behave like cells in human brains.

The brain's innate motion building blocks provide a critical head start in motor skill development

A number of recent studies of motor learning have lent support to the idea that human beings learn motor skills by relying on an internal vocabulary of movement building blocks that enable them to quickly master different movements.

How important is this built-in vocabulary of movement building blocks? Without it, learning even simple motor skills would take weeks, months, even years. For example, in the simplest case where a muscle is either contracted or relaxed, there are 2^{600} possible motor activation patterns (600 muscles in the body), more than the number of atoms in the known universe. With the building blocks that effectively reduce the number of possible motor patterns, a toddler can quickly learn to walk, a Sunday hacker can improve one's golf swing, a teenage girl can learn to play field hockey, and a senior citizen can learn to dance.

This fascinating picture of how the brain interacts with the musculoskeletal system to develop motor skills is also emerging from research conducted by Postdoctoral Fellow William J. Kargo, Ph.D., and Associate Fellow Douglas A. Nitz, Ph.D.

"When we decided to investigate this exciting area of brain function, we suspected there had to be some underlying system either innately specified or learned through development, which provides a tremendous boost in learning new motor skills," Kargo says. "Otherwise, even something as seemingly simple as picking up a coffee cup and taking a drink would overwhelm our ability to learn, as it involves the activation of more than 40 arm and hand muscles."

Kargo and his team discovered evidence for such building blocks when they measured the brain and muscle activity of rats that were given a fairly complex and novel motor task. They showed that even the earliest motor activation patterns for the skill could be described as the sequential combination of a small number of muscle groupings or building blocks. Improvement in or mastery of the skill (from 20% to 80% success rates) resulted not only from fine-tuning the timing and magnitude of the pre-specified building blocks, but also from assembling new muscle groupings that were subsequently stored in the brain for use in learning other skills.

"We've learned that you don't have to construct a motor skill from scratch. We can essentially 'borrow' building blocks that are already stored in the brain to attempt the novel skill. Then, with practice, we can fine tune the building blocks and the way in which they are combined," said Kargo.

Postdoctoral Fellow William J. Kargo, Ph.D., logs data from a bank of computers that tracks brain and muscle activity in rats.

Although the research is in its early stages, Kargo does envision important applications in the future. For example, it could eventually help victims of stroke – where areas of the brain that store motor activation patterns or the building blocks have been damaged – to re-learn motor skills they have lost.

"Another exciting and promising application – one that isn't too far down the road – will be in the field of neural prosthetics. A person will be able to use one's own brain cells to transmit signals electronically, controlling motor activation patterns for an artificial limb in a manner similar to the real limb."

Looking for **Mr. Carnegie**

What's in a name? The Rockefeller University in New York City. Jules Stein Eye Institute at UCLA. Dana-Farber Cancer Institute in Boston. Scripps Institution of Oceanography at UCSD. Beckman Institutes at Caltech, City of Hope, Illinois, UC-Irvine, and Stanford. Scripps Green Hospital. Norris Cancer Center and Keck School of Medicine at USC. Packard Children's Hospital at Stanford.

These are some of the nation's leading medical and scientific institutions that have become virtual household words across the country. All have been blessed with magnificent donations from major benefactors. And few would argue with the conclusion that the prominent association of the benefactor's name – apart from major funds contributed – helped each institution to achieve international distinction.

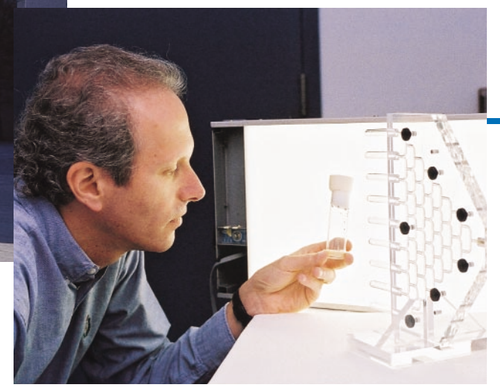
But what about those biomedical centers not yet named for a major philanthropist or prominent public figure? The Neurosciences Institute in La Jolla, California, is such an organization. And it is now eager to find a benefactor willing to provide funding at a level sufficient for the Institute to bear the donor's name on a permanent basis.

"The Neurosciences Institute represents an extraordinary investment opportunity for someone interested in promoting breakthrough discoveries involving the human brain and nervous system. We're looking for a special someone who values the critical role of basic research in modern civilization. History has shown that basic research is the critical foundation for most major medical advances such as open heart surgery and antibiotics, not to mention countless inventions like Teflon®, GORE-TEX®, transistors, and synthetic fabric, which we all take for granted," explains David Mitchell, Institute Relations Director at The Neurosciences Institute. "The funds we're seeking via a naming gift will give our scientists greater freedom to pursue their work without having to write frequent grant requests and fill out reports – something that diverts enormous time and energy away from their research pursuits. But just as important is that a naming gift will give the Institute a distinctive identity that our work merits."

The non-profit Institute, originally located in midtown Manhattan in New York City, selected the vibrant coastal research center of La Jolla over Princeton, New Jersey, Berkeley, California, and Cambridge, Massachusetts as its new hometown when it relocated to San Diego in 1993. Under the leadership of its founder and director, Nobel Laureate Gerald M. Edelman, M.D., Ph.D., the Institute occupies a stunning modern facility whose award-winning design has made it, along with its older neighbor The Salk Institute, one of San Diego's most popular destinations for fans of great architecture.

> "We're looking for a special someone who values the critical role of basic research in modern civilization. History has shown that basic research is the critical foundation for most major medical advances such as open heart surgery and antibiotics, not to mention countless inventions like Teflon®, GORE-TEX®, transistors, and synthetic fabric, which we all take for granted."
>
> David L. Mitchell
> Director, Institute Relations

Since it was established in 1981, The Neurosciences Institute has received worldwide recognition for its many noteworthy discoveries involving the human brain. It also is the home and sponsor of one of the world's most distinguished academies of brain scientists, the Neurosciences Research Program. But despite its stellar reputation in research circles, the Institute lacks a name that differentiates it from dozens of other brain research centers throughout North America. Says Mitchell, "The Neurosciences Institute is a pretty special place. Most biomedical research centers are large and divided into lots of departments filled with specialists who may or may not have much contact with one another. These centers are funded largely by short-term grants from the federal government, primarily to look at specific medical problems."



"In vivid contrast, we are intentionally quite small, relatively speaking – no more than 40 resident scientists at any given time. We rely primarily on private support as the best means to encourage major breakthroughs without having to deal with cumbersome bureaucratic policies and procedures that typically accompany government grants. Our scientists work closely as an interdisciplinary group, with no artificial divisions to separate them. We don't investigate particular diseases or disorders; that type of research is already well covered in medical schools and other biomedical centers. Instead, we're dedicated to understanding how the human brain works at a fundamental level. This requires research initiatives that take place over an extended period – as long as 10 years or more. We believe that this long-range approach is critical to opening the door to curing or preventing such tragic diseases as Alzheimer's, Parkinson's, autism, dyslexia, depression, addiction, schizophrenia, and countless other problems that afflict millions of people."

Continues Mitchell, "Put another way, could Albert Einstein have obtained a government grant to develop his revolutionary theories? Or could Einstein have made his discoveries today while funded by a government grant? I sincerely doubt it."

The Neurosciences Institute is currently searching for someone to personalize the Institute's name, as part of a long-term effort to raise funds in support of its unique research agenda. The qualifications for the privilege of naming the Institute are twofold. First, one should be committed to the Institute's unique organizational structure and mode of operation. Second, one will be asked to underwrite approximately half of the Institute's research budget of $6.5 million per year for an extended period – or, to provide a permanent endowment fund of $50 million or more.

The Neurosciences Institute is currently searching for someone to personalize the Institute's name, as part of a long-term effort to raise funds in support of its unique research agenda.

What has the Institute done to deserve a donation large enough to permanently rename it?

Since moving to La Jolla in the mid-1990s, The Neurosciences Institute has announced major discoveries at a rate exceeding many other better known brain research centers:

- Its work in understanding the basis of consciousness – and the unknown role of sleep in human life – is pioneering.
- It has developed the world's most sophisticated robot-like machines controlled by realistic central nervous systems and capable of learning through experience. These advanced brain-based devices are being used to investigate how brain activity gives rise to behavior and learning processes.
- Of keen interest to those with spinal cord injuries, it has developed the principles underlying some of the most advanced prototypes of prosthetic devices that are 'wired' into the brain. This work may ultimately help amputees and paraplegics live more normal lives.
- It is widely regarded for its work in understanding the role of genes versus environment in determining behavior.
- For those interested in the so-called "Mozart Effect," the Institute's work involving music and the human brain is revealing the importance of music in speech development and recognition. These findings may lead to a better understanding of the neural basis of disorders such as autism and certain types of dyslexia.

How have the Institute's efforts to obtain a naming gift progressed thus far?

Says Mitchell, "We've talked to a good number of individuals and private foundations about the possibility of a major funding relationship with the Institute. In many instances, we've found that we're competing with the lure of the leading research universities, teaching hospitals, or established cultural organizations where strong ties already exist. In several cases, the stock market decline has impeded their ability to make any large charitable commitments for the time being. Most often, we have simply not had sufficient time to develop the kind of deep relationship that typically precedes a substantial donation.

"All this is perfectly understandable. However, I believe firmly that we'll ultimately succeed in our quest, since there are people out there who will identify with our distinctive values and our special approach to science. Twenty-five years from now, I expect to look back on this quest for a naming gift as a turning point in conquering one or more of the major disorders that affect our brain. Which disease? It's impossible to predict. But whichever one it might be, just think of the countless lives that will be saved as a result of one benefactor's vision and generosity!"

Nameless in San Diego? For now, maybe. But hopefully not for that much longer.

Two genetic suspects

are identified in mystery of why we need to sleep

Like sleuths in an endlessly complex Agatha Christie novel, scientists at The Neurosciences Institute have been trying to solve the mystery of why we need to sleep. Now, following a two-year investigation, they have identified two genetic suspects that may one day make it possible to prevent the consequences of sleep deprivation.

The work presented in a recent issue of *Nature*, a leading scientific journal, built upon their previous research which had shown that sleep in the fruit fly is eerily similar to mammalian sleep, right down to the level of which genes are activated. Now they have demonstrated that flies, like mammals, will die if they don't sleep.

"The significance of the study is that sleep is an important part of life and that without it you will die," says lead project scientist Paul J. Shaw, Ph.D., Associate Fellow. "Sleep is so important that it has survived throughout evolution, even though it is a costly behavior. While animals sleep, they can't forage for food, take care of their young or engage in any number of other vital biological activities."

In addition to finding that sleep is vitally important in the fruit fly, the investigators identified two genes that play such an important role in sleep function that flies will die after only a few hours of sleep deprivation when these genes are eliminated or reduced. Although the genes were identified in the fruit fly, both genes have counterparts in human beings.

One of the genes has previously been shown to play an important role controlling our internal clock. Among other things, the clock sends out signals that tell us when it is time to wake up and when it is time to go to sleep.

"For many years, most scientists have believed that the sleep and clock mechanisms were independent, although it was widely recognized that they could influence one another," Shaw says. "Our data suggest a much more intimate relationship."

The other gene they identified has been shown to play an important role in protecting the body against stress.

Associate Fellow Paul J. Shaw, Ph.D. (left), confers with Senior Research Technician Donald Robinson.

When the investigators applied stressors, such as heat or low oxygen and food levels, before they deprived the flies of sleep, the flies survived.

The findings now offer scientists a 'hook' to examine more advanced possibilities for sleep-related afflictions that affect humans. For example, their findings may suggest treatments and behavior modifications that eliminate or minimize the effects of night-shift work, sleeplessness and jet lag, to name a few.

The next research phase of Shaw and his colleagues, Ralph Greenspan and Donald Robinson, at The Neurosciences Institute, is to pin down the mechanisms by which these genes increase and/or protect against the lethal effects of sleep deprivation. Co-author of the paper, Giulio Tononi, formerly at the Institute, is now at the University of Wisconsin – Madison's Department of Psychiatry.

"The take-home message is that sleep serves a vital biological role, perhaps as important as eating," says Shaw. "Short-changing sleep in order to have more time available to accomplish other tasks is very dangerous and will ultimately fail. In other words, SLEEP!"

July 11, 2002 Library Roundtable:

"The Cosmos and the Brain: Exploring our Final Frontiers" by Daniel S. Goldin

Dan Goldin with Institute Founder and Director Gerald Edelman

From left, Sylvia Kane, Hyman Gaylis, and Rhoda Gaylis

Dan Goldin addresses a crowd of 350 in the auditorium.

Daniel S. Goldin, immediate past Administrator of NASA and a Visiting Fellow at The Neurosciences Institute, gave a fascinating glimpse of uncharted territory with his presentation, "The Cosmos and the Brain: Exploring our Final Frontiers." Goldin proposed the idea that there are two exciting destinations humankind has not yet conquered: understanding the origins of the universe and understanding how the brain works. Says Goldin, "Who among us has not stared up at the night sky and wondered 'Are we alone? And where did we come from?' We also don't understand fully how our brain works and how it interconnects with our body, our environment and our life experiences. The next quarter century promises revolutionary scientific and technical progress in answering these questions. Research on the human brain may even complement our efforts to unlock the door to the heavens."

Institute Relations Director Dave Mitchell, Mary Carrington, and Richard Hill

Donna Knierim, Tom Durler, and Berit Durler

Dan Goldin, Elaine Galinson, Larry Sherman, and Murray Galison

September 17, 2002 Library Roundtable:

"Eyes Believe What They See; Ears Believe Others" by Paul J. Orfalea

Paul J. Orfalea, Founder and Chairperson Emeritus of Kinko's, Inc., provided Library Roundtable guests with an inspirational look at how he overcame dyslexia and relied on creativity and thinking 'outside the box' to develop the 1,100-outlet Kinko's copying chain into one of the world's most successful business services companies. Today, Orfalea is involved in a number of philanthropic and community pursuits, including teaching and an effort to improve education.

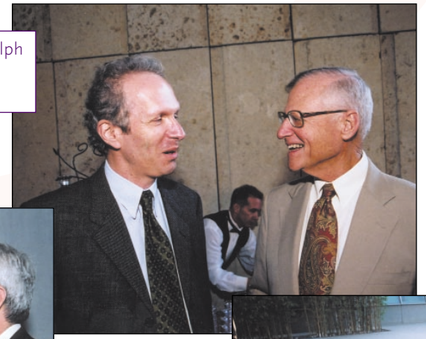
"Schools have gotten anal. They're obsessed with testing," Orfalea said. "We want kids to learn the alphabet in the womb. We're taking away so much imagination from our children. Let them play. Let's get some art out there in the schools, some music. This is the only time in their life they can use their imagination."

Paul Orfalea describes how he founded Kinko's near the UC – Santa Barbara campus in 1970

Reinette Levine, Linda Satz, Institute Trustee Joseph Satz and Marvin Levine

Roundtable guests at the cocktail reception following Paul Orfalea's address

Kathleen Bell Flynn and Steve Flynn



Cullman Senior Fellow Ralph Greenspan with Institute Trustee Peter Elllsworth

Institute Trustee Martin Dickinson, Carol Dickinson, and Dan Goldin, who delivered the previous Roundtable talk on July 11

Roundtable guests at the cocktail reception following Paul Orfalea's address

Associate Fellow Niraj Desai (left), with Institute Trustee Leon Jaroff

From left, Walter and Judy Munk, Lucy and Jim Haugh

From left, Robert and Nina Noble, Jean Collins, and Institute Trustee Mila Collins

Jane and Tom Fetter

From left, Burnham Fellow Ani Patel, Institute Trustee Jinx Ecke and Bob McGivern

Sally Gall (left) with Institute Trustee Faye Wilson

Institute Trustee Ira Weinstein (left) with Board Chairman and Trustee Bill Walsh

Spring Governing Board Meeting

The Neurosciences Research Foundation, Inc. board meeting was held over the weekend of May 3-5 in La Jolla, as one of two major meetings the Institute's governing board holds each year. (The fall meeting was held November 15-17 in New York City.)

A special dinner was held on Saturday, May 4 in conjunction with the board meeting to which board members and all donors of $1,000 or more were invited. Before an *al fresco* dinner in the Auditorium's loggia, the 125 guests were treated to a private jazz concert in the Auditorium by the Holly Hofmann – Mike Wofford Quartet.

On both Saturday and Sunday mornings, trustees, spouses, and donors heard thirteen different presentations by Institute Fellows on a variety of topics. Examples of the talks included: "Why Sleep?" "The Situation with Stem Cells;" "Action and Interaction in the Brain;" "Networking the Genes;" and "How Does the Brain Work?"

Martin C. **Dickinson**

On May 4, 2002, the governing board of The Neurosciences Institute elected Martin C. Dickinson as a trustee of the Neurosciences Research Foundation, Inc. (NRF).

A San Diego native who was raised on the family ranch in Chula Vista until moving to La Jolla in 1943, Dickinson is actively involved in a variety of business and civic activities in San Diego and Oklahoma.

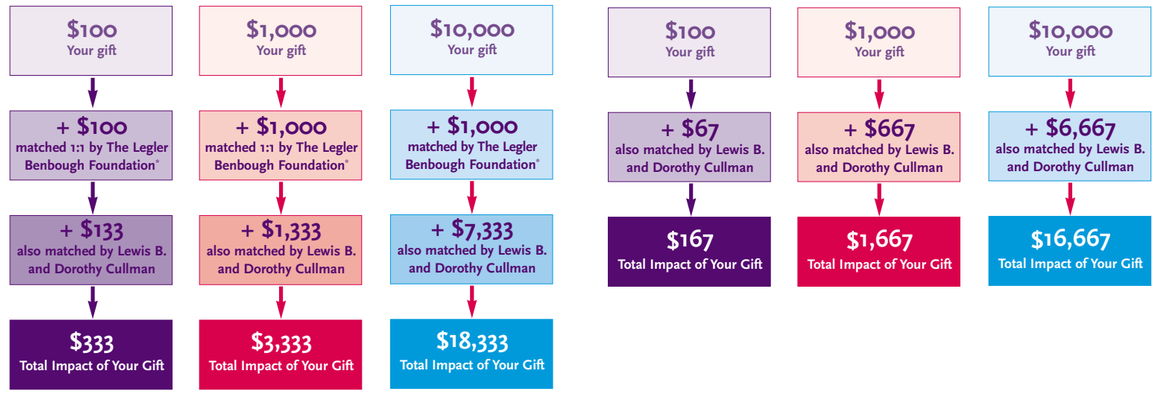
On the business front, Dickinson serves as director of Gaylord Entertainment Company (NYSE), Oklahoma Publishing Company, H.G. Fenton Company and Broadmoor Hotel Corporation. He is currently vice chairman of Legacy Bank and previously was a director and senior executive with Scripps Bank of La Jolla.

On the eleemosynary side, Dickinson is president of the Donald C. and Elizabeth Dickinson Foundation and the National Cowboy and Western Heritage Museum in Oklahoma City. He is also a director of the Rancho Santa Fe Foundation and is chairman of the Scripps Cancer Center Development Council. Previously, he chaired the Scripps Foundation for Medicine and Science and served as a trustee of the Mercy Hospital Foundation, ScrippsHealth, and the Kraemer Endowment Foundation. Dickinson also served as president of the San Diego Historical Society and as chairman of the San Diego Intermuseum Council.

A former officer in the U.S. Navy, Dickinson graduated from Pomona College (B.A.) and Stanford University (M.B.A.) before pursuing a career in banking with Security Pacific Bank and La Jolla Bank & Trust. He and his wife, Carol, reside in Rancho Santa Fe and have six children and seven grandchildren.

Cullman and Benbough **Challenges**

Leverage Your Gift to The Neurosciences Institute



* The Legler Benbough Foundation Challenge applies only to San Diego County residents, matching the first $1,000 of one's donations.

Progress Report: The Campaign for The Neurosciences Institute

In July 2000, the Institute's Board of Trustees approved a fundraising campaign to expand the family of contributors and to provide private funding necessary to carry out the Institute's research goals and objectives over the next several years. By December 31, 2005, the campaign will seek a minimum of $35 million from private sources, which can be used to underwrite the Institute's critical initiatives in brain research as well as its cultural and educational programs for the San Diego community. As of October 31, 2002, more than 300 individuals, foundations, and business firms had made gifts and pledges totaling $18,781,700 – representing 54% of the campaign goal.

In support of this fund raising effort, NRF Board chairman William D. Walsh, together with his wife, Jane, pledged $1 million to the campaign in May 2002, their second commitment of $1 million to this venture.

The Neurosciences Institute also seeks to enlarge its permanent endowment fund so that at least half of the Institute's annual operating budget can eventually be offset through income from the endowment. Though gifts for endowment are not officially part of the campaign, the Institute invites donations of gifts for endowment from interested parties. On pages 6-8 of *BrainMatters*, "Looking for Mr. Carnegie" describes an opportunity to rename The Neurosciences Institute in recognition of a contribution of $50 million toward the Institute's endowment.

Campaign Goal by December 31, 2005: $35,000,000

Gifts and Pledges as of October 31, 2002: $18,781,700

Asterisk (*) preceding donor's name denotes donor as a first-time contributor

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$2,000,000

William D. and Jane Walsh, Atherton, California

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$500,000 - $999,999

*Dr. David Clayson (dec.), New York, New York

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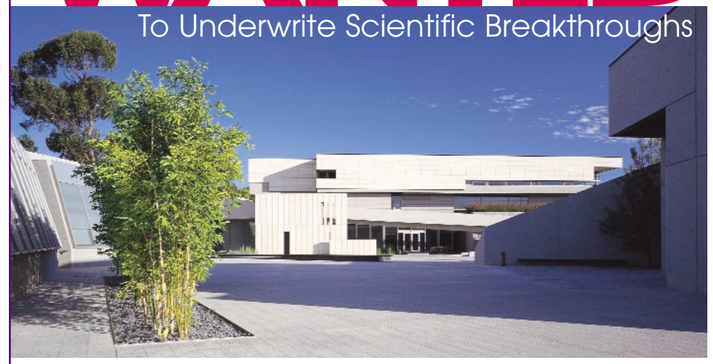

The Organization:

The Neurosciences Institute...

- internationally renowned for pioneering brain research to benefit humanity
- dedicated to major advances in understanding how the human brain works
- founded and directed by a Nobel Laureate in Medicine
- research campus in La Jolla, California has won numerous architectural awards
- funded entirely by private contributions
- independent, not-for-profit under IRS Sections 501(c)(3), 509(a)(1), and 170(b)(1)(A)(vi)

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The Opportunity:

The Neurosciences Institute invites charitable donations from those who seek ground-breaking discoveries in brain science. Areas of research currently underway include:

- **Consciousness and attention:** To understand the brain bases of what makes us human, and to enhance learning and memory
- **Sleep states:** To improve vigilance, well-being, and job performance
- **Motor-sensory coordination:** To develop innovative treatments for muscular and movement disorders
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Donations of **all** sizes will be matched 2:3 by another private source. A contribution of $50 million or more will entitle the donor to rename the Institute. Other prominent naming opportunities are available to recognize gifts of $10 million, $5 million, $2 million, and $1 million.

Interested parties should contact:

David L. Mitchell
Director, Institute Relations
The Neurosciences Institute
10640 John Jay Hopkins Drive
San Diego, CA 92121
Tel: (858) 626-2020
Fax: (858) 626-2013
Email: mitchell@nsi.edu

A MOST **Distinctive** VISITOR

Many visitors to The Neurosciences Institute come to appreciate the architecture at close hand. This visitor, *Buteo jamaicensis calurus* (red-tailed hawk), also enjoyed a brief dip in the local "spa." The hillside by the auditorium, and other landscaped areas, provide housing for voles and similar small rodents, which are a major food source for these raptors. The red-tail is widely distributed throughout North and Central America.

The Neurosciences Institute

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