Dear Friends and Colleagues:

I am pleased to announce that we recently changed our name to the Comprehensive Center on Brain Aging to reflect the extensive and broad-ranging scope of research and clinical programs being cohesively integrated within the auspices of our Center. Often, I’m asked what sets our Center apart from similar centers in the country. If I had to answer this question in one word, I would say, innovation. Quite honestly, I don’t believe a center exists that compares to ours when you take into account our areas of innovative leadership: world-class patient-focused care; more than 30 years of breakthrough research; and continued investment in education. The bottom line: we are innovators, creators, leaders of change.

What is innovation in research? To us, it means creativity, ingenuity, breakthroughs. It means shaking things up, upheaving the status quo, thinking of new measures, new methods, new ways of seeing things and being fearless in transforming the world I science as we know it. In many cases, innovation requires that we put aside what we think we know and start with a blank slate. We’re not here to tweak, adjust or refine. We believe in order to reach our goal — Alzheimer’s disease will be a treatable or preventable disease not to be feared as it is now — we have to discover new frontiers and forge unprecedented pathways to progress.

And so, this issue is dedicated to innovation. As you glance through the following pages, you’ll read about our clinical and research advances — a novel program focused on cognitive remediation and the sharpening of memory skills for those concerned about memory loss. You’ll also read about our multi-disciplinary and collaborative research focusing on the tau protein and its relationship and impact on AD. And in keeping with our theme, I think you’ll be enlightened by the work undertaken by a group of our researchers studying early behavioral detection of Alzheimer’s. Speaking of unconventional approaches, also included in this issue is a very special and touching story of hope that focuses on bringing together persons with dementia and their caregivers, uniting them in song. These are just a few of our newsworthy stories of innovation.

Like all research, the ultimate value lies in our potential to save lives and improve the quality of each life. For us, that’s life-changing innovation.

Warm regards,

Ralph A. Nixon, M.D., Ph.D.
Director, Comprehensive Center on Brain Aging

DONOR PROFILE

The Pearl I. Barlow Center for Memory Evaluation and Treatment Celebrates Important Milestone

Through the generosity of the late Pearl Ida Barlow, in May 2007, the Silberstein Alzheimer’s Institute at NYU Langone Medical Center inaugurated a formidable clinical operation, The Pearl I. Barlow Center for Memory Evaluation and Treatment. Today, the Barlow Center is recognized as New York City’s most comprehensive treatment center for memory disorders of all origins, providing patients the next generation of patient-focused medical care encompassing best practices in medicine, psychiatry and neurology.

As the Barlow Center celebrates its fifth anniversary, we spoke with Dr. Richard Amelar, Pearl Barlow’s nephew, to learn more about the Center’s founding and to gain insight into the life of Mrs. Barlow, her roots, and the woman she was.

EDITOR: The Barlow Center impacts the lives of many with dementia and NYU is grateful for your generous gift and honored by your investment. What can you share with our readers about your aunt and your family?

MRS. PEARL I. BARLOW: My aunt, Pearl, was my mother’s baby sister, born in Chicago in 1912. My mother, the oldest of eight, was born Theresa Edelman, in Hungary in 1897.

Continued on Page 5
Untangling the Role of Tau in Alzheimer’s Disease

One of the hallmarks of Alzheimer’s disease (AD) is the neurofibrillary tangle, a dense clump of proteins comprised mainly of an abnormally altered version of the tau protein. Growing in acceptance in the Alzheimer’s scientific community is the tau hypothesis, the idea that tau protein abnormalities initiate the disease cascade. Researchers at NYU’s Comprehensive Center on Brain Aging are collaborating in numerous ways and working on multiple fronts to untangle the enigma that tau poses in order to develop drugs and therapies that can stop or significantly delay the progression of Alzheimer’s by short-circuiting the way the disease forges forward.

Tau is a prime target for disease modifying therapies in AD. In the following few paragraphs, highlighted is the novel and diverse research on the tau protein led by four NYU research teams, representing a wide spectrum of approaches and in-depth studies — the most extensive and comprehensive of any medical institution in the country.

Tau normally plays a crucial role in maintaining the structural framework and transport system within nerve cells. While tau is modified by the attachment of phosphate molecules (a process called phosphorylation), excessive phosphorylation appears to contribute to tangle formation and prevents tau from carrying out its normal function. This results in a communication malfunction between neurons, leading to cell death. Studies have shown that the extent of tau phosphorylation is closely related to the severity of AD, thus suggesting that the ability to reduce the amounts of phosphorylated tau could be a therapeutic benefit.

One promising therapeutic strategy being developed by Einar M. Sigurdsson, Ph.D., Associate Professor, Departments of Physiology and Neuroscience and Psychiatry, focuses on a vaccine treatment targeting the neurofibrillary tangle. Harnessing the immune system to remove disease causing tau protein, an approach pioneered by Dr. Sigurdsson and his team, has recently become attractive as a potential therapy for Alzheimer’s disease and related tau diseases. Using newly developed antibodies that bind to abnormal tau and promote its elimination — in mice specially bred to produce abnormal tau — the researchers have been able to slow tau accumulation in these mouse brains and prevent memory decline. Dr. Sigurdsson explains, “clearing abnormal clumps of tau from brain cells is a promising therapeutic approach. Our findings indicate that immunotherapy targeting tau is very feasible for Alzheimer’s and related diseases, and will likely be assessed in clinical trials in the near future.” Studies pioneered by Dr. Sigurdsson’s lab have been confirmed by several other laboratories.

Another significant area of study led by Stephen D. Ginsberg, Ph.D., Associate Professor in the Departments of Psychiatry and Physiology and Neuroscience, takes a deeper look at the activity of genes related to tau function in the Alzheimer’s disease brain to gain insights into the still unknown molecular mechanisms underlying tauopathy. The researchers microdissected neurons either predisposed to developing tau tangles or relatively resistant to tangle formation. From the miniscule amounts of genetic material isolated from these neurons, the researchers applied a sophisticated method to measure the levels of RNA (similar to DNA) corresponding to individual genes in an array containing hundreds of genes potentially relevant to AD. Comparison of tau gene profiles dissected from neurons from individuals with either no memory impairment, mild cognitive impairment (suspected very mild AD), or AD, demonstrated that the gene expression patterns for different forms of tau abnormally shifted in neurons destined to develop tangles, but not in normally aging neurons. Such a shift could promote tangle formation. Further analyses in mice link tau anomalies to changes in genes regulating synapses — the connections critical for neuron-to-neuron communications that support memory formation. Connect- ing tau-related events to genes promoting synapse degeneration is a valuable step toward developing new therapeutic approaches for the disease.

Another promising area of tau study at NYU involves synaptic plasticity, which refers to molecular changes that synapses undergo in response to brain activity. The lab of Charles A. Hoeffer, Ph.D., Assistant Professor in the Department of Physiology and Neuroscience, in collaboration with the Sigurdsson lab, tested synaptic plasticity in mice carrying a human tau gene with a specific mutation found in individuals with an inherited dementia caused by tau. In the brains of these mice, the tau protein forms neurofibrillary tangles and is excessively phosphorylated. Surprisingly, the researchers found that these mice had increased synaptic plasticity in the hippocampus, an area within the brain that is crucial for memory formation. These observations suggest that the synapses were over-excited, which can be a basis for memory decline. Further work indicates that the problem may lie in the loss of a certain type of hippocampal neuron that normally inhibits the activity of other neurons. Such analyses will enable researchers and physicians to design more effective AD therapies that target precise cells or molecular lesions affected by tau mutations.

A fourth NYU research team focuses on the pathological actions of tau, using as a model the largest known synapse, which is found in squid. Studies by Professor Rodolfo R. Llinás, M.D., Ph.D., Thomas and Suzanne Murphy Professor of Neuroscience, and Professor Mutsuyuki Sugimori, M.D., Ph.D., both from the Department of Physiology and Neuroscience, in collaboration with Herman Moreno, M.D. from SUNY Downstate Medical Center reveal that when human tau (H-tau) is directly injected into the squid synapse, it becomes phosphorylated and remodeled, and rapidly blocks the ability of synapses to release chemicals essential for communication with neighboring neurons. The remodeled H-tau also forms filaments resembling the “straight filaments” of tau seen in AD and related conditions. Working with a Japanese pharmaceutical company, Dr. Llinás and colleagues have now identified a promising drug that blocks tau phosphorylation, inhibits the H-tau remodeling, and restores the ability of the synapse to release its chemical “communications.” The novel human tau remodeling demonstrated in Dr. Llinás’ research is an invaluable clue allowing the identification of additional therapeutic agents to treat and/or prevent tau-related neurofibrillary degeneration.

While more scientific study needs to be done, potential new treatment targets that can change the course of AD and its progression by slowing or preventing neuron death are in sight. “Our goal is to further develop these studies and move candidate therapies expeditiously into clinical trials. The hope is that more potent disease modifying treatments and prevention strategies based on tau modification will become available in the coming years,” noted Dr. Ralph A. Nixon, Director of the Comprehensive Center on Brain Aging.
Dr. Nixon Named as Alzheimer’s Association MSAC Chairman and Appointed to the Association’s National Board of Directors

Ralph A. Nixon, Ph.D., M.D., professor in the Departments of Psychiatry and Cell Biology, director of the NYU Comprehensive Center on Brain Aging and the Silberstein Alzheimer’s Institute has been named chair of the Alzheimer’s Association Medical and Scientific Advisory Council (MSAC) and has also been appointed to the Association’s national Board of Directors.

Dr. Nixon is director of Research and director of the Center for Dementia Research at the Nathan S. Kline Institute for Psychiatric Research. He has served, since 2008, as vice chair of the MSAC and is a founding member of the Alzheimer’s Association International Society to Advance Alzheimer’s Research and Treatment (ISTAART), a professional organization for individuals interested in Alzheimer’s and dementia science.

Alzheimer’s Association and private foundations, focuses on how proteases modify the function of proteins and eliminate damaged proteins from brain cells — a process that is disrupted in Alzheimer’s disease and a promising target of new therapies for the disease. His work has led to the recent discovery of how mutations in the presenilin 1 gene cause early-onset Alzheimer’s disease. Dr. Nixon has published more than 230 papers and sits on the editorial boards of six scientific journals.

Blas Frangione Young Investigator Merit Award

Recognizing the achievements of outstanding young investigators in the field of brain aging research, the inaugural 2012 Blas Frangione Young Investigator Merit Award was presented to Guang Yang, Ph.D., Assistant Professor, Department of Anesthesiology, NYU Langone. Dr. Yang received an unrestricted prize of $5,000 to be used for research purposes, and was given the honor of presenting her research at the Center’s annual Research Day in March. Her scientific study focuses on understanding the mechanism of synaptic loss and cognitive dysfunction in aging and neurodegenerative diseases. She has a broad background in neurobiology, with specific training and expertise in neuronal and glial structure imaging.

The Blas Frangione Young Investigator Merit Award was founded to recognize early career NYU scientists who show promise in the field as “out-of-the-box” thinkers. The Award provides support for the next generation of exceptionally visionary thinkers with “high-risk/high-reward” ideas that have the potential to significantly impact our understanding of and/or approaches to the prevention, diagnosis and treatment of Alzheimer’s, Parkinson’s or related neurodegenerative disease.

Did You Know?

A Mediterranean diet can lower your risk of Alzheimer’s by 40 percent?

A Mediterranean diet — rich in fruits, vegetables, olive oil, legumes, whole grains and fish — offers cardiovascular benefits and studies show that it may also benefit your brain by:

- Slowing cognitive decline in older adults
- Reducing the risk of mild cognitive impairment (MCI), a transitional stage between the cognitive decline of normal aging and the more serious memory problems caused by dementia or Alzheimer’s disease
- Reducing the risk of MCI progressing into Alzheimer’s disease

Source: Alzheimer’s Association, 2010 statistics
The Unforgettables: With a Song in Their Hearts, People With Dementia and Their Caregivers Join in Harmony

Dr. Mary Mittelman, director of the Psychosocial Research and Support Program at the Comprehensive Center on Brain Aging, believes that research may prove that music and social interaction can be of significant benefit to people suffering from dementia and their family members. With that in mind, she and her fellow colleagues have created a unique chorus in New York City, the first of its kind for people with dementia and their family members and friends. The chorus members named themselves The Unforgettables. “The pleasure this process has given participants was clear from the start,” said Dr. Mittelman, who has been conducting research at the NYU School of Medicine on how to help family caregivers of people with dementia for more than 25 years. “The chorus has proven to be a wonderful place to be, where no one feels stigmatized.” People with dementia and caregivers were initially recruited through outreach that involved a number of local organizations, including the New York City chapter of the Alzheimer’s Association and NYU support groups. Chorus members meet once a week to practice and are led by two conductor-directors. They’re taught standard techniques to enhance breathing, vocalization and performance, just like any other choir. The chorus rehearses for 13 weeks for a concert that features nearly 20 songs. To date, three public performances have been staged. The first concert included Fly Me to the Moon, Smile, and Besame Mucho. The second concert in December featured music appropriate to the holiday season; three participants with dementia sang solos. “There’s a certain camaraderie,” noted Howard Smith, a choral member who cares for his wife, Lois, diagnosed with Alzheimer’s about two years ago. “Lois is there with people with the same problems. And it’s comforting for her and the other patients, and even for the caregivers. Because it means we’re not alone.” Dr. Mittelman agrees, “That sense of inclusiveness is key.” “Too often,” she said, “caregivers are afraid to go to a normal event with a person with dementia. And so he ends up being discounted, or discounts himself, as people exclude him from social events and he has fewer and fewer activities to participate in and becomes more and more isolated.”

As Dr. Mittelman points out, “This is a pilot study. The goal of the Psychosocial Research and Support program is to see to what extent non-drug therapies can help people with dementia and their families. We know there is no cure for Alzheimer’s or dementia yet, but there is the potential to improve quality of life and the relationship between the person with dementia and the family caregiver,” both of which she is actively studying through the choral group. If successful, this novel program could be a prototype for others to emulate, and it could be a great source of enjoyment and connection for participants. Dr. Mittelman and colleagues expect it will help participants continue to partake of other activities together and improve their moods and relationships. The choral program was designed to ensure a high quality and rewarding experience for the singers as well as provide a structure that maximizes the synergy and skills of the leaders. The goal is also to enrich and educate the wider community through the concerts and be a model for replication in other communities.

The working group, dedicated to the investigation of music as a therapeutic activity for people with dementia and their family members includes: Mary Mittelman, Dr. PH, NYU Langone Medical Center; Cynthia Epstein Smith, LCSW, NYU Langone Medical Center; Jan Maier, RN, MPH, Research Triangle Institute; Concetta Tomaino, DA, Institute for Music and Neurologic Function; and Kendra Ray, M.A., Metropolitan Jewish Health Care.

New Specialty Program for Sharpening Memory

Dr. Stella Karantzoulis

Program led by Stella Karantzoulis, Ph.D., Assistant Professor of Neurology, Clinical Neuropsychologist and Associate Director of the Barlow Center. This program is designed for those individuals with concerns that their memory is not as sharp as it once was and for those with mild cognitive impairments. “The primary goal of these sessions is to identify strengths and weaknesses with memory, and implement interventions to enable each patient to reach his/her highest potential,” said Dr. Karantzoulis, who teaches various memory strategies to help individuals compensate for their memory weaknesses, as well as educates people on the importance of lifestyle factors (e.g., diet, sleep, exercise) on cognitive function. While memory decline is often the most common focus, she also uses coaching strategies to improve other neuro-cognitive abilities such as attention, working memory, cognitive flexibility and planning.

She explains, “Our patient-tailored approach includes didactic, pencil-and-paper and computer tasks mainly in a group format.” The main objective is to provide individuals with lifetime skills and strategies, and help
The Pearl I. Barlow Center for Memory Evaluation and Treatment Celebrates Important Milestone

Continued from Page 1

She came with her family to Chicago in 1906. My mother’s first job after high school was as a secretary to the man who later became my father, Joseph Amelar. He worked for the Armour Meat Packing Company’s export division. They married in 1917 when Pearl was only five years old. My mother and father then moved to New York where there were better opportunities in the exporting business, I, their only child, was born in the Bronx in 1927.

Pearl, as a young unmarried woman in Chicago, suffered from fibroid tumors. She’d had a hysterectomy to remove them, and therefore never had any children. Starting out, she worked as a secretary to Louis Greenberg, a brewhery owner. After she had worked for him for 20 years, and his wife had died, he married Pearl. Unfortunately, soon after, he passed away.

So, Pearl left Chicago and went to Florida. There, she bought a hotel resort in Hollywood. She married her manager Al Barlow. He, too, soon died. She sold the hotel resort and then owned and ran restaurants in Palm Beach. Living “at home” until she married, a large part of the responsibility of caring for her aging parents fell on Pearl. Therefore, she wanted her money, after she died, to help the elderly with medical problems. She entrusted her bequest to my discretion. I was the first born of her nieces and nephews. I was the son she never had. And, she was the big sister I never had.

Why did you decide to direct your gift towards dementia and Alzheimer’s disease care?

It was Pearl’s wish that her money be directed to benefit the elderly and aging sick. That was very important to her. She left her estate in my hands and in keeping with her wishes, I felt strongly about directing my gift to dementia care and to NYU.

So, Mrs. Barlow did not have Alzheimer’s?

That is correct. The decision was based mostly on her wishes to help people combined with my loyalty towards NYU.

Why NYU?

It was my way of “giving back.” I went to NYU for my medical schooling, graduated in 1950 and continued at NYU in the Department of Urology under the mentorship of Dr. Robert Hotchkiss, who was then the Chief of Urology. I trained under him and continued my professional career at NYU becoming a male infertility specialist. It was through Dr. Hotchkiss that I got my start in the field, and male infertility became my life’s work… my life’s journey. I feel very indebted to Dr. Hotchkiss and to NYU and this was an opportunity for me to show my appreciation to the school that helped me gain success and happiness in life.

What inspired you to establish a dedicated dementia center?

After my aunt passed away, I remember meeting with NYU’s Office of Development and they mentioned to me a very active research program on dementia and Alzheimer’s. I was interested in what they had to say. They then introduced me to Dr. Ralph Nixon, Director of the Silberstein Alzheimer’s Institute. I met with Dr. Nixon and was immediately impressed with him and his plans to establish a new clinical care facility. More importantly, in that initial meeting, one thing stood out about Dr. Nixon … he cared deeply and genuinely, had compassion and was strongly committed to the Silberstein Institute. I knew then that we wanted to move forward and be a part of his plan. The Silberstein Institute had decades of pioneering research behind it, but no organized patient care program associated with it at that time. Therefore, this made perfect sense.

How did the opening of the Barlow Center impact the work that was being done on Alzheimer’s research at NYU?

The Silberstein Alzheimer’s Institute had always been at the forefront of research advances in the dementia field — from advancing the scientific community’s understanding of the genetic and molecular structure of the disease to developing state-of-the-art brain imaging and clinical assessment techniques. Their investigators continue to be top-ranked in the areas of clinical treatment, early diagnosis, genetic and molecular causes and drug discovery. In 2007, in order to bring research advances directly to the patient, with Barlow funding, the Silberstein Institute inaugurated the Pearl I. Barlow Center providing clinical care of memory impairment and age-related brain disorders.

The Center’s innovative Cognitive Remediation Program is effective at treating individuals who want to improve:

- Thinking
- Social Skills
- Memory
- Relationships
- Concentration
- Quality of Life
- Everyday Tasks

The Pearl I. Barlow Center for Memory Evaluation and Treatment Celebrates Important Milestone

How do you feel now about your gift and your decision?

I’m extremely proud of what the Barlow Center is doing and what the researchers and clinicians are working on and accomplishing at the Center. Under Dr. Nixon’s leadership, I feel confident that we gave our gift to the best possible institution. He is committed to increasing the public’s awareness of the disease; further expanding the Center’s research and clinical capabilities; as well as strengthening caregiver support programs. In some small way, I hope my aunt’s gift will help shape this mission.

Alzheimer’s is a devastating disease — for those that suffer from it and those that suffer alongside. I’m sure my aunt would also be pleased that her monies are being used for such a worthwhile cause.

For our readers, many of whom are Barlow patients or caregivers, what words of advice would you give in terms of philanthropic planning and giving?

I would say no matter how large or small your gift is, it is meaningful and brings great benefit to the recipient. There are various ways in which to donate your estate either during your lifetime or after to have a lasting impact on generations to follow. I suggest thinking through the variety of options and then tailor your gift to best suit your objectives. Personally speaking, it was very helpful for me to meet with NYU’s Development Office and let them know our intentions and purpose, and in turn they were able to better guide me in directing our gift. When you give money to a cause you feel deeply about, you give hope, support progress and advance momentum.

What one event comes to mind as a special memory of Mrs. Barlow?

When I was a medical school student, I had a month of vacation time, and Pearl invited me and a classmate of mine to drive down to Mexico with her. You can imagine how thrilled I was. There we were, the three of us, driving from Chicago, which is where she lived at the time, to Mexico. We had a ball. She always liked to travel and have adventures.

How do you remember your aunt?

I think of her as a warm, affectionate, generous person. A good, caring friend and a wonderful aunt.
Path of Progress: Early Behavioral Detection of Alzheimer’s Disease

As we know, Alzheimer’s disease (AD) is characterized behaviorally by gradual and eventually devastating memory loss, and neurologically by neuron loss, plaques and tangles. Prior to the disease being diagnosed, its hallmark behavioral symptom is a gradual decline in declarative memory — conscious long-term memory for everyday experiences. This memory impairment is thought to result from a slowly progressing neuropathology that occurs first in the medial temporal lobe structures of the brain critical for declarative memory, and later in the frontal, lateral temporal and parietal cortices of the brain.

Extensive cellular damage occurs before clinical diagnosis, therefore early diagnosis is extremely important to optimizing the benefit of treatments for Alzheimer’s disease. Hence, early detection, especially if it can be done non-invasively, has become increasingly important in treating AD. While biological measures, namely MRI (Magnetic Resonance Imaging), PET (Position Emission Tomography) scans, and CSF (Cerebral Spinal Fluid) biomarkers, have emerged as promising tools for pre-symptomatic diagnosis, these techniques tend to be intrusive as well as costly.

To gain leverage on this problem, a multi-disciplinary team of researchers has initiated a pioneering study exploring the potential of behavioral tasks that depend on the functioning of some of the brain areas affected in the earliest stages of AD. The entorhinal cortex is a region of the brain located on the underside of the cortex near the hippocampus. It serves as the main conduit between the hippocampus and the neocortex, a selection of tasks that are very sensitive to the integrity of these areas and are currently investigating their sensitivity to neuroimaging and biomarker abnormalities (MRI volume loss, PET hypometabolism, and abnormal CSF levels) consistent with very early AD.

Primary Focus
Two parallel and complementary lines of studies, one in humans and one in rodents, are under way to address the investigators’ goal. In the human research, the team uses a selection of tasks that are very sensitive to the functioning of some of the brain areas affected in the earliest stages of AD. The participants are deemed “cognitively normal” based on clinical evaluation, but are categorized as having high vs. low risk of having very early AD based on biological measures (e.g., assessment of brain atrophy using magnetic resonance imaging; assessment of brain metabolism using positron emission tomography; profiling of AD-related proteins using lumbar puncture sampling of cerebral spinal fluid). High-risk participants, compared to their low-risk counterparts, are expected to exhibit significant deficits on these tasks.

In the complementary animal research, investigators test the hypothesis that behavioral deficits in tasks analogous to those used in the human research exist in a transgenic (genetically modified) mouse model of AD, and that these deficits precede deposition of amyloid (protein linked to AD). Using various microscopy techniques, the research team will further verify that such deficits are accompanied by early changes in the entorhinal cortex and in its projection to the hippocampus. This parallel line of research will provide a better understanding of brain changes that cause the earliest deficits in AD.

Additionally, the research team recently initiated piloting efforts to develop tasks sensitive to the integrity of a set of brain regions (including the precuneus, posterior cingulate, and retrosplenial cortex) called the Default Network. Several brain regions in the Default Network, particularly the precuneus, are prominent sites of amyloid pathology in AD and show functional changes far earlier than clinical diagnosis. Therefore, tasks that probe the functioning of these brain regions will be powerful tools for behavioral detection of preclinical AD.

Findings
To date, the investigators have collected some initial feasibility data on two of their experimental tasks from 28 cognitively normal participants who have had MRI as part of their clinical evaluations and who also had measurement of CSF (cerebrospinal fluid) biomarkers. Preliminary results are promising and findings have recently been presented at the Fourth Conference on Clinical Trials in Alzheimer’s Disease (CTAD).

Potential for Clinical Impact
The research team expects their research to provide an important first step in the development of non-invasive, cost-effective behavioral methods for detecting preclinical AD. When further validated in larger longitudinal outcome studies, these methods will greatly facilitate the development of treatments to prevent AD. Results will also be used to support preclinical drug testing using behavioral tasks, including drugs that may have failed when administered to more advanced AD patients. Such drugs could advance rapidly to clinical trials that would employ the same behavioral measures to demonstrate clinical efficacy in pre-symptomatic individuals.

The research team includes: Steven Ferris, Ph.D., Professor, NYU Langone Medical Center; Director, Alzheimer’s Disease Center (ADC); Stella Karantouulis, Ph.D., Clinical Neuropsychologist, The Pearl I. Barlow Center; Huyan Lao, Ph.D., Adjunct Assistant Professor (CCNY) and Post-doctoral Fellow, ADC; Catherine Myers, Ph.D., Research Scientist, VA New Jersey Health Care System; Susan De Santi, Ph.D., Adjunct Associate Professor, NYU Langone; Helen Scharfman, Ph.D., Professor, NYU Langone and Research Scientist, Nathan Kline Institute; and Ashita Gurnani, B.A., Research Coordinator, ADC.

Several brain regions, including the hippocampal area as well as the default network, particularly the precuneus, are areas affected earliest in AD pathology, even before clinical diagnosis.
The Comprehensive Center on Brain Aging hosted its first Healthy Brain Aging community event in recognition of National Alzheimer's Disease Awareness month. More than 200 people attended the fair and went through the circuit to the various tables, kiosks and screening booths which offered memory screenings, Body Mass Index (BMI)/obesity evaluations, blood pressure screenings, lung capacity/lung age testing and much more. The chair yoga session was in high demand and the presentations by Drs. Ralph A. Nixon and James E. Galvin focused on lifestyle modifications/healthy brain aging and an update on research advances on AD. The event was designed to provide the community with information on brain aging and related diseases, and to bring awareness of healthy lifestyle modifications that may potentially delay the onset of Alzheimer’s.

Healthy Brain Aging Fair: Collaboration Yields Success

Collaborative Team of Nathan Kline Institute (NKI) Investigators Awarded $10M Program Project Grant

A unified team of investigators from the Center for Dementia Research at Nathan S. Kline Institute for Psychiatric Research (NKI), in collaboration with NYU Langone Medical Center researchers, representing various departments and administrative units, was recently awarded a $10 million program project grant (P01), over five years, by the National Institutes of Health (NIH) to further their research focusing on the cell and molecular pathology of Alzheimer’s disease. The significance of this grant is that it represents synergistic research programs working in concert, designed to achieve results unattainable by investigators working independently.

Ralph A. Nixon, Ph.D., M.D., is designated as the principal investigator, bearing responsibility for the scientific and fiscal management of the program project grant. Dr. Nixon will lead a team of 21 scientists and affiliated scientists focusing on four interrelated projects. The Project and Core Leaders (Paul M. Mathews, Ph.D.; Ralph A. Nixon, Ph.D., M.D.; Efrat Levy, Ph.D.; and Stephen D. Ginsberg, Ph.D.) with differing areas of expertise will be collaborating on this broad scale project, pooling talents and resources. Additionally, Ana Maria Cuervo, M.D., Ph.D., at Albert Einstein College of Medicine will participate as a consortium principal investigator.

"Addressing an urgent need for additional perspectives on effective therapies for this mind-robbing disease, our Program advances a novel biological framework for understanding how Alzheimer’s develops and identifies new directions for the therapy of AD and possibly other aging-related diseases," said Dr. Nixon. He added, "In recent studies, we have unequivocally linked the genes causing early onset Alzheimer’s disease directly to functions within endocytic and autophagic pathways of the lysosomal system (cell's waste disposal and recycling system), documenting specific impairment of these functions beginning at the earliest stages of AD. We propose to validate further our novel conceptual framework that positions the lysosomal system as a common primary target for disruption by diverse genetic and environmental AD-risk factors."

Presently, no effective treatment exists to either slow or prevent the progression of Alzheimer’s disease. "Validation for one or more of these new approaches will have significant impact on realizing therapeutics for Alzheimer’s disease and other major aging-related neurodegenerative diseases," said Dr. Nixon.

Please join us in this race against time. Your gift will be put to work immediately, making a tangible impact on the lives of those suffering from Alzheimer’s and their families. Your support will aid the researchers working on the front lines of discovery, allowing them to quickly pursue promising laboratory studies and clinical trials.

Each step we take in advancing Alzheimer’s research we hope will prove beneficial for you or someone you love — today or in the future.

Annual Federal Funding for Research

<table>
<thead>
<tr>
<th>Research Area</th>
<th>Amount</th>
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<tr>
<td>Cancer Research</td>
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<tr>
<td>Cardiovascular Disease Research</td>
<td>$4 Billion</td>
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<tr>
<td>HIV/AIDS Research</td>
<td>$3 Billion</td>
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<tr>
<td>Alzheimer’s Research</td>
<td>$450 Million</td>
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Source: Alzheimer’s Association

Please join us in Our Mission

Your support is vital to fund our pioneering research and clinical programs. Please join us in our mission to eliminate Alzheimer’s and make a monetary gift to support life-changing research at our Center, so that generations to follow will know a world without Alzheimer’s.

Funding for research on Alzheimer’s disease and related disorders is less than two percent of the National Institutes of Health budget. Private funding is now more critical than ever before.

- Chronic underinvestment for research is leaving promising investigations unfunded and delaying progress toward a treatment or cure.
- We increasingly rely on charitable gifts to continue our Center’s research and patient-focused programs.
- There is no cure for Alzheimer’s and there are no preventative treatments. Therefore, it is imperative that we continue to search for therapies to stop or reverse disease progression.

Please commit.

For more information on ways to give, including gifts, estates, memorial gifts, and gifts of securities, please visit our secure online donation page: Giving.nyumc.org/sai

Or Contact: Alie Freund
NYU Comprehensive Center on Brain Aging
145 East 32nd Street, 5th Floor
New York, NY 10016
alexandra.freund@nyumc.org
212-263-2615

Your generosity will make a difference.

A publication of NYU Langone Medical Center | Comprehensive Center on Brain Aging
There seem to be many different Alzheimer’s drugs on the market. Is one more effective than the other?

Although the treatments available today can alleviate the symptoms of Alzheimer’s disease and slow progression, there is no treatment available that actually stops the progression of the disease. Two different types of drugs have been found to delay the progression of the disease. Unfortunately, these medications don’t work for all patients. Approved by the Food and Drug Administration (FDA), one type seems to work best in the earlier stages of the disease, while the other is reserved for treatment of late stage AD.

Alzheimer’s disease alters the brain in many ways. One of the changes results in a decrease in the levels of acetylcholine, a chemical messenger that’s believed to be important for alertness, memory, thought and judgment. This is when we usually prescribe cholinesterase (ko-lin-ES-tur-ase) inhibitors, which are a type of drug that improves the effectiveness of acetylcholine either by increasing the amount of it in the brain or by enhancing nerve cells’ response to it. Cholinesterase inhibitors can’t reverse Alzheimer’s disease and don’t stop the death of nerve cells. And because the brain produces less acetylcholine as the disease progresses, the medications lose their effectiveness over time. These drugs are marketed as donepezil (Aricept), galantamine (Razadyne) and rivastigmine (Exelon).

The second type of drug is Memantine (Namenda). Our researchers at the Silberstein Alzheimer’s Institute played an important role in the clinical trials leading to the drug’s approval. Memantine works by regulating the activity of glutamate, a messenger chemical involved in all brain function, including learning and memory. Until we can find a cure or halt the progression of AD, slowing the downward spiral remains the only benefit drugs can offer. But for many families, even temporary improvements can help extend the amount of quality time they have with their loved ones.

Letters to the Editor: We encourage you to write to us — voice your comments and feedback on articles you have read in our newsletters. We will select a few for publication in each issue. Letters may be submitted via email to camy.sleeman@nyumc.org. We reserve the right to edit letters for length.

Your Involvement Matters

We, at the Comprehensive Center on Brain Aging, are committed to combating Alzheimer’s disease, Parkinson’s disease and other neurodegenerative cognitive disorders.

We hope you will join us in this endeavor, and therefore we ask for your help. Please, would you commit through a philanthropic donation and/or getting involved in a research study? Your involvement today can benefit the lives of many for years to come.

For more information or financial planning for gifts and bequests, please contact Alie Freund at 212.263.2615 or alexandra.freund@nyumc.org.