Newsletter of the Brain Research Foundation
Vol. 5, No. 2 2004

brain waves

In This Issue

What is ALS?

Amyotrophic lateral sclerosis (ALS) is a disease that many people have heard of–especially when you say, "Lou Gehrig's disease"–but few actually know what it is.

In 1939, Lou Gehrig brought attention to ALS when he unexpectedly retired from baseball at the age of 42. The country was stunned to learn that the "Iron Horse," who hadn't missed a game in over 13 years, was suffering from such a devastating disease.

Chicago broadcasting legend John Drury was recently diagnosed with ALS. On July 29, 2004, the Brain Research Foundation hosted the John Drury Benefit for ALS to educate and raise funds for this disease (details on page 4).

ALS is a progressive neurodegenerative disease, which attacks the motor neurons that provide voluntary movement. As these nerves die, muscle movement control decreases, leading to eventual paralysis.

Symptoms:
- Progressive weakness or difficulty in coordination
- Changes in speech
- Weight loss or loss of muscle mass

Facts:
- 30,000 Americans afflicted
- Mean age of onset in the 50s
- 10% of cases are hereditary
- Average survival is 3 to 5 years

Research:
- Several ongoing clinical drug trials
- Ongoing stem cell research as a treatment for ALS
- New genes identified as the cause of familial ALS. These genes may provide insight into sporadic ALS.

dear friends

In addition to funding brain research, the Brain Research Foundation strives to educate the community about neurological disorders and recent developments in neuroscience. Over the past year, we have informed the public through seminars, newsletters and an annual report.

In April, John & Martha Mabie and Tom & Hope Reynolds, in partnership with the University of Chicago and the Brain Research Foundation, hosted *Exploring the Mind: Memory and Aging*. The evening gave attendees a chance to learn the newest discoveries in Alzheimer's research from the experts at the University of Chicago.

Not only does the Brain Research Foundation encourage the general public to learn more about neuroscience, we also recognize the importance of promoting this exciting field to the next generation of scientists. Recently, the Foundation had an opportunity to sponsor students who chose to pursue neuroscience projects in the Summer Research Program at the University of Chicago. This program was established to expose students to medical research, and hopefully spark their interest to continue in this area. By supporting the students of today, the Foundation is investing in the neuroscientists of the future.

Mark your calendars on November 5th for the 6th Annual Neuroscience Day. The Brain Research Foundation is proud to sponsor this day of scientific seminars. Speakers will include David Holtzman, M.D., Washington University and Nobel Laureate Paul Greengard, Ph.D., Rockefeller University, as well as various members of the Brain Research Institute at the University of Chicago. I hope some of you will join me in learning about the latest research at the University and throughout the nation.

Finally, I am very proud to announce that the Brain Research Foundation 2002-2003 Annual Report, designed by Liska + Associates Chicago, won the 2004 *American Graphic Design Award* for excellence in communication and graphic design. I hope everyone enjoyed reading it as much as I enjoyed putting it together.

We will continue to educate and inform as we learn more about the latest in brain research.

Sincerely,

Terre A. Sharma, Ph.D.
Executive Director

2004 Seed Grant Recipients

Sean P. Cook, Ph.D.
Anesthesia and Critical Care
A novel ion channel target for the sensation of pain

Daniel J. Curry, M.D.
Surgery
The ultrastructural effect and distribution of intrathecal and intravenous poloxamer 188 in the rat model of excitotoxic brain injury

Morris B. Goldman, M.D.
Psychiatry
Identifying novel therapeutic targets in an alternative phenotype of schizophrenia

Jackie K. Gollan, Ph.D.
Psychiatry
Early life stress and emotion and stress regulation in depression

Naoum Issa, M.D., Ph.D.
Neurobiology, Pharmacology & Physiology
Cortical limits on dynamic visual acuity

Maciej Lesniak, M.D.
Surgery
Preclinical evaluation of cytoryn (ReGel/IL-2) in malignant glioma

R. Loch Macdonald, M.D., Ph.D.
Surgery
Role of ephrins in brain arteriovenous malformations

Charles J. Marcuccilli, M.D., Ph.D.
Pediatrics
Electrophysiological characterization of pediatric neocortical neurons

Promising Research on Alzheimer's Disease

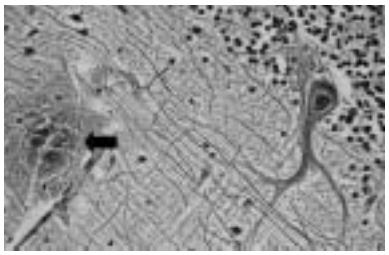


Figure 1

On April 19, 2004, John & Martha Mabie and Tom & Hope Reynolds, in partnership with the University of Chicago and the Brain Research Foundation, hosted *Exploring the Mind: Memory and Aging*. The evening gave participants a chance to learn the newest discoveries in Alzheimer's research from the experts at the University of Chicago.

Dr. Sangram Sisodia, Professor in the Department of Neurobiology, Pharmacology & Physiology, discussed how he is utilizing a transgenic animal model that exhibits some of the characteristics of Alzheimer's disease to uncover how to stop the progression of this disease. His laboratory addressed the idea that a stimulating environment might improve the outcome of transgenic animals exhibiting features of Alzheimer's disease. They discovered that the transgenic mice housed in enriched environments–cages with toys, exercise wheel and playmates–displayed smaller plaques in the brain, one of the pathological hallmarks of Alzheimer's, than the transgenic mice housed in cages without stimulants. Closer observation determined that the mice benefited more if they were active within the enriched cages. Mice that tended to observe, not participate, showed greater Alzheimer's pathology.

Dr. Ana Solodkin, Research Associate (Assistant Professor) in the Department of Neurology, is perfecting an imaging technique–Diffusion Tensor Imaging (DTI)–to detect structural changes in the brain of patients with Alzheimer's disease. Dr. Solodkin uses this imaging method to determine how areas of the brain are relating to each other. More specifically, she will be studying the perforant pathway. This pathway is affected very early on in Alzheimer's disease. The goal is to be able to use DTI to determine anatomical alterations before atrophy and degeneration is too extreme. Earlier recognition of the disease will hopefully lead to successful therapeutic interventions.

Dr. James Mastrianni, Assistant Professor in the Department of Neurology, spoke about the common occurrence of plaque formation in age-related neurodegenerative disorders. His laboratory studies prion disease as a model of neurodegenerative disease. When prion protein becomes misfolded and pathogenic, it can aggregate together or with normal prion protein to form fibrils, which can further accumulate to create larger masses called plaques (Figure 1). These plaques can compromise brain function.

Michael S. McCloskey, Ph.D.
Psychiatry
Functional magnetic resonance imaging of aggression in subjects with and without intermittent explosive disorder

Kourosh Rezania, M.D.
Neurology
Impaired glucose tolerance in idiopathic neuropathy

Axel Rosengart, M.D., Ph.D.
Neurology
Targeted drug delivery based on a novel vascular stent in medicated magnetic carriers

Nancy B. Schwartz, Ph.D.
Pediatrics
Glial precursor migration and differentiation during brain development and injury: Role of aggrecan

Kamal Sharma, Ph.D.
Neurobiology, Pharmacology & Physiology
The role of SMN protein in determination of motor neuron subtype identity

Paul R. Vezina, Ph.D.
Psychiatry
Calcium-mediated second messengers and enhanced self-administration of amphetamine

Zheng Xie, M.D., Ph.D.
Anesthesia and Critical Care
Molecular mechanisms for catecholamine release by anesthetics

Yimin Zou, Ph.D.
Neurobiology, Pharmacology & Physiology
Guidance of corticospinal cord axons in the spinal cord

Women's Council Seed Grant Recipient

Angèle Parent, Ph.D.
Neurobiology, Pharmacology & Physiology
Presenilin regulates nicotinic and glutamatergic receptors: potential therapeutic target for Alzheimer's

To interrupt the formation of plaques, Dr. Mastrianni is working with a protein chemist to design peptides (small proteins) that will bind to the pathogenic protein to block further aggregation. The goal: to stop the cycle of pathogenic protein production and halt the progression of prion disease. This exciting work has the potential to change the way we view and treat all neurodegenerative diseases.

Common questions:

1. *What is the prevalence of Alzheimer's disease in the United States?*
   According to a study published in the 2003 issue of *Archives of Neurology*, an estimated 4.5 million Americans have Alzheimer's disease. The number of Americans with Alzheimer's disease will continue to grow–by 2050 the number could range from 11.3 million to 16 million.

2. *Cholesterol-lowering drugs have been in the news lately. Should we start taking Lipitor™ now to prevent Alzheimer's disease?*
   Possibly, but only if your cholesterol is elevated. Studies are ongoing, but so far it looks like taking such drugs long before the disease starts may be protective. Once the disease symptoms begin, it appears to be too late for these drugs to work.

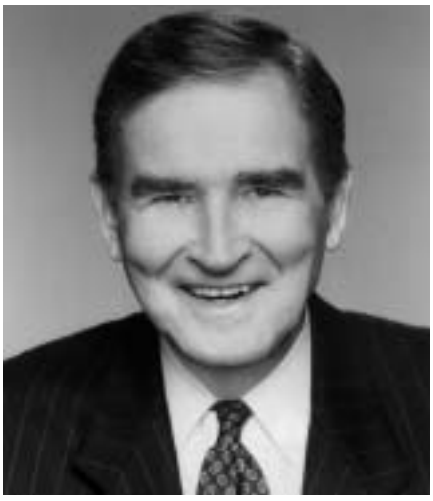
3. *Do only people with Alzheimer's disease develop plaques? Or is some plaque formation typical with aging?*
   Protein aggregation into clumps is a common feature of all neurodegenerative diseases, such as Parkinson's disease, Huntington's disease, Alzheimer's disease, and others. Recent work suggests that the toxic feature of these relates to extremely small aggregates long before the obvious plaques are deposited in the brains. Even with normal aging, Alzheimer-related plaques have been found in the brains of healthy people. These findings suggest that Alzheimer's disease is a continuum of damage occurring within the aged brain, but most people do NOT develop Alzheimer's disease, so there must be something different about those people that develop a large plaque burden.

1. Alan Krashesky, Kathy Brock 2. Martin Koldyke, Jay Levine, Gwen Knapp, Jules Knapp, Tom Reynolds 3. Mary Mathie, Frank Mathie
4. ABC 7 Chicago table 5. John McDonough & daughter, Anne McDonough 6. Ann Drury

John Drury Benefit for ALS

Chicago Newscasters Support One of Their Own

John Drury is a distinguished newscaster and Chicago legend who came into our homes and kept us informed for over forty years. After retiring, John Drury learned that he was suffering from a neuromuscular disease, amyotrophic lateral sclerosis (ALS, also known as Lou Gehrig's disease). John Drury and his family partnered with the Brain Research Foundation to raise awareness and funds for this devastating disorder.



John Drury

On July 29, 2004, the Brain Research Foundation hosted the John Drury Benefit for ALS at the Ritz-Carlton Chicago. Over 120 guests and friends were in attendance, including news personalities from ABC7 Chicago, CBS2 Chicago and NBC5 Chicago. Masters of Ceremonies Kathy Brock and Alan Krashesky of ABC7 Chicago spoke to the audience about John Drury and introduced his longtime friends and fellow newscasters, Frank Mathie and Paul Meincke, whose words brought back fond memories of working with such a remarkable man. One of the highlights of the evening was videotape produced by ABC7 that featured John Drury's career through the years and captured his spirit–then and now.

The Brain Research Foundation would like to thank Mr. and Mrs. John Drury, ABC7 Chicago and BRF board members. Your tremendous support and participation helped make this event a success.

food for thought

Women's Council Luncheon

On May 12, 2004, the Women's Council of the Brain Research Foundation held their annual spring luncheon at Spiaggia. The theme for this luncheon was: *Autism–Hope Through Understanding*. Dr. Thomas Owley, Assistant Professor of Child and Adolescent Psychiatry, University of Chicago, Dr. Kathleen J. Millen, Assistant Professor of Human Genetics, University of Chicago and Sharon Rosenbloom, author of "Souls–Beneath and Beyond Autism," spoke to over 50 guests at the luncheon, providing insight on the theories and causes of autism.

For more information on the Brain Research Foundation, please call (773) 834-6750 or visit our website at www.brainresearchfdn.org.

Holiday Luncheon

The Women's Council of the Brain Research Foundation Holiday Luncheon will be held on Thursday, December 2, 2004, at the home of Carol Fessler. We hope you will come to socialize over food and drinks. The luncheon will begin at 11:30 a.m.

For more information contact Lydia Johns at (773) 702-6355.

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