

Parkinson Report



Official Journal of the National Parkinson Foundation

Vol. XVII, Issue 3, Summer 2006

The Impact
of Research



"Captain"
Nick Frasso
with his boat,
the Shake n' Bait

Help Hook the Cure Fishing Derby Back by Popular Demand!



Nick Frasso is a fisherman with a sense of humor. Diagnosed with Parkinson disease at age 48, he refused to give in to its seriousness. So he named his boat the *Shake n' Bait*. He says humor keeps everything in perspective.

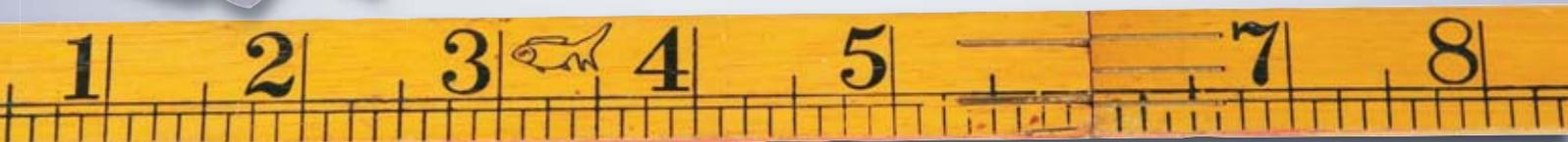
Determined to eradicate the disease, Captain Nick and his friends at the Winthrop Lodge of Elks in Winthrop, Massachusetts, are holding their second annual *Help Hook the Cure Fishing Derby* on Saturday, August 19, 2006, as a fundraiser for the National Parkinson Foundation.

Nick's humor is infectious and carries over into the rules:

- **Fish must be freshly caught.**
- **No frozen fish accepted.**
- **Fish must be caught during official tournament hours.**

Last year, Nick and the Elks hoped to raise \$3,000 for NPF and exceeded their expectations, donating \$9,000! This year, they hope to raise at least \$20,000. In addition, they are selling gold "fish hook" tie pins to raise extra funds.

Read more about the *Help Hook the Cure Fishing Derby* at <http://www.parkinson.org/>. Click on Events, or contact Nick directly at n.frasso@comcast.net.



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www.parkinson.org



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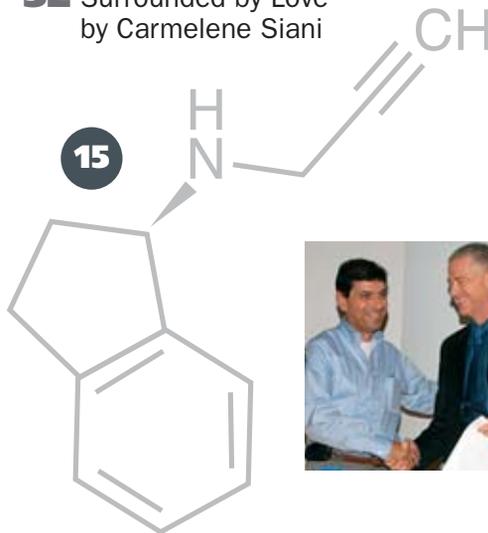
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STAY
NEW
TREN
DING

Parkinson Report

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Every effort is being made to avoid duplication of mailing labels; however, occasional duplications are inevitable. If you receive an extra copy of the *Parkinson Report*, please pass it along to a friend or colleague. We would appreciate your taking the time to inform us as well, so that our mailing lists can be adjusted and funds saved.

Parkinson Information Lines

In U.S., Canada and the Caribbean

(800) 327-4545

In Miami, Florida

(305) 243-6666

On the Internet

<http://www.parkinson.org>

Joint Message of the Chairman, the Chairman Emeritus, and the President



Paul F. Oreffice



Nathan Slewett



Daniel Arty

Research – featured in this issue of the *Parkinson Report* – has been and remains a top priority for the National Parkinson Foundation. Although NPF remains committed to improving the quality of life for those who must deal with Parkinson disease every day – patients, family members, and caregivers – our commitment to finding the cause and cure for Parkinson disease through research remains strong.

Over the years, NPF has funded tens of millions of dollars in Parkinson-related research. All of the research grant applications that are submitted to us are evaluated by our outstanding Scientific Advisory Board, composed of a dedicated group of nationally recognized scientists who volunteer their time and talents for this crucial task. Last year we implemented a new Large Grants research program, funded by our Board of Directors, with an appropriation of \$3 million. This year we implemented yet another new Mega-Grants research program, with grants up to \$1 million over three years for highly innovative proposals capable of moving the state of the science in significant steps rather than incrementally. Our Board of Directors approved an appropriation of \$5 million to fund that program, and four grants totaling \$2 million were awarded this past May.

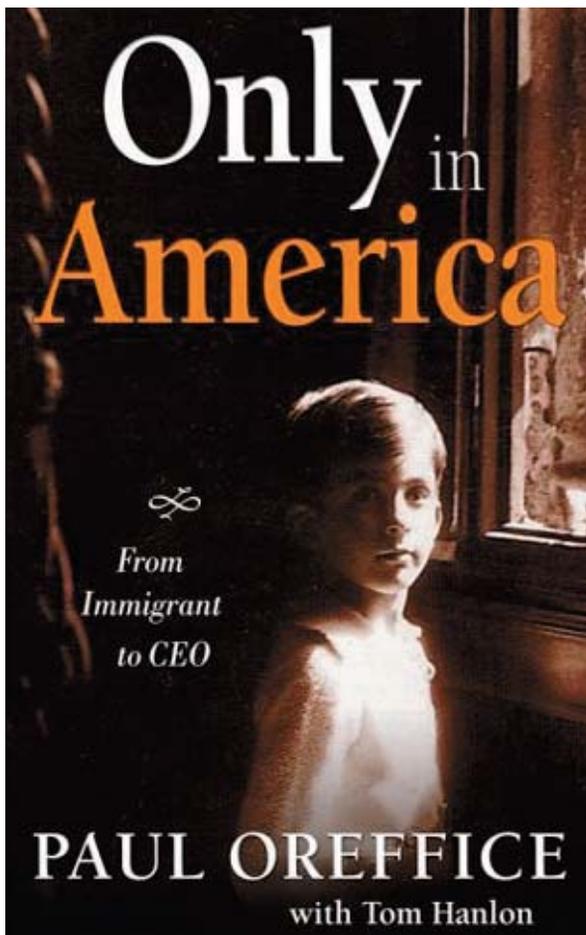
The Large Grants program and the Mega Grants program are in addition to the ways by which we have traditionally funded Parkinson-related research: through our network of national and international Centers of Excellence, and through our annual individual grants program for scientists who are in the early stages of their careers and who propose meaningful high-risk/high-yield projects. All NPF grants are peer-reviewed and are required to be of the highest scientific caliber as a precondition to being funded.

For fiscal year 2006-07, which began this past July 1st, our Board of Directors has already approved new research grants totaling \$4,172,877 – an amount which does not include the multiple-year grants previously awarded. We have also approved a similar amount, \$4,339,880, for Parkinson-related patient care, outreach, and education. If money speaks louder than words, then the monetary commitments that we have made and continue to make at the National Parkinson Foundation are the clearest examples of our determination to eradicate this disease from the face of the Earth – an effort made possible only through the generosity of our donors. To them, we extend our deepest gratitude on behalf of all who benefit from their generosity.

Paul F. Oreffice
Chairman

Nathan Slewett
Chairman Emeritus

Daniel Arty
President



Paul F. Oreffice, Chairman of the Board of Directors of the National Parkinson Foundation (NPF), is well known for his role in helping to develop NPF into a prominent international organization, respected by scientists and researchers throughout the world.

What many may not realize is that Mr. Oreffice is a classic example of the American dream fulfilled. In his new book, *Only in America*, he recounts his inspirational stories of emigrating to America from his native Venice, Italy, at age 12. Though he arrived with limited knowledge of the English language, he reveals that the difficulties he experienced in his early years formed the basis of his managerial style and led to his success as CEO of Dow Chemical Company.

Through his own will and determination, he became a U.S. citizen, served in the U.S. Army, earned a B.S. degree in chemical engineering from Purdue University, and was awarded numerous honorary doctoral

degrees. He received Indiana's highest honor, the Sagamore of the Wabash Award, for his service to education, as well as the three highest awards granted by the world's chemical organizations: the International Palladium Medal, the Chemical Industry Medal, and the Centenary Medal.

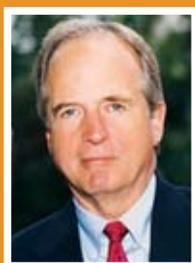
Recognizing Mr. Oreffice's abiding commitment to the Parkinson community, the National Parkinson Foundation awarded him a Lifetime Achievement Award in 2002. Mr. Oreffice is generously donating 1,000 copies with autographed bookplates to the National Parkinson Foundation. All proceeds will benefit the Foundation. For \$25, purchasers will receive a copy of the book and a charitable gift receipt for \$12.50. Which is based on the \$25 retail price of the book.

Now you can read and be inspired by his tale, as well as benefit Parkinson research through your donation.



"Only in America is the story of the Land of Opportunity and of an immigrant boy who made the most of it. Paul Oreffice is an American original, and his account of his rise to the pinnacle of business leadership is filled with drama, inspiration, and wisdom."

Gerald Ford,
38th President of the United States



"Paul Oreffice affirms that the American Dream is alive and well. You won't be able to put it down."

Peter Ueberroth,
Former Commissioner of Major League Baseball

There are several ways to order your copy of *Only in America*:

By credit card:

Order online at www.parkinson.org.

By mail:

Please mail your check for \$(US)25 per copy (which includes a \$12.50 charitable donation), payable to the National Parkinson Foundation, to:

National Parkinson Foundation
Attn: Only In America
1501 N.W. 9th Avenue
Miami, Florida 33136

By email:

Please send your request to publications@parkinson.org.





NATIONAL
PARKINSON
FOUNDATION
Research, Care, and Hope, Worldwide

NPF Awards More Than \$9 Million In New Grants

The NPF Board of Directors announces the awarding of \$9,063,928 in new grants for Parkinson-related research, care, and outreach worldwide over the next two years. In addition, grants totaling \$87,500 were awarded to 12 NPF Chapters around the country for projects ranging from mental health to educational programs, exercise sessions, publications, patient screening, and respite services.

Research grants totaled \$4,561,548 and were awarded as follows:

- \$1,181,548 to 18 NPF Centers of Excellence worldwide.
- \$2,000,000 for four "Mega Projects" at Case Western Reserve University, Dana-Farber Cancer Institute, Northwestern University, and Emory University.
- \$900,000 for the University of Miami/NPF Brain Bank.
- \$480,000 to 12 individual researchers from various countries for "high-risk/high-yield" scientific proposals.

The complete listing of NPF Center Grants (including research, comprehensive care, and outreach, where appropriate), as well as the complete listings of individual research program and Mega Projects recipients, with descriptions of each

project funded, can be found on the following pages. All NPF research grants are peer-reviewed and must be of the highest scientific caliber. All grants are subject to strict standards of reporting and accountability.

Comprehensive Care grants totaled \$2,357,722 and were awarded as follows:

- \$1,457,722 to 27 NPF Centers of Excellence and Care Centers worldwide.
- \$900,000 to the University of Miami clinical program.

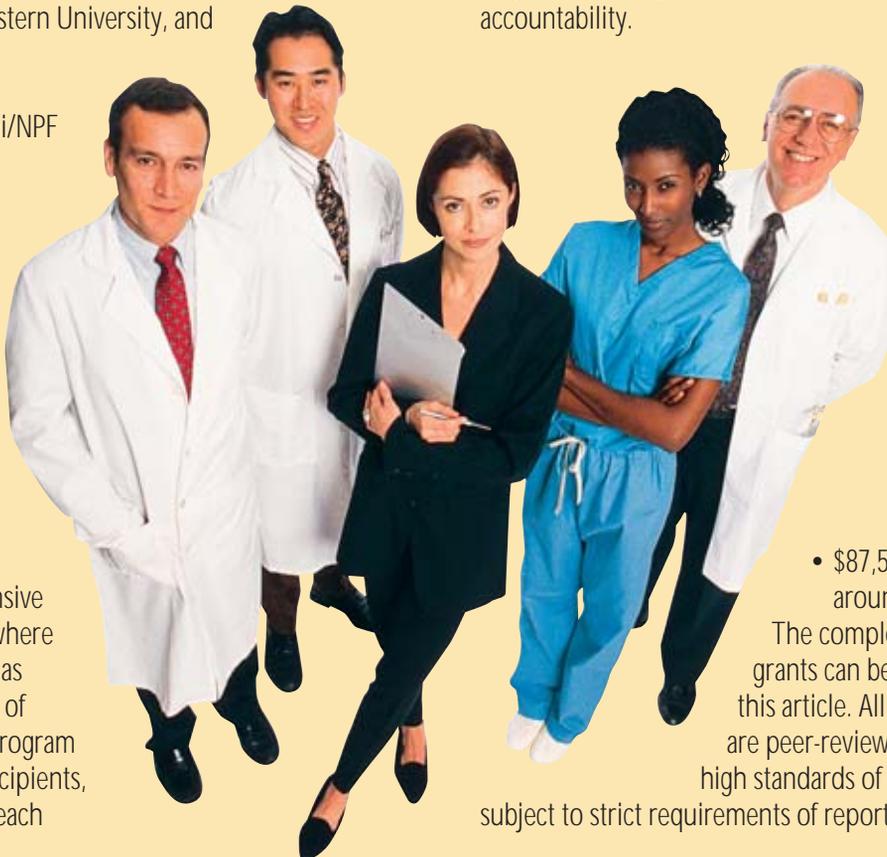
All NPF comprehensive care grants are peer-reviewed and must be used to provide the highest-caliber care possible. All grants are subject to strict standards of reporting and accountability.

Outreach, education, and Chapter grants

totaled \$2,232,158 and were awarded as follows:

- \$2,144,658 to 41 NPF Centers of Excellence, Care Centers, and Outreach Centers worldwide.
- \$87,500 to 12 NPF Chapters around the country.

The complete listing of Chapter grants can be found at the end of this article. All NPF outreach grants are peer-reviewed and must adhere to high standards of service. All grants are subject to strict requirements of reporting and accountability.



Mark D. Bevan, Ph.D., Thomas Wichmann, M.D. - Northwestern University*“Cellular Mechanisms Underlying the Therapeutic Benefit of High-Frequency Stimulation of the Subthalamic Nucleus for Parkinson Disease”*

High-frequency electrical stimulation (HFS) of the subthalamic nucleus (STN) is the preferred surgical intervention in the treatment of Parkinson disease (PD) but the precise cellular mechanisms underlying its therapeutic efficacy are poorly defined. Application of state-of-the-art cellular electrophysiological techniques will be employed to address the effects of HFS on STN neurons and on synaptic communication within and outside the STN in animal models of PD. By conducting experiments in a brain slice preparation, the cellular mechanisms and neurotransmitter receptors engaged by HFS will be determined with the greatest possible precision. Data of direct clinical relevance will be provided by parallel electrophysiological and microdialysis studies in awake, behaving animals. Taken together, these studies will deepen everyone's understanding of the factors underlying the efficacy of HFS of the STN for PD, which will guide further development of HFS protocols and reveal drug targets for future nonsurgical treatments for PD.

Bruce Spiegelman, Ph.D., David Simon, M.D., Ph.D. - Dana-Farber Cancer Institute*“PGC-1alpha and Neuroprotection in Parkinson Disease”*

PGC-1 alpha is a gene that functions to increase oxygen consumption by many cells including nerve cells. This team has most recently found that it also decreases the production of reactive oxygen species by cells. Reactive oxygen species are very toxic products of oxygen that have been implicated as a cause of death in many neurodegenerative disorders, including Parkinson disease. In a genetic model in mice, they have shown that mice having less PGC-1 alpha are supersensitive to toxins that damage cells of the substantia nigra (SN), the part of the brain damaged in PD. This new work will ask if raising the levels of PGC-1 alpha in mice will render the SN resistant to damage with a variety of agents that cause PD. These data may establish a new paradigm for how to spare cells of the SN in PD.

Shu G. Chen, Ph.D., Amy L. Wilson-Delfosse, Ph.D., Kevan M. Shokat, Ph.D. - Case Western Reserve University*“Uncovering the pathogenic role of LRRK2 in Parkinson Disease using molecular and chemical genetic approaches”*

Mutations in LRRK2 (leucine-rich repeat kinase 2) are thus far the most frequent cause of autosomal dominant and late-onset Parkinson disease (PD). LRRK2 is a novel protein kinase that potentially controls important biological processes through phosphorylation of protein substrates. Despite the genetic significance of LRRK2 in the development of PD, neither the activation mechanisms nor cellular substrates for LRRK2 have

been elucidated. This collaborative research project will address these issues using a combination of molecular and chemical genetic approaches. The team will characterize the in vitro mode of LRRK2 activation and regulation by its internal functional domains following overexpression of LRRK2 in mammalian cells. Afterward, the direct substrates of LRRK2 will be further identified using ATP analogs and genetically engineered LRRK2. Hopefully, these studies will not only provide molecular insights into the biological functions of LRRK2 relevant to PD pathogenesis, but also discover LRRK2 substrates as potential therapeutic targets for PD.

Yoland Smith, Ph.D., Thomas Wichmann, M.D., Leonard Howell, Ph.D., Gilles Tamagnan, Ph.D. - Emory University*“Metabotropic Glutamate Receptors: Novel Targets for Parkinson Disease Pharmacotherapy”*

The motor signs of Parkinson disease (PD) result from loss of midbrain dopaminergic neurons, and, consequently, most current antiparkinsonian treatment strategies are still based on replacing or restoring dopaminergic transmission with L-DOPA or dopamine receptor agonists. These treatments are highly effective, but also result in disabling long-term side effects, such as the development of dyskinesias, and may induce or exaggerate cognitive problems in PD. It is well established that abnormal glutamatergic transmission is an important consequence of dopamine loss. Abnormally patterned activity of neurons in the basal ganglia that strongly depend on glutamatergic transmission, is crucial for the expression of parkinsonian motor signs. Based on these insights, glutamate receptor antagonists have been assessed for their therapeutic potential in animal models of PD. Unfortunately, because of their widespread distribution and requirement for normal brain functioning, blockade of glutamate receptors that mediate fast excitatory neurotransmission have failed in clinical trials in humans largely because of unacceptable side effects and/or limited efficacy. Recently, a new group of glutamate receptors, called metabotropic glutamate receptors (mGluRs), have become targets of great interest for treatments of neurologic and psychiatric diseases. Preclinical rodent studies have provided strong evidence that agents acting at these receptors are very promising targets for symptomatic and neuroprotective therapies in PD. As a step forward in the development of novel nondopaminergic drug therapy of PD, a combination of behavioral and electrophysiological techniques will be used to assess the antiparkinsonian efficacy of specific mGluRs antagonists in MPTP-treated nonhuman primates, considered as the “gold standard” model of PD. This team will also test whether the effects of another highly promising group of nondopaminergic agents, adenosine A2a receptor antagonists, are synergistic with those of mGluR antagonists. Finally, they will combine in vivo PET scanning and quantitative postmortem analyses to assess the neuroprotective properties of these drugs on dopaminergic neuron degeneration. In summary, these preclinical studies will provide solid evidence that mGluR antagonists are new class of non-dopaminergic drugs that can be used to treat the symptoms and the progression of Parkinson disease in humans.

INDIVIDUAL RESEARCH GRANTS 2006-07

Katherine Sturm-Ramirez, Ph.D. - St. Jude Children's Research Hospital

"Is H5N1 influenza virus a novel etiological agent in the development of experimental parkinsonism?"

The etiology of Parkinson disease is multivariate, ranging from identified genetic mutations to strict environmental causation and exposure to viruses. Most influenza infection in humans cause respiratory disease, but occasionally the brain can also be affected. The greatest influenza pandemic of the 20th century, the Spanish Flu, occurred in 1918. It is estimated that about 25-30 percent of the world population was infected and upward of 40 million people died in less than a year. About the same time, the world was hit by an unusual epidemic of neurological diseases. Circumstantial and epidemiological evidence links post-encephalitic Parkinsonism to the 1918 influenza pandemic, but a causal link was never formally proven as the pandemic occurred before the advent of modern virology. Interestingly, the virus that caused the Spanish Flu pandemic was recently resurrected in the laboratory and detailed analysis shows that it was most likely an avian influenza virus passed directly from a bird to a human, followed by mutations that allowed this strain to efficiently transmit from human to human.



In light of the recent events involving another avian influenza strain, the highly pathogenic H5N1, this finding is of great concern. With the current risk of a human influenza pandemic due to H5N1 that is currently spreading rapidly throughout the world, the potential for another outbreak of postencephalitic parkinsonism is significant. The goal of this research is to investigate if infection with avian H5N1 influenza viruses can either directly or indirectly lead to the death of neurons in the substantia nigra pars compacta, a hallmark of Parkinson disease in a mammalian species.

Andrea Kuhn, M.D. - University College London

"Frequency-specific effects of electrical brain stimulation on neuronal oscillations and motor performance in patients with Parkinson Disease"

The study aims to further elucidate the mechanism of two new treatments for Parkinson disease (PD), deep brain stimulation and motor cortex stimulation. Recent results propose that motor deficits in PD patients may be related to increased oscillatory neuronal activity in the so-called beta frequency band (13-30 Hz) in the basal ganglia. The research will test whether frequency-specific brain stimulation, namely at high frequency, may suppress the pathologically enhanced beta activity and whether the stimulation effect is correlated to improvement in motor symptoms.

Benjamin N. R. Cheyette, M.D., Ph.D. - University of California San Francisco

"Dact1/Dpr1 in Dopaminergic Development"

Parkinson disease is caused by inadequate numbers or functioning of dopamine neurons located in the ventral midbrain. Of particular interest is a member of the Dpr/Frodo gene family, which is present in the developing midbrain at the time of dopamine cell generation during development. A mutation in this gene in mice has been genetically engineered. The mutant mice have an abnormal expansion of the midbrain at birth. With support from the National Parkinson Foundation the researchers are studying the causes of midbrain expansion in this mouse line, focusing on mutant effects on cell communication that have consequences for dopamine cell generation and survival. By understanding the role of these molecules in normal dopamine cell development and maintenance, perhaps they will open new windows into the biological causes of Parkinson disease, and new doors to potential cures.

Eric Vilain, M.D., Ph.D. - University of California, Los Angeles

"Role of the male-specific transcription factor SRY on dopaminergic function: implications for gender differences in Parkinson Disease"

INDIVIDUAL RESEARCH GRANTS 2006-07

Parkinson disease occurs 1.5 times more often in men than women. Understanding what causes this striking difference may lead to discover causes of Parkinson disease that are specific to men or women, and may ultimately help tailor treatment to the patient's gender. There is evidence that SRY, the gene that is present exclusively in males on the Y chromosome and that is responsible for the presence of testicles, is also found in men's brains. SRY has been found in the same cells that make dopamine and that are lost when Parkinson disease develops. These researchers have also discovered that SRY can turn on Tyrosine Hydroxylase, an enzyme that is essential for dopamine production. It is possible that there are gender-specific ways to control the production of dopamine: SRY in males and a different factor in females. This proposal will test if there are indeed male- and female-specific ways to make dopamine, and if they can compensate for each other.

**Robert Malenka, M.D., Ph.D. -
Stanford University School of Medicine**

“Synaptic Function and Plasticity in Indirect and Direct Pathway Striatal Neurons”

The basal ganglia are an interconnected set of brain regions that are critical for the proper control of movement. Individual cells in the striatum, which is the largest of the basal ganglia regions, can be categorized based on their connections with other basal ganglia regions. Cells that are connected directly to output areas of the basal ganglia are known as “direct pathway” cells, whereas cells that connect to intermediate basal ganglia areas are known as “indirect pathway” cells. Proper control of movement is thought to require balanced activity in direct and indirect pathway cells. This balanced activation is normally fine-tuned by dopamine, an important brain chemical that can regulate cell activity. However, in Parkinson disease, dopamine is lost, and activity in the basal ganglia becomes imbalanced. These studies will investigate the properties of cells and their inputs in the direct and indirect pathways, both under normal conditions and in the absence of dopamine. In particular, these scientists will focus on mechanisms that independently modulate activity in these pathways, with the aim of discovering new drug targets that can restore balance to these brain circuits in the absence of dopamine.

**Lachlan Thompson, Ph.D. -
Wallenberg Neuroscience Center, Lund University**

“Identification and selective isolation of dopamine neuron progenitors from foetal midbrain for transplantation in animal models of Parkinson Disease”

The foetal midbrain contains a highly mixed population of cells in various states of differentiation including, for example: proliferating stem cells, progenitor cells and more mature neurons and glia.



Following transplantation, some of these cells give rise to the dopaminergic neurons that can very effectively restore motor function in PD patients. In order to identify these cells, this project makes use of a variety of transgenic reporter mice in which green fluorescent protein is expressed only in certain cell types at specific stages of differentiation within the foetal midbrain. Through the technique of ‘fluorescence activated cell sorting (FACS)’, this will allow the researchers to selectively isolate subfractions of cells from the foetal midbrain, based on their differentiation state, and identify which cell type is best suited to giving rise to mature dopamine neurons following transplantation. The results from this project will be highly relevant for current efforts in the field to develop safe and effective protocols for transplantation therapy of PD using embryonic stem (ES) cells, where there is likely to be a need to obtain purified populations of transplantable dopamine neuron progenitors from mixed preparations of expanded ES cells.

**Margaret Rice, Ph.D. -
New York University School of Medicine**

“Mitochondrial Dysfunction and Somatodendritic Dopamine Release”

Mitochondrial dysfunction is implicated in Parkinson disease, possibly via oxidative stress resulting from generation of reactive oxygen species, like hydrogen peroxide. Normally, activity-dependent hydrogen peroxide is produced in dopamine neurons to provide an inhibitory signal that regulates neuronal firing rate. This team will examine whether false peroxide signaling during mitochondrial dysfunction, mimicked by the pesticide rotenone, leads to excessive inhibition of dopamine neurotransmission by suppressing dopamine neuron activity and consequent dopamine release.

INDIVIDUAL RESEARCH GRANTS 2006-07

Youren Tong, Ph.D. - Brigham and Women's Hospital, Harvard Medical School

"Generation and characterization of LRRK2 Transgenic and Knockin Mice"

Parkinson disease (PD) is the most common movement disorder characterized by resting tremor, rigidity, and bradykinesia. Most PD cases occur sporadically; however, several genes associated with monogenetic forms of the disease have been identified. Clinical symptoms of the familial forms of PD are essentially indistinguishable from those of the sporadic forms. Generations of genetic mouse models recapitulating the central features of PD, therefore, would be invaluable for the elucidation of the pathogenic mechanisms underlying the selective dysfunction and degeneration of dopaminergic (DA) neurons. Recently, at least seven disease-segregating missense mutations in human LRRK2 have been identified, which are autosomally and dominantly inherited and the most common genetic cause of the late-onset PD. To investigate the pathogenic mechanism by which mutations in LRRK2 cause PD, this researcher has proposed to generate transgenic mice overexpressing human mutant (R1441C) or wild-type LRRK2 as well as knockin mice, in which a commonly found mutant form (R1441C) of LRRK2 is expressed under the control of the endogenous regulatory elements. These mice will be analyzed for PD-relevant phenotypes, such as impaired locomotor activity, protein aggregation, mitochondrial dysfunction, and DA neuron degeneration. The study of the LRRK2 mutant mice would provide a meaningful contribution to the understanding of the sporadic as well as the familial form of PD.

Zachary Baquet, Ph.D. - St. Jude Children's Research Hospital

"Analysis of immune system response in a mouse model of Parkinson Disease"

The root causes and contributing factors of the neurodegenerative disorder Parkinson disease are unknown. Recent studies demonstrated that a part of the body's immune system, the activated T-cells, are capable of lessening the neurotoxic effects of MPTP, the neurotoxin that is most used to model Parkinson disease in mammals. With this grant this research team seeks to experimentally determine the role that T-cells and other components of the immune system, isolated in both genetically modified and chemically induced models, play in both the etiology and progression of experimental Parkinson disease. As in previous work, their studies will utilize the MPTP model in mice to examine how these different components of the immune system impact the cells of the substantia nigra. The goal is to find ways to slow the progression of this disease thus providing for a better quality of life for its sufferers.

Wanli W. Smith, M.D., Ph.D. - Johns Hopkins University School of Medicine

"Mutant LRRK2 toxicity and kinase activity"

Mutations in the leucine-rich repeat kinase 2 (LRRK2) gene cause Parkinson Disease (PD). The mutation could be responsible for up to five percent of PD in people with a family history of the disorder and may account for one to two percent of cases in individuals who do not have a family history of the disease. The LRRK2 gene provides instructions for making a protein called dardarin (LRRK2). The gene is presumably active in the brain, but little is known about the LRRK2 gene or LRRK2 protein (dardarin). Last year, this group and others found that LRRK2 protein has an enzyme activity known as kinase. Like other members of the kinase family, LRRK2 may help control other proteins' activities by transferring small groups called phosphates onto them. They recently found that mutant LRRK2 protein causes neuronal death. In this proposal, it will be determined whether alteration of LRRK2 kinase activity influences mutant LRRK2-induced cell death using genetic and cell culture approaches. These studies will enlarge knowledge in the scientific community of LRRK2 kinase function, will help elucidate the pathogenesis of LRRK2-associated neuronal loss in PD, and will provide the new avenues to develop new PD therapeutic strategies by regulation of LRRK2 kinase activity.

NPF CENTER GRANTS 2006-07

Centers Of Excellence

Centro Neurológico Hospital Francés - Laboratory of Experimental Parkinsonism
Buenos Aires, Argentina
\$25,000

Victorian Comprehensive Parkinson's Program
Cheltenham, Victoria, Australia
\$152,350

Centre for Movement Disorders
Markham Stouffville Hospital
Markham, Ontario, Canada
\$157,000

Toronto Western Hospital Movement Disorders Center
Toronto, Ontario, Canada
\$195,000

Pacific Parkinson's Research Centre, University of British Columbia
Vancouver, British Columbia, Canada
\$204,732

Neurologie et Thérapeutique Expérimentale - Université Pierre et Marie Curie and INSERM UMR 679
Paris, France
\$40,000

Tel Aviv Sourasky Medical Center
Tel Aviv, Israel
\$195,000

Nijmegen Parkinson Center
Nijmegen, Netherlands
\$100,490

Muhammad Ali Parkinson Center Barrows Neurological Institute
Phoenix, Arizona
\$100,000

The Parkinson's Disease and Other Movement Disorders Center University of Southern California
Los Angeles, California
\$50,000

Parkinson's Disease Clinic and Research Center University of California at San Francisco
San Francisco, California
\$115,000

Georgetown University Hospital
Washington, D.C.
\$80,000

University of Florida Parkinson's Disease and Movement Disorders Center
Gainesville, Florida
\$194,408

University of South Florida Parkinson's Disease & Movement Disorders Center
Tampa, Florida
\$60,000

Medical College of Georgia Department of Neurology, Movement Disorders Program
Augusta, Georgia
\$100,000

Parkinson Disease Center of Excellence at Kuakini Medical Center
Honolulu, Hawaii
\$160,430

Northwestern University Parkinson's Disease & Movement Disorders Center
Chicago, Illinois
\$100,000

University of Kansas Medical Center
Kansas City, Kansas
\$135,000

Johns Hopkins Parkinson's Disease and Movement Disorders Center
Baltimore, Maryland
\$50,000

Massachusetts General Hospital NPF Center of Excellence, Harvard Medical School
Boston, Massachusetts
\$115,000

Parkinson's Disease & Movement Disorders Center, Beth Israel Deaconess Medical Center
Boston, Massachusetts
\$104,755

Struthers Parkinson's Center
Golden Valley, Minnesota
\$199,946

Parkinson's Disease and Related Disorders Center at Kings County Hospital/SUNY Downstate Medical Center
Brooklyn, New York
\$213,800

The Betty and Morton Yarmon Center for Parkinson's Disease at Beth Israel Medical Center
New York, New York
\$86,000

University of Rochester Medical Center, Department of Neurology Movement and Inherited Neurological Disorders Unit
Rochester, New York
\$205,747

University of North Carolina at Chapel Hill School of Medicine
Chapel Hill, North Carolina
\$101,820

Center for Neurological Restoration, Cleveland Clinic Foundation
Cleveland, Ohio
\$105,030

Oregon Health & Science University, Parkinson Center of Oregon
Portland, Oregon
\$144,126

The Parkinson's Disease and Movement Disorders Center, University of Pennsylvania, Pennsylvania Hospital
Philadelphia, Pennsylvania
\$84,066

National Parkinson Foundation Center of Excellence at Vanderbilt University Medical
Nashville, Tennessee
\$160,000

Parkinson's Disease Center & Movement Disorders Clinic at Baylor College of Medicine
Houston, Texas
\$110,500

Care Centers

Parkinson, Memory & Movement Disorders Center Notre Dame des Secours Hospital
Byblos/Jbeil, Lebanon
\$42,700

The Parkinson Center at Hoag Hospital
Newport Beach, California
\$125,000

Colorado Neurological Institute Movement Disorders Center
Englewood, Colorado
\$50,000

Parkinson's Clinic of the Ozarks
Springfield, Missouri
\$52,716

Bellevue Center for Parkinson and Related Movement Disorders
New York, New York
\$128,312

Plummer Movement Disorders Center at Scott & White Hospital/Texas A&M Health Science Center
Temple, Texas
\$115,000

Regional Parkinson Center at Aurora Sinai Medical Center
Milwaukee, Wisconsin
\$50,000

Outreach Centers

The Parkinson's Center at Florida Atlantic University
Boca Raton, Florida
\$50,000

Lee Parkinson's Care Program
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\$65,000

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Parkinson Center Florida Hospital Neuroscience Institute
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\$50,000

Tallahassee Memorial Parkinson Center
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\$50,000

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\$50,000

Parkinson Foundation of the National Capital Area
McLean, Virginia
\$65,000

Total Center Grants Awarded: \$4,783,928

NPF CHAPTER GRANTS 2006-07

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Portland, Oregon
\$9,000

Parkinson Association of Southwest Florida, Inc.

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\$2,500

National Parkinson Foundation, Orange County Chapter

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\$7,000

Southeast Parkinson Disease Association, Inc.

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Colorado Springs, Colorado
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Parkinson Support Group of Upstate New York

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Kingdor National Parkinson Foundation

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Parkinson's Association of Western New York

Buffalo, New York
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NPF CENTERS OF EXCELLENCE

Muhammad Ali
Parkinson Center
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and Other Movement
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Parkinson's Disease Clinic
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University of California at
San Francisco
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Parkinson's Disease and
Movement Disorders Center
Gainesville, Florida

University of South Florida
Parkinson's Disease &
Movement Disorders Center
Tampa, Florida

Medical College of Georgia,
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Program
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Movement Disorders Center
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Movement Disorders Center,
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Boston, Massachusetts

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Struthers Parkinson's Center
Golden Valley, Minnesota

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Related Disorders Center at
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Downstate Medical Center
Brooklyn, New York

The Betty and Morton Yarmon
Center for Parkinson's
Disease at Beth Israel
Medical Center
New York, New York

University of Rochester
Medical Center, Department
of Neurology Movement
and Inherited Neurological
Disorders Unit
Rochester, New York

University of North Carolina
at Chapel Hill School of
Medicine
Chapel Hill, North Carolina

Center for Neurological
Restoration, Cleveland Clinic
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Cleveland, Ohio

Oregon Health & Science
University, Parkinson Center
of Oregon
Portland, Oregon

The Parkinson's Disease and
Movement Disorders Center,
University of Pennsylvania,
Pennsylvania Hospital
Philadelphia, Pennsylvania

National Parkinson
Foundation Center of
Excellence at Vanderbilt
University Medical
Nashville, Tennessee

Parkinson's Disease Center &
Movement Disorders Clinic at
Baylor College of Medicine
Houston, Texas

INTERNATIONAL CENTERS OF EXCELLENCE

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Experimental Parkinsonism
Buenos Aires, Argentina

Victorian Comprehensive
Parkinson's Program
Cheltenham, Victoria, Australia

Centre for Movement
Disorders
Markham, Ontario, Canada

Toronto Western Hospital
Movement Disorders Center
Toronto, Ontario, Canada

Pacific Parkinson's Research
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Columbia
Vancouver, British Columbia,
Canada

Kings College London
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Neurologie et Thérapeutique
Expérimentale - Université
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INSERM UMR 679
Paris, France

Rabin Medical Center
Petah-Tiqva, Israel

Tel Aviv Sourasky Medical
Center
Tel Aviv, Israel

Nijmegen Parkinson Center
Nijmegen, Netherlands

Parkinson's Disease and
Movement Disorders Centre,
National Neuroscience
Institute
Singapore

NPF ANNOUNCES Two New Centers of Excellence

New Centers Join Fight Against Parkinson, Lead in Groundbreaking Research and Innovative Care

The National Parkinson Foundation (NPF) has announced two new Centers of Excellence, a designation awarded by NPF to healthcare institutions that meet criteria for excellence in Parkinson-related research, comprehensive care, and outreach. The new centers are:

- *University of Michigan* (Ann Arbor, Michigan)
- *Parkinson's Disease and Movement Disorders Centre, National Neuroscience Institute* (Singapore)

"A Center of Excellence is chosen because it is a regional hub and leader in the provision of innovative models, setting a gold standard for care, outreach, and research," said Jose Garcia-Pedrosa, chief operating officer of NPF. "Additionally, each Center must also share our commitment to developing comprehensive interdisciplinary teams that will interact holistically with each other."

NPF has also designated two new Care Centers and one new Outreach Center. The Booth Gardner Parkinson's Care Center in Kirkland, Washington, and the Winnipeg Regional Health Authority in Winnipeg, Manitoba, will now serve as NPF Care Centers, devoted to providing both comprehensive care and outreach for Parkinson disease. The University of Buffalo in Buffalo, New York, has been designated as an NPF

Outreach Center, providing direct support and services to address the unique challenges faced by the patients and families living in communities within the surrounding areas.

Currently, NPF has a total of 36 Centers of Excellence, ten Care Centers, and eight Outreach Centers located at premier medical and academic institutions throughout the world. This year alone, NPF has awarded a total of 86 grants to its Centers, accounting for more than \$5.1 million.

Founded in 1957 and headquartered in Miami, the National Parkinson Foundation's dual mission is to find the cause of and cure for Parkinson disease, as well as to improve the quality of life for those afflicted with the debilitating disease. NPF has invested over \$100 million in the fulfillment of its mission and is dedicated to providing care, education, and support services for persons whose lives are affected by Parkinson. Currently, the centerpiece of NPF's research, care, and delivery system is its international network of 54 institutions worldwide that have achieved designation as NPF Centers of Excellence, Care Centers, or Outreach Centers and through its 41 affiliated Chapters.

For a complete list of all NPF Centers and affiliated Chapters or to learn more about NPF's designation criteria, visit www.parkinson.org.

NPF CARE CENTERS

Parkinson, Memory & Movement Disorders Center
Byblos/Jbeil, Lebanon

The Parkinson Center at Hoag Hospital
Newport Beach, California

Colorado Neurological Institute Movement Disorders Center
Englewood, Colorado

Parkinson's Clinic of the Ozarks
Springfield, Missouri

Health South Parkinson/Movement Disorder Center and Deep Brain Stimulation Program
Albuquerque, New Mexico

Bellevue Center for Parkinson and Related Movement Disorders
New York, New York

Plummer Movement Disorders Center at Scott & White Hospital/Texas A&M Health Science Center
Temple, Texas

Booth Gardner Parkinson's Care Center
Kirkland, Washington

Regional Parkinson Center at Aurora Sinai Medical Center
Milwaukee, Wisconsin

NPF OUTREACH CENTERS

The Parkinson's Center at Florida Atlantic University
Boca Raton, Florida

Lee Parkinson's Care Program
Fort Myers, Florida

Parkinson Association of Southwest Florida
Naples, Florida

Parkinson Center Florida Hospital Neuroscience Institute
Orlando, Florida

Tallahassee Memorial Parkinson Center
Tallahassee, Florida

Nevada Neuroscience Foundation
Henderson, Nevada

University at Buffalo, Depts. of Neurology/Neurosurgery
Buffalo, New York

Parkinson Foundation of the National Capital Area
McLean, Virginia

NPF CHAPTERS

Arizona Chapter of the National Parkinson Foundation
Phoenix, Arizona
480-607-1960

Kingdor National Parkinson Foundation
Nassau, Bahamas
242-393-2515

Los Angeles Alliance Against Parkinson's Disease
Los Angeles, California
323-851-3230

National Parkinson Foundation - Orange County Chapter
Newport Beach, California
949-764-6998

NORCAL NPF Chapter
Redding, California
530-229-0878

Parkinson Network of Mount Diablo
Walnut Creek, California
925-939-4210

Parkinson Association of Northern California
Sacramento, California
916-489-0226

Colorado Parkinson Foundation, Inc.
Colorado Springs, Colorado
719-884-0103

South Palm Beach County Chapter of NPF
Boca Raton, Florida
561-482-2867

The Parkinson Association of Greater Daytona Beach
Daytona Beach, Florida
386-252-8959

Parkinson Association of Southwest Florida, Inc.
Naples, Florida
239-254-7791

Southeast Parkinson Disease Association
Orlando, Florida
407-489-4124

St. Augustine Parkinson's Disease Support Group
St. Augustine, Florida
904-824-7776

North Florida Parkinson Awareness Group
Tallahassee, Florida
850-385-8186

Alzheimer/Parkinson Association of Indian River County, Inc.
Vero Beach, Florida
772-563-0505

Central Savannah River Area (CSRA) Parkinson Support Group
Grovetown, Georgia
706-721-1238

Northwest Georgia Parkinson Disease Association
Rome, Georgia
706-235-3164

Hawaii Parkinson Association
Honolulu, Hawaii
808-528-0935

Parkinson Foundation of the Heartland
Overland Park, Kansas
913-341-8828

Northeast Kansas Parkinson Association
Topeka, Kansas
785-267-6916

Eljay Foundation for Parkinson Syndrome Awareness
Lake Charles, Louisiana
337-310-2440

Northeast Parkinson's and Caregivers, Inc.
Bondville, Massachusetts
413-289-2006

Cape Cod Chapter, Inc. of the National Parkinson Foundation
East Dennis, Massachusetts
508-385-2333

Parkinson's Association of West Michigan
Grand Rapids, Michigan
800-617-8711

Parkinson Association of Minnesota
Golden Valley, Minnesota
763-545-1272

Parkinson's Group of the Ozarks
Springfield, Missouri
417-885-9595

Brooklyn Parkinson Group
Brooklyn, New York
718-522-0553

Parkinson's Association of Western New York, Inc.
Depew, New York
716-684-0650

Parkinson Support Group of Syracuse New York, Inc.
Clay, New York
315-652-6857

Parkinson's Support Group of Upstate New York, Inc.
Rochester, New York
585-234-5355

Midwest Parkinson's Awareness of Northeast Ohio Alliance, Ohio
Alliance, Ohio
330-823-8989

Parkinson's Resources of Oregon
Portland, Oregon
503-413-6656

The Parkinson Council - Philadelphia Chapter
Bala Cynwyd, Pennsylvania
610-668-4292

Lehigh Valley Parkinson Support Group
Allentown, Pennsylvania
610-868-3510

Parkinson Chapter of Greater Pittsburgh
Pittsburgh, Pennsylvania
412-365-2086

Asociación Puertorriqueña de Parkinson
Carolina, Puerto Rico
787-768-5565

Fundación Puertorriqueña de Parkinson, Inc.
San Juan, Puerto Rico
787-764-4898

Parkinson Association of South Dakota
Sioux Falls, South Dakota
605-328-4227

Parkinson Foundation of the National Capital Area
McLean, Virginia
703-891-0821

Parkinson Educational Society of Puget Sound
Olympia, Washington
360-491-9700

Wisconsin Parkinson Association
Milwaukee, Wisconsin
414-219-7061

NPF WELCOMES TWO NEW CHAPTERS

Parkinson's Association of West Michigan

260 Jefferson Ave. S.E., Suite 210

Grand Rapids, MI 49503

Tel: 616-954-8077

Fax: 616-954-2346

Toll Free: 800-617-8711

www.parkinsonsassociationwmi.org

pawmmtc@iserv.net

Mary T. Chubinski, Executive Director



Established in 1983, the Parkinson's Association of West Michigan (PAWM) serves persons with Parkinson and their families and the health care community. The vision and direction of the active, volunteer board of directors and the staff are to make available to every family affected by Parkinson in West Michigan quality health care and support services, while providing education about specific and unique care issues for physicians and other allied health care professionals and the general public.

PAWM offers:

- support groups for information
- a bi-monthly newsletter, which ensures that even those who are home-bound receive current information
- exercise programs specially designed for Parkinson
- in-services/resources provided to educate the community about Parkinson disease
- lending library of current resources about Parkinson and its management

- special projects and guest speakers, which further our mission of education
- information and referral

North Florida Parkinson Awareness Group

P.O. Box 14722

Tallahassee, FL 32317

Tel: 850-385-8186

randyregina57@comcast.net

www.nfpag.org

Randy McCoy, Chapter President



Organized in November 2005, the North Florida Parkinson Awareness Group (NFPAG) is committed to providing support, friendship, information, and advocacy for all people with Parkinson disease and their families, caregivers, and friends. Based in Tallahassee, Florida, NFPAG seeks to serve as a resource for not only northern Florida residents, but also those in southern Georgia and southeastern Alabama. In addition to being the state capital, Tallahassee is home to the primary educational and medical facilities for this mostly rural region. NFPAG members use their knowledge and experience to educate state legislators and influence policymakers so they can make better informed decisions that affect the lives of PD patients and their families.

NFPAG members are active in two support groups in the region, as well as Tai Chi classes and a Parkinson Choir.

4th Annual Young-Onset Parkinson Network Conference Living Today - Fighting For Our Future!

July 6 – 8, 2006

Hyatt Regency Reston

Washington, D.C. Metro Area

The National Parkinson Foundation would like to thank the following sponsors for their generous underwriting of the 2006 YOPN Conference:

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Karl and Angela Robb

Professor Ann Graybiel Named NPF's Harold S. Diamond Professor

New Selma and Lynn Diamond Research Fellows Also Named

McGovern Institute Investigator **Ann Graybiel, Ph.D.**, the Walter A. Rosenblith Professor of Neuroscience at Massachusetts Institute of Technology, has added a new professorship to her name in recognition of her important contributions to the understanding and treatment of Parkinson disease. The National Parkinson Foundation (NPF) recently awarded her the **Harold S. Diamond Professorship**, created in honor of **Ms. Lynn Diamond** of New York City and named after her late father.

"I am humbled and incredibly honored to receive this award," Graybiel commented. "My hope is that our lab's work will help patients with Parkinson disease."

"It is NPF that is honored to have such a close and lengthy association with a world-class scientist like Dr. Graybiel," commented Jose Garcia-Pedrosa, NPF's chief operating officer.

Professor Graybiel is considered one of the world's leading experts on the basal ganglia, the complex and inaccessible parts of the brain affected in people suffering from Parkinson disease and related conditions. Her group is using experimental models of Parkinson disease, addiction, and habit formation to study how animals learn to perform familiar tasks and how their neuronal circuits respond to drugs that affect the dopamine system.

The basal ganglia not only influence movement; they also are critical brain centers involved in motivation. "It's a great puzzle," said Graybiel, who was awarded the National Medal of Science in 2002, the nation's highest science award. "Somehow the same or related circuitry that gets damaged in Parkinson disease is also involved in habit formation, addiction, and procedural learning."

A *magna cum laude* graduate of Harvard University,



Ann Graybiel, Ph.D.

Dr. Graybiel earned her Ph.D. in psychology and brain science from the Massachusetts Institute of Technology. She is the recipient of more than two dozen honors and awards, including an Honorary Doctor of Science degree from Tufts University. She serves on numerous Editorial and Advisory Boards, and has hundreds of papers and other publications to her credit.

NPF Harold S. Diamond Professor, Ann Graybiel, will work with two postdoctoral fellows, **Mark Ruffo, Ph.D.**, and **Ken-ichi Amemori, Ph.D.**, who have been named the Selma Diamond and

Lynn Diamond Research Fellows, respectively.

NPF Selma Diamond Fellow Mark Ruffo will record in the primate basal ganglia and cerebral cortex simultaneously with state-of-the-art electrophysiological methods. The goal of his work is to identify activity occurring at multiple sites in the cortico-basal ganglia network that is dysfunctional in Parkinson disease. This basic research will allow an understanding of how the different parts work together successfully to underlie so many different aspects of behavior. A graduate of Georgetown University, Dr. Ruffo completed his Ph.D. degree in neurobiology and behavior at the University of Washington.

NPF Lynn Diamond Fellow Ken-ichi Amemori will utilize similar methods to pinpoint the neural activity in this network that is associated with decision for action, a function progressively deficient as Parkinson disease advances. This kind of work is very closely allied to neurologic and neurosurgical approaches to treating Parkinson disease. A native of Japan, Dr. Amemori earned his undergraduate degree in physics from Kyoto University and his Ph.D. in computational neuroscience from Japan's Nara Institute of Science and Technology. ▲

What Patients Need to Know About Rasagiline



By **Hubert H. Fernandez, M.D.**
Daily Columnist, Ask
The Doctor Forum,
NPF; Co-Director,
Movement Disorders
Center; Director, Clinical Trials for
Movement Disorders, Department
of Neurology McKnight Brain
Institute/University of Florida,
Gainesville, Florida

Introduction

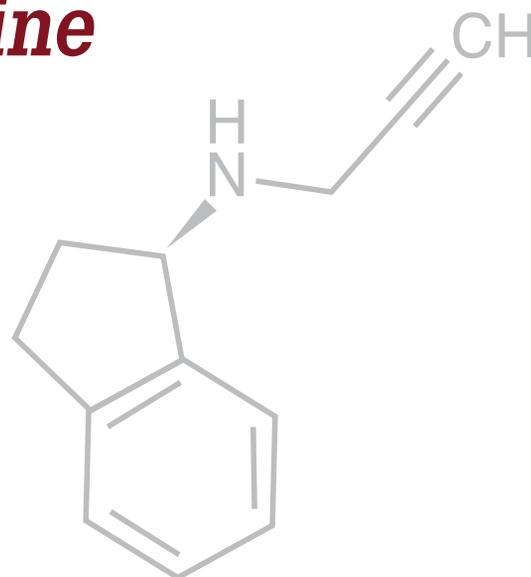
Parkinson's disease (PD) is characterized by progressive degeneration of dopaminergic neurons within the substantia nigra (a deep brain structure located in the midbrain) and degeneration within other basal ganglia circuits. The dopamine deficiency in particular seems to contribute to an imbalance in the motor circuits and to the development of parkinsonian symptoms, including tremor, bradykinesia, and rigidity. Thus, most, if not all, commercially available medications attempt to correct this imbalance by either replacing dopamine (by using a drug called levodopa), stimulating dopamine receptors (such as dopamine agonists) or preventing its breakdown. The prevention of its breakdown allows more dopamine to be available in the brain (MAO inhibitors like rasagiline function in this way).

How rasagiline works and what makes it different from selegiline

Upon release from neurons, dopamine is predominantly

degraded by the enzyme, monoamine oxidase (MAO). There are two types of MAO enzymes, MAO-A and MAO-B. MAO-A plays a major role outside the brain in deactivating circulating catecholamines (chemicals like epinephrine and norepinephrine) and dietary substances that raise blood pressure (such as tyramine). Thus, medications that inhibit the MAO-A enzyme can induce a hypertensive crisis (the "cheese reaction") when food rich in tyramine is ingested. This ingestion blocks tyramine's main deactivating mechanism, allowing it to freely work on the blood vessels to increase blood pressure. MAO-A also contributes to the breakdown of dopamine, norepinephrine, and serotonin in the brain, but it is the MAO-B enzyme that accounts for the majority of MAO activity within the human brain and for the breakdown of dopamine. Therefore, selectively inhibiting the MAO-B enzyme results in the elevation of dopamine concentrations. "Selective" inhibition means that it only inhibits the MAO-B and not MAO-A, and should therefore not be prone to causing the "cheese effect," regardless of one's diet.

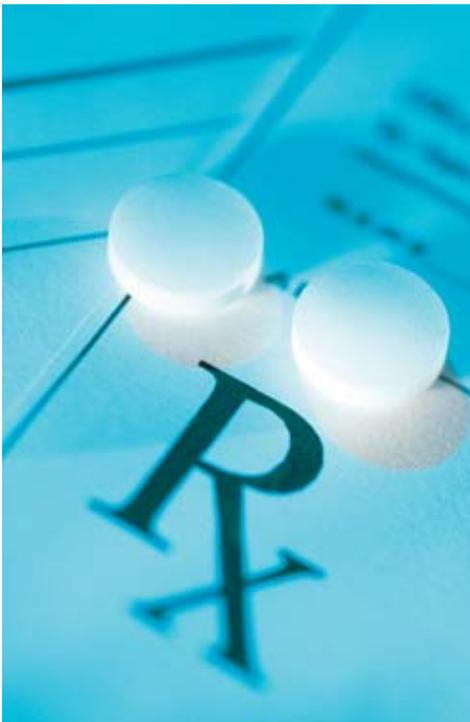
Selegiline (Eldepryl) is the first selective MAO-B inhibitor to be approved for use in PD in the United States. The chemical structure of selegiline is derived from methamphetamine. Thus, when selegiline is eventually broken down it is metabolized into amphetamine derivatives. These amphetamine metabolites have



been associated with cardiac and psychiatric effects in patients with PD. Similarly, rasagiline, is also a selective but "second-generation" MAO-B inhibitor. Unlike selegiline, the major metabolite of rasagiline, aminoindan, has no amphetamine features. Thus, the hope is that rasagiline would be better tolerated by PD patients because it is not broken down into amphetamine derivatives. Indeed, clinical trials have shown once-daily administration of rasagiline is efficacious and well tolerated as monotherapy in patients with early PD and as adjunctive therapy in levodopa-treated patients with motor fluctuations. Additionally, rasagiline has been shown to exhibit neuroprotective activity in several in vivo and in vitro models, but its neuroprotective effect (saving neurons in the brain from dying) in PD patients remains to be defined.

The pharmacology of rasagiline

Both rasagiline and selegiline are rapidly absorbed in the



In human clinical studies, there is at the very least suggestive evidence that rasagiline may slow disease progression in PD.

gastrointestinal tract and readily cross the blood-brain barrier in order to act inside the brain. Both drugs undergo extensive metabolism via the liver; therefore, both drugs should be used with caution in patients with mild hepatic impairment and should probably be avoided in patients with moderate hepatic impairment. Rasagiline is broken down primarily through a mechanism called CYP 1A2. Therefore, co-administration of rasagiline and other drugs that are also inhibitors of CYP 1A2 (such as cimetidine, ciprofloxacin, fluvoxamine) may increase the concentration of rasagiline, and physicians and patients should be aware of this effect. The opposite however is true with co-administration of drugs that are CYP 1A2 inducers (such as omeprazole), and these substances act to reduce rasagiline concentration.

Is rasagiline really neuroprotective?

In addition to their symptomatic effects, both rasagiline and selegiline

have been extensively studied for their potential neuroprotective properties. For example, by virtue of their capacity to inhibit MAO-B, both rasagiline and selegiline prevent the destruction of dopaminergic cells in MPTP-treated animal models of PD. In the MPTP animal model of PD, MPTP is converted by the MAO-B enzyme to a harmful chemical called MPP⁺, which generates hydrogen peroxide and other free radicals. These substances lead to neuronal death and parkinsonian symptoms. In monkeys, pretreatment with rasagiline or selegiline prevented the MPTP conversion to the harmful chemical, MPP⁺, and prevented the emergence of parkinsonian signs.

The drug breakdown is a distinguishing feature between rasagiline and selegiline. Rasagiline is metabolized to aminoindan whereas selegiline is metabolized to derivatives of amphetamine. While rasagiline, and selegiline have both shown neuroprotective and “anti-apoptotic” (or anti-programmed cell

death) properties, in vitro models show that amphetamines may block the neuroprotective effects of selegiline whereas aminoindan does not in the case of rasagiline. More research is needed in this area.

In human clinical studies, there is at the very least suggestive evidence that rasagiline may slow disease progression in PD.

The clinical efficacy of rasagiline

Monotherapy in Early PD

The pivotal clinical study of rasagiline monotherapy in patients with early PD was the Rasagiline [then called TVP-1012] in Early Monotherapy for Parkinson’s Disease Outpatients (TEMPO) study. TEMPO was a 12-month, double-masked, randomized, delayed-start study followed by open-label extension.

TEMPO enrolled 404 PD patients and employed a delayed-start design to evaluate the potential disease-slowing effects of rasagiline in addition to its efficacy and safety in untreated patients with early PD. The idea was to find out if patients who received rasagiline earlier were better off after 12 months when compared to those who received rasagiline later. Patients were randomized to receive once-daily rasagiline 1 mg, 2 mg, or placebo for six months. After six months, the placebo-treated group was switched to rasagiline 2 mg/day, and all patients received active treatment for the next six months. The primary measure of efficacy was change in the Unified Parkinson Disease Rating Scale (UPDRS) score, a standard measurement of PD motor and functional severity.

During the six-month placebo-controlled phase of TEMPO, both rasagiline doses were superior to placebo for improvement in the UPDRS scores. However, the

interesting finding was seen at 12 months when all patients were already taking rasagiline. The patients treated with rasagiline 2 mg for 12 months had significantly better UPDRS scores than patients who first received placebo for six months. They also had better scores than the rasagiline 2 mg for six months group although this difference was not as large.

These data suggest the neuroprotective effects of rasagiline demonstrated in experimental systems may translate into clinically meaningful disease-slowing effect in PD patients. If rasagiline effects were purely symptomatic, then six months of rasagiline treatment would have allowed patients who initially received placebo to eventually catch up to those who received rasagiline from the start, and no difference in UPDRS scores at 12 months would be expected. These findings, which suggest a disease-modifying effect would need to be confirmed in a larger, better-designed clinical trial specifically looking at rasagiline's neuroprotective effect.

Overall, 85 percent of patients entered the open-label extension of TEMPO. Preliminary data from 398 patients treated with at least one dose of rasagiline (some patients receiving rasagiline for up to 6.5 years) have been reported. Of patients who completed two years of treatment, 46 percent still did not require additional dopaminergic therapy. Over the 6.5-year period, the mean annual deterioration in UPDRS scores in patients not receiving additional dopaminergic therapy was two to three points per year, which was much less when compared to other clinical studies than commonly reported decreasing rates of 8-12 points/year in placebo-treated patients with early PD.

Adjunct Therapy to Levodopa in Advanced PD

Two large, randomized, double-blind, placebo-controlled trials of rasagiline as adjunct therapy to levodopa have been conducted. The Lasting Effect in Adjunct Therapy with Rasagiline Given Once Daily (LARGO) study was an 18-week, randomized, double-blind study comparing rasagiline, entacapone (Comtan) and placebo in 687 levodopa-treated patients experiencing motor fluctuations. The primary outcome measure was mean change in daily "off" time.

Rasagiline 1 mg significantly reduced "off" time by an average of 1.18 hours, compared with the placebo reduction of 0.4 hours; and

despite optimized dopaminergic therapy. Unlike LARGO, PRESTO had no active comparator. Patients were randomized to rasagiline 0.5 mg/day or 1 mg/day, or placebo. Again, the primary efficacy measure was mean change from baseline in total daily "off" time.

Patients treated with 1 mg rasagiline experienced 1.8 hours less "off" time, and those treated with 0.5 mg rasagiline had 1.4 hours less "off" time, which were both significantly better than the decrease reported for placebo (-0.9 hours).

LARGO and PRESTO results indicated that short-term rasagiline treatment provides benefit to patients with advanced, fluctuating PD. Further study is needed to determine

LARGO and PRESTO results indicated that short-term rasagiline treatment provides benefit to patients with advanced, fluctuating PD.

increased daily "on" time without troublesome dyskinesias by 0.85 hours. Although the study was not designed to directly compare rasagiline and entacapone, their clinical effects on levodopa-related motor fluctuations were roughly equivalent. These treatment effects with both drugs were similar to those reported in other trials of entacapone and other drugs known to improve fluctuations, such as pramipexole and other dopamine agonists.

Like LARGO, the Parkinson's Rasagiline: Efficacy and Safety in the Treatment of "Off" (PRESTO) study enrolled 472 levodopa-treated patients with motor fluctuations

the effects of long-term rasagiline treatment in these patients.

The clinical safety of rasagiline

A total of 530 PD patients in the TEMPO, LARGO, and PRESTO studies were treated with the recommended rasagiline dose (1 mg/day) for a total of 212 "patient years." Of them, the number of patients discontinuing treatment due to adverse events was not significantly different between placebo and active treatment groups.

Rasagiline monotherapy has an adverse event profile similar to that observed with placebo. The most

frequently reported adverse events in patients treated with rasagiline in TEMPO at 12 months were infection, headache, unintentional injury, and dizziness. At 6.5 years, only 11.3 percent of rasagiline patients had withdrawn from TEMPO due to an adverse event.

The most frequent adverse events in studies of rasagiline 1 mg adjunct therapy, that reported at least two percent more frequently than placebo, included abdominal pain, accidental injury, positional

with other anti-parkinsonian medications and to delay levodopa use, especially in younger patients.

Rasagiline compares favorably with PD medications in other drug classes. Anticholinergic drugs are associated with increased risk of cognitive dysfunction, hallucinations, paranoia and confusion, particularly in older patients. Moreover, they are most effective for resting tremor but have marginal efficacy on the other cardinal motor symptoms of PD. In contrast, rasagiline is uncommonly

convenience of once-daily dosing compared with multiple daily entacapone doses. When used with levodopa, rasagiline appears to confer a lower risk of dyskinesia than the dopamine agonists.

As a neuroprotective agent, rasagiline still needs to be evaluated in a larger clinical trial to determine if the preliminary data suggesting its disease-modifying effect will hold up in a well-powered longitudinal study. ▲

Editor's Note: Dr. Hubert Fernandez may be reached at: fernandez@neurology.ufl.edu.

Rasagiline is uncommonly associated with cognitive or psychiatric side effects and is generally safe in older patients.

low blood pressure, constipation, vomiting, weight loss, and dyskinesia. Unlike selegiline, rasagiline is not associated with amphetamine-like side effects. In clinical studies, rates of dizziness, positional low blood pressure, confusion, and hallucinations associated with rasagiline were no different from rates with placebo.

The long-term safety of rasagiline continues to be monitored in ongoing clinical studies now of several years' duration.

Where does rasagiline belong in the PD armamentarium?

Levodopa remains the gold standard of symptomatic therapy in PD. However, with chronic treatment and advancing disease, the therapeutic window for levodopa narrows, and the risks of motor fluctuations and dopaminergic adverse events may increase. Therefore, it has become common practice to begin therapy

associated with cognitive or psychiatric side effects, is generally safe in older patients, and has broader symptomatic effects.

Dopamine agonists are considered the most effective symptomatic therapy (other than levodopa) in early PD. Additionally, they may reduce the risk of developing motor complications and dyskinesias associated with levodopa therapy. Whether rasagiline delays the onset of motor complications with levodopa has not been established. Compared with dopamine agonists, rasagiline has more convenient once-daily dosing, and does not require dose-titration. Moreover, rasagiline is probably less likely to cause the neuropsychiatric side effects observed with dopamine agonists (such as somnolence, "sleep attacks," hallucinations, psychosis).

As adjunctive therapy, rasagiline reduces "off" time in patients with motor fluctuations to a comparable level as entacapone, but offers the

REFERENCE LIST

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GDNF for Parkinson Disease

By **Franz F. Hefti, Ph.D.**, and
Cynthia A. Rask, M.D.

Thousands of researchers and physicians worldwide are working very hard to bring better and more effective treatment to Parkinson disease patients. There has been substantial progress in many diverse disease areas, and in particular, in new therapies for cardiovascular diseases and cancer.

For Parkinson disease alone, it can be roughly estimated that hundreds of researchers in academia and in industry devote the majority of their energies to trying to find cures, or at least better treatments. This massive effort has brought forward important new understandings of Parkinson disease and will very likely lead to better treatments. However, bringing new and effective drugs to patients is a very difficult and complex process.

It often generates unpredictable challenges of scientific, ethical and legal principles, and it typically takes many years to succeed in bringing a new therapy to market.

The challenges experienced with glial derived neurotrophic factor (GDNF) provide an excellent example of the difficulties encountered when discovering and developing new drugs. GDNF has been tested in Parkinson patients, due to its positive effects on specific types of nerve cells and very encouraging findings in animal models. In the human studies, positive and negative results were obtained. Animal studies testing the safety of GDNF raised concerns about toxicity.

The biotechnology company sponsoring the drug, Amgen Inc., located in Thousand Oaks, California, decided to at least temporarily put the program on

hold¹. Several academic researchers have taken issue with this decision and have expressed the view that further studies in patients may be warranted². Some of the patients who experienced positive effects of GDNF have accused the company of denying them effective treatment³. Who is right in this difficult dispute? Is there a right or wrong position?

What Is GDNF?

GDNF is a molecule that belongs to the group of neurotrophic factors. These factors are natural proteins occurring in the brain, which are able to regulate survival and regeneration of nerve cells. GDNF is the abbreviation for “glial cell line-derived neurotrophic factor,” a name that reflects its history. GDNF was originally purified in 1993⁴ from cells derived from the rat brain and grown in culture dishes. GDNF



attracted strong interest from researchers in Parkinson disease, since it is particularly effective for promoting survival and regeneration of the dopamine-producing cells in the brain (the group of nerve cells which degenerate in Parkinson disease). The beneficial effects of GDNF were demonstrated first on isolated cells grown in culture dishes. Subsequently, GDNF was shown to effectively stimulate regeneration of the dopamine-producing cells in animal models of Parkinson disease.

The positive findings with GDNF administered to the animal models were first reported in 1995⁵. They were published in leading scientific journals such as *Nature* and immediately attracted a lot of attention, and were regarded as a significant breakthrough for Parkinson research. The animal studies fueled speculation that GDNF might be beneficial in treatment. If affirmative, GDNF treatment would be expected to slow down or stop the disease progression, an achievement the current drugs had not met.

Unfortunately, giving GDNF to Parkinson patients was not straight forward, since the substance

could not be taken orally or given by injection into a vein, muscle or skin. GDNF is a protein, a large molecule, which is digested when taken as a pill, and which is incapable of reaching the brain when injected into muscle, other tissue, or the bloodstream. To reach the dopamine-producing cells in the brain, and to treat them effectively, GDNF has to be given directly into the brain, in the vicinity of the cells that scientists were trying to treat.

In small animals, rats and mice for example, researchers were able to inject GDNF with a special syringe that placed it directly into the brain. In larger animals such as monkeys, a pump device was implanted under the skin in anesthetized animals, and a tiny tube was inserted through the skull to deliver GDNF directly to the desired brain areas. These procedures were well tolerated by the animals and were in line with bioethical requirements established by the National Institutes of Health.

Clinical Studies with GDNF

To be able to give GDNF to humans it is necessary to implant a special

device. Patients undergo surgery (to implant two pumps), each about the size of a hockey puck, under their skin in the abdominal region. The pumps are filled with GDNF and can be refilled by injections through the skin. GDNF is delivered from the pumps to the brain by small tubes that run under the skin from the abdomen up to the head, through small openings in the skull, and then into the brain to the areas occupied by the dopamine-producing cells. The operation is relatively minor, easily tolerated and done under general anesthesia. However, it is not entirely risk free. There may be rare complications of bleeding in the brain, infections and movement of the tubing, and, once implanted, the pump and delivery devices cannot easily be removed and may become a minor factor of physical or emotional discomfort for patients. Common sense and medical ethics indicate that the pump devices should only be implanted in patients with a clear medical need, and those who have given full informed consent to be part of an institutional review board-approved research trial.

Three human studies have been conducted to date. In all the studies, the human protein GDNF, produced in vitro with bioengineering procedures by Amgen, was used. The technically precise description of the protein is “recombinant methionyl human GDNF” which was given the name “liatermin.” In the first study⁶, five patients were treated for two years in a so-called open-label protocol. With this protocol, the patients and the physician taking care of them all were aware that all patients were receiving the drug (we call that open label). The design did not distinguish between actual drug effects and placebo effects.

There were improvements in

all five patients and there were no significant negative effects. The study received an abundance of media attention and triggered strong interest in further evaluations of the therapeutic potential of GDNF. The second study⁷, which also used an open-label protocol, evaluated the effects of GDNF given to one side of the brain in ten Parkinson patients. After six months of treatment, most of the ten patients showed improvements of their disease state. The improvements were seen on both sides of the body, even though GDNF was infused on one side of the brain only. The third study⁸ was the largest and most significant one. It used a randomized double-blinded protocol, in which 17 patients received the drug and 17 other patients received an infusion of placebo (salt water). Neither the patients nor the physicians evaluating them after the surgery knew whether the patient was receiving the drug or placebo. After six months of treatment, there was no overall difference in the Parkinson symptoms and signs on neurological examinations between the patient group that received GDNF or the patient group that received placebo. A small positive effect of the GDNF therapy was observed on brain imaging studies, in which the dopamine-producing nerve cells were visualized with a radioactive agent. A small number of patients experienced adverse events due to the implanted pump device. Otherwise, the implantation and treatment was well tolerated.

Summarizing the clinical studies, it is possible to conclude that the GDNF treatment, comprised of the implanted pump device and the actual drug, were well tolerated. (A small number of patients experienced problems with the pump device.) Regarding efficacy

of the treatment, it was difficult to draw a definitive conclusion. There were signs suggestive of biochemical effects on the brain seen in the imaging studies, but there was no conclusive evidence that GDNF treatment provided meaningful benefit to Parkinson patients. Positive findings in open-label studies have been observed before in Parkinson patients given a variety of other therapies, prompting many experts to discount results from such studies and to focus entirely on data from double-blinded trials. The positive findings in the open-label studies were attributed mainly to a “placebo effect,” which occurred to some extent in nearly all previous Parkinson disease clinical studies⁹. The placebo effect reflects the psychological anticipation of a beneficial effect, which can then be translated into improvements in the signs and symptoms of the disease. A positive effect of GDNF on Parkinson symptoms as compared to the placebo effect was expected in the double-blinded studies, but it could not be proven. Nevertheless, the small positive effect in the imaging signaled that GDNF had what we think was a positive biochemical effect on the brain.

Safety Risks

The clinical studies with GDNF revealed limited risks associated with the pump device. In addition, the double-blinded study pointed to a further risk, the formation of antibodies against GDNF in treated patients. In a small number of patients, the immune system produced neutralizing antibodies which recognized and bound to GDNF. Anti-drug antibodies are sometimes observed with biologic molecules such as GDNF, and they do not necessarily limit the use of the drug. However,

these antibodies create reason for concern, since they may inactivate naturally occurring GDNF in the body of patients and potentially lead to detrimental effects. Outside of the brain, GDNF is involved in sensory functions such as touch, heat and pain sensitivity. If antibodies interfere with GDNF outside the brain, they might alter these sensations. Although it is a theoretical concern at this point, it needs to be kept in mind for future studies with GDNF.

All drugs are tested extensively in animals before they are given to human patients. In addition, there are further long-term toxicity studies that are conducted in animals in parallel to the initial clinical studies. In such a study, high doses of GDNF, up to approximately six times higher than those given to humans, were infused into the brain of monkeys for six months in a similar way as the drug was given to human patients. The treatment produced an unexpected degenerative change in some of the monkeys receiving the highest doses. These changes were seen in the cerebellum, a part of the brain involved in the control of motor behavior and balance. There were no behavioral consequences of this change and its significance was hard to gauge. Imaging studies of Parkinson patients treated with GDNF did not show any abnormalities in the cerebellum¹⁰. However, the results of the imaging study do not rule out the possibility that GDNF has a detrimental effect on the human brain.

Based on the negative result of the double-blinded clinical study and based on the risks that are potentially associated with GDNF, Amgen Inc., the company producing the drug, decided to temporarily halt the program and re-evaluate

the overall situation. The risk to continue was determined to be too high even for those patients who had implanted pumps, and had reported positive effects presumably due to the GDNF. This decision reflected a careful risk/benefit analysis, which every biotechnology and pharmaceutical company is required to perform in order to receive permission from regulatory agencies to continue a study or redesign a new study. Amgen's decision to at least temporarily halt the GDNF studies received substantial press coverage because some of the patients who participated in the clinical trial strongly argued that they deserved continued access to the drug. These events triggered intense, still ongoing discussions in the expert communities of academic physicians, the biotechnology and pharmaceutical companies, and the regulatory agencies.

What's Next?

Patients are the customers of the biotechnology and pharmaceutical companies, and these companies are therefore very responsive to patient comments and input. The patients and their advocates who requested continuation of the GDNF studies had an influential voice. In addition to the patient advocates, many academic researchers vocalized concerns about the halting of the program.

First, they argued that the negative double-blinded study did not provide a conclusive negative result. Indeed, patients were treated for six months only, making it possible to argue that beneficial effects might have been observed following longer treatment intervals. However, the initial studies showed positive effects after only three months of treatment.

A second argument related to the details of the infusion device. The

tubing used to deliver GDNF to the brain distributed the drug over a small brain area only. Experts in this technology have argued that a different design of the end of the tubing from which GDNF flowed would distribute the drug more widely and produce improved results.

A third argument was linked to the patient population included in the clinical studies. It is possible, although not certain, that patients of different age and suffering from different degrees of severity of Parkinson disease may show a better result (failure could have been due to patient selection).

The pros and cons of continuing GDNF studies are being discussed widely, in informal discussions; in formal interactions between the company, the regulatory agencies and the clinical experts; and in public exchanges in the scientific literature¹¹. It is not possible to predict the outcome at this point in time. However, the Parkinson community should be assured that the voices of the experts and the patients are being heard. The broadly distributed decision mechanisms in drug trials, which involve companies, academic experts, governmental experts, regulatory agencies, and patient advocates, can be expected to lead to a reasonable, ethical and widely accepted decision.

Whatever the outcome of the ongoing discussions, the GDNF program will continue in a general way. The findings obtained in animal models of the disease make a compelling case that GDNF has a beneficial effect on the dopamine-producing cells affected by Parkinson disease. Delivery of GDNF with pumps may yet prove to be the right approach. If not, it may be possible to provide GDNF to the brain with other technologies, including gene therapy. Molecules similar to GDNF

may be useful, given by pump infusions or other delivery devices. The scientific literature is full of examples of publications showing beneficial effects of such approaches in animal models of Parkinson disease. For example, Ceregene Inc., a small biotechnology company located in San Diego, California, is currently pursuing the administration of neurturin, a molecule belonging to the same protein family as GDNF, by gene delivery¹². The current controversy about GDNF infusion therapy is an important step in developing optimal therapy for patients with Parkinson disease. ▲

Editor's Note: *Dr. Hefti, a member of the NPF Centers Review and Scientific Advisory Boards, is executive vice president of drug development at Rinat Neuroscience Corp., a biotechnology company located in South San Francisco, California. Previously, he held senior executive positions in drug discovery at Merck & Co. and Genentech Inc. Before joining industry, he was a professor at the University of Southern California and the University of Miami. Dr. Rask currently works as consultant in the biopharmaceutical industry. Until recently she was a division director in the Center for Biologics Evaluation and Research at the FDA and, before that, supervised drug development programs at Genentech Inc. and Abbott Laboratories. The authors wish to thank their colleagues in academia and industry who reviewed the manuscript and provided many helpful comments.*

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COMMUNITY



Tel-Aviv Sourasky Medical Center

Tel-Aviv, Israel

The NPF Parkinson Center at Tel-Aviv Sourasky Medical Center is a tertiary medical center with 1,200 inpatient beds and a large outpatient clinical service. Founded nine years ago, the center is closely affiliated with Tel-Aviv University's Sackler School of Medicine; seven Parkinson Center personnel hold joint appointments in the medical center and in the medical school.

The Parkinson Center and its Laboratory for Gait & Neurodynamics are both located in an outpatient area of the hospital, promoting close interactions among researchers and clinicians. Five certified neurologists provide medical care to patients with PD and their families. Four nurses support the activities of the center, including a clinical coordinator, a nurse who runs the DBS program and two nurses who support drug studies and genetic research. Additional staff members include a social worker, a speech and swallowing pathologist, a neuropsychologist, a dietitian, three physical therapists, and four secretaries.

The laboratory is directed by two senior Ph.D. scientists, with assistance from four research assistants, two Ph.D. students, and seven master's students. In addition, a research group investigates the interplay between occupation, genetics, and the risk of developing PD, and collaborates with the genetic institute on the genetics of PD.

About 200 PD patients and their caregivers are seen by the Parkinson Center staff each month. A very active speech and swallowing disturbances clinic provides evaluations and treatment including FEES evaluation of swallowing, one-on-one treatment sessions, group therapy

for speech and communication, and LSVT sessions. Support groups are conducted throughout the year by the Parkinson nurse specialist and the social worker.

Working together with its Laboratory for Gait & Neurodynamics, the center's clinical research focuses on the characterization, mechanisms, and treatment of freezing of gait in parkinsonism as well as on the risk factors for falls and near falls. A major emphasis is placed on the contribution of stride-to-stride rhythmicity, coordination of the left and right legs, and cognitive function. Scientists examine the role of cognition, especially executive function, on walking and fall risk in PD patients, and potential therapeutic interventions including pharmacologic and rehabilitation techniques.

The center is currently involved in five prospective, double blind, phase III, multicenter drug studies for all stages of PD, and four long-term, open-label studies, all sponsored by drug companies.

The center's research also investigates the causes of orthostatic hypotension and loss of consciousness, with specific interest in the brain's regulation of cerebral blood flow and the contribution of post-prandial hypotension to gait disturbances and falls. Researchers study psychosis and behavioral problems, including impulse control disturbances. For example, researchers recently observed that 14 percent of the center's patients have underrecognized and undertreated hypersexuality. In parallel, researchers are developing a genetic research branch, having recently established a DNA bank of the center's PD patients and many of their spouses. ▲



Nir Giladi, M.D. (right), director of the Movement Disorders Unit - NPF Parkinson Center, greets Gabriel I. Barbash, M.D., MPH (left), director general, Tel-Aviv Sourasky Medical Center



The multidisciplinary staff of the Movement Disorders Unit - NPF Parkinson Center take care of more than 2,000 persons with PD and their families.



Parkinson Center Nijmegen (ParC)

Radboud University Nijmegen Medical Center
Nijmegen, The Netherlands

A tertiary referral center for patients with Parkinson disease (PD) for more than 30 years, ParC is proud to be a National Parkinson Foundation Center of Excellence – the first NPF Center of Excellence in the Netherlands. Its longstanding mission includes four components:

- to improve the quality of life of people with PD (and their families),
- to conduct high quality Parkinson research,
- to improve the efficacy of interventions to benefit Parkinson patients, and
- to spread news about the disease and its treatment.

On June 28, 2006, ParC held a conference to celebrate the opening of its new multidisciplinary Day Care unit. Participants heard presentations from noted national and international experts and viewed part of the documentary, “*Bridge Over Midnight Trembles*,” about the life of well-known Australian actor and PD patient, Richard Moir. Joining ParC’s Medical Director, Bastiaan R. Bloem, M.D., Ph.D., as conference speakers were ParC Scientific Director Dr. M. Munneke as well as colleagues from the European Parkinson’s Disease Association, the Dutch Parkinson Foundation, Stichting Parkinson Nederland, Radboud University Nijmegen Medical Center, and many others.

In addition to the June event, the dedicated ParC staff organized a conference on March 24th to honor the work of the now-retired Parkinson specialist Dr. MWIM Horstink, who received the “Miep van der Grohe Award” (for excellent health care for Parkinson patients) from the Dutch Parkinson Foundation earlier this year.

The center’s main research focuses on gait and

balance control in PD and other movement disorders. The center has a fully equipped, state-of-the-art laboratory where comprehensive analyses of walking and balance can be performed. Intervention studies concentrate on drug therapy, neurosurgery, physiotherapy, and deep brain stimulation techniques.

Additional studies address different aspects of motor impairment in Parkinson disease, such as handwriting, pointing movements of the arms, mental rotation processes and mechanisms underlying motor preparation. Another research area focuses on clinically relevant elements of PD, such as the pathophysiology and treatment of sweating and drooling in PD.

In recognition of his outstanding research into the pathophysiology of Parkinson disease, ParC’s medical director, Dr. Bloem, received the 2002 “Professor Hans Lakke Award” from the Dutch Parkinson Foundation.

ParC is proud to offer patients and their families high quality, individualized care by a dedicated multidisciplinary team of health professionals, consisting of neurologists; Parkinson nurses; speech, physical, occupational, and sex therapists; rehabilitation medicine professionals; neuropsychologists and if needed, a psychiatrist; dietitians; and social workers. The multidisciplinary team is led by team coordinator, Mrs. Monique Schmidt.

A special feature of ParC’s approach is the development of a dedicated regional network (called ParkNet) consisting of a small group of health professionals, all trained by the center, and who all work within 15 minutes travel time of the patients’ homes. This ensures that ParC’s

multidisciplinary health plan can be conveniently implemented within the direct vicinity of the patient’s home.

Another outstanding feature of ParC’s approach is its use of communication technology to provide information about Parkinson disease to both patients and professionals. Using ICT technology, bundled under the term ParkinsonWeb, the center has established electronic patient files, and designed an up-to-date website and an e-health care service, both of which will become operative later this year.▲



Dr. Bastiaan R. Bloem welcomes participants to the June 28th conference in celebration of ParC’s new Day Care unit.



Mw. Mary Baker, President, European Parkinson’s Disease Association, was a featured speaker.



Victorian Comprehensive Parkinson's Program

Cheltenham, Victoria, Australia

A National Parkinson Foundation Center of Excellence since 2005, the Victorian Comprehensive Parkinson's Program (VCP) offers services to people with Parkinson disease from Victoria, South Australia, Tasmania, and the Australian Capital Territory.

The Movement Disorders Program was founded in 1993 and a research arm was added the following year. It has continued to grow and develop over the past 12 years and, currently, the program operates on two campuses, providing services to over 1,200 persons with Parkinson disease and offering support to more than 500 caregivers, in both the public and the private health sectors.

Inpatient, outpatient, community, and outreach services are offered, along with educational and support programs in urban and rural areas. These services are provided by skilled professionals who work within multi- and/or trans-disciplinary teams, and who offer individual guidance and therapeutic intervention based on thorough assessments and consultations with the patient and family. In addition, a holiday program offers a range of vacations and recreational activities for people with PD and their caregivers.

Joining Professor Robert Iansek, a founding member of the program and its medical director, are five additional medical professionals: a neurologist, a geriatrician, a psycho-geriatrician, a psychiatrist, and a neurosurgeon. The program also has five dedicated nursing staff and 23 allied health staff members (including physiotherapy, occupational therapy, speech pathology, social work, and neuropsychology disciplines) to support the many outpatient, community, and outreach programs that are offered.

Each of the public and the private sectors of the program employs a coordinator who coordinates the outpatient and outreach facilities within community-based programs, and provides information, education and support to people with PD, their families, other health

professionals, and the wider community.

The Geriatric Research Unit operates within the Movement Disorders Program, and is staffed with a manager/biomechanist, a post-doctoral research fellow, and two research physiotherapists. The overall thrust of research has been toward the improved understanding of basal ganglia function and its malfunction in PD. Previous research from this department has demonstrated that decreased step length is the primary deficit in gait in people with PD. Gait rehabilitation programs now use conscious attention and/or visual cues to increase step length to improve walking speed and pattern. Investigations into concurrent tasks during walking have confirmed the need for directed attention during dual-task performance, and a recently completed project yielded results suggesting that festination and freezing of gait in people with PD result from a combination of hypokinesia and sequence effect, and that visual cues may eliminate festination and freezing of gait. Current research topics include:

- A systematic investigation of gait: What can the spatiotemporal variable of gait tell us about central control of gait and the impact of Parkinson disease?
- Step variability leading up to, and during, a planned stop in Parkinson's gait.
- Normal walking patterns of adults in Victoria.
- Effect of stride length on festination and freezing of gait.
- Deep Brain Stimulation – impact on function and quality of life.
- Under development: an investigation into central control of automatic and attentional gait using Positron Emission Tomography (PET) in healthy and PD persons.

Research within the VCP has generated the publication of textbooks, patient handbooks, instructive videos, presentations at educational seminars and conferences, and numerous journal articles. ▲



Back row, (L) to (R): Anna Murphy (PhD), manager, Gait Laboratory; Professor Robert Iansek, director, Movement Disorders Program (MDC); Jan Flynn, administration officer, MDC; Dianne Cameron, research physiotherapist, Geriatric Research Unit (GRU); front row, (L) to (R): Mary Danoudis, physiotherapist, MDP and GRU; Kerry Jervis, administration officer, MDP; Barbara Went, coordinator, MDP; Barbara Winkler, occupational therapist, MDP; Frances Huxham (PhD), post-doctorate research fellow, MDP and GRU; Camilla Page, administration officer, GRU.

Physiotherapist, Margaret Bruce, with a PD patient.



The Top Questions and Answers from NPF's "Ask the Doctor" Forum



Hubert H. Fernandez, M.D.



Kelly D. Foote, M.D.



Michael S. Okun, M.D.

By **Hubert H. Fernandez, M.D.**, **Kelly D. Foote, M.D.**, and **Michael S. Okun, M.D.**, University of Florida Movement Disorders Center, a National Parkinson Foundation Center of Excellence

Thousands of people with Parkinson disease write to us online at the "Ask the Doctor" forum. It is a free service where we are able to answer questions from patients, family members, and health professionals about Parkinson disease. This forum is designed to deliver needed information all over the globe, and it is our privilege and honor to present to you some of the "Top Questions" from the last few months. We encourage you to log on to www.parkinson.org and sign up to receive our daily e-mail summary of the day's questions and answers.

Q. *Glutathione for Parkinson Disease?*

Could you tell me what dosage and strength of glutathione to take? I am willing to give it a try. Thanks.

A. This drug is currently being used for research and is under investigation at the University of South Florida with Dr. Robert Hauser, if you want to join his study. For details, call Terry McClain, ARNP, at 813-844-8070.

It is given intravenously through a vein, and I do not recommend it for PD patients until more data comes forward. There are people administering the drug, but I do not recommend it at this time without further data.

Q. *Sleep Problems and Parkinson Disease?*

At times, PD patients on Sinemet may verbalize and/or have vivid dreams while deep sleeping.

Is this "par for the course" and normal for someone who has been taking Sinemet for three years? Is it the Sinemet that causes this? Is it

best to "live with it," or take some other medication to reduce it?

A. It's par for the course and these sleep problems can be made worse with Sinemet and agonists. Therefore, some people choose not to take a night-time dose of a dopamine agonist.

Many with Parkinson disease have this REM (rapid eye movement)-sleep behavioral disorder (acting out their dreams), even prior to diagnosis.

Most of my patients respond to a bedtime dose of clonazepam, but be cautious, as this can have side effects. Some patients need a sleep study for diagnosis and treatment.

Q. *Shortness of Breath and Parkinson Disease?*

I am a 44-year-old, single mother of three teenage boys and I have been experiencing shortness of breath. I was even sent to the Emergency Room the other day because they thought I was having a stroke. I saw three doctors about this problem and no one told me it was due to my Parkinson's. I have had Parkinson for 12 years now and

I have just started experiencing this problem. I wanted to let other PD patients know, and would you please explain it further.

A. Shortness of breath can be seen in Parkinson disease. In many cases, it is linked to Parkinson disease anxiety. Many PD experts give Sinemet, agonists, and extenders at more frequent intervals (every two, three, or four hours). One strategy is to reduce the off time and wearing off that can precipitate the anxiety/shortness of breath. The dose or frequency of medications can be changed. In some situations, adding a benzodiazepine like clonazepam or Xanax can be helpful.

The shortness of breath can sometimes be pulmonary or cardiac so a complete medical workup is needed by your internist. If medication changes do not help, the addition of a psychiatrist may also expand your options.

Finally, in some cases expiratory muscle strength training by someone like Chris Sapienza can be helpful to strengthen those muscles. Contact Chris at sapienza@csd.ufl.edu.

Q. Weight Gain and DBS?

I am a 47-year-old wife and mother of two young boys. I was diagnosed with PD at 44, but my symptoms started nearly two years before that. I am strongly considering having DBS. I know that it is associated with weight gain, but I don't know how much. Do people gain a lot? Why does DBS cause weight gain? Does anyone know? It certainly won't stop me from having the surgery, and I will obviously have to eat more carefully, but I'd like to know, if possible. Thank you.

A. Well, I regret to confirm that you may have to be a little more careful about watching what you eat after DBS. It is true that people who are treated with DBS for Parkinson disease tend to gain weight. The average patient gains ten to 15 pounds after DBS. Interestingly, the average Parkinson patient loses five to ten pounds after being started on dopaminergic medication.

Research at the University of Minnesota and in Bordeaux, France, suggest that this weight gain is related to decreased resting energy expenditure (REE, or metabolic rate) following DBS. This is presumably because the tremor and dyskinesia that are relieved by DBS were burning a significant amount of energy.

I am sure that this is part of the explanation, but I believe there are multiple factors involved. With increasing awareness of this common DBS-related weight gain, we are now emphasizing the need for

proactive management of body weight in PD patients undergoing DBS. The weight gain is avoidable if you're careful – not all of our patients are gaining significant weight.

Q. Number of Programming Sessions Needed for DBS?

My wife had DBS surgery last June for severe essential tremor in both hands (the right hand was targeted in the surgery), and has had two programming sessions. The resulting benefit is real (and better than before the surgery), but not ideal.

We understand that it can take numerous programming sessions before the optimum benefit is reached. In your knowledge and experience, please give us a ballpark figure of the number of programming sessions (on average) needed for optimum results.

A. Thank you for the question. As you might expect, the number of programming sessions required to achieve optimal benefit from DBS depends upon the patient, the surgery, and the programmer. A more experienced programmer is likely to maximize DBS benefit in fewer sessions. An electrode that is perfectly placed in the brain will be easier and more efficient to program. And a patient with essential tremor (ET) on minimal medication will be far less complicated to program than a patient with advanced Parkinson disease who is on a complex medication regimen that needs to be adjusted simultaneously with programming to find the right combination of medications and stimulation that will maximize the outcome for that patient.

For ET, I would say that maximum benefit can usually be reached after three or four programming sessions. PD is more complicated and commonly requires between five and ten programming sessions with concurrent medication adjustments to optimize the therapy. These are just ballpark estimates, of course, and patients vary quite a bit. If predicted benefit is not achieved after several programming visits, it may be due to a suboptimally-placed electrode. (No amount of expert programming can compensate for a poorly placed electrode.)

The information published in this "Ask the Doctor" Forum is not intended to replace, and should not be interpreted or relied upon as, professional advice, whether medical or otherwise. Accordingly, please consult your own professional for all advice concerning medical, legal, or other matters published in connection with this Forum. NPF assumes no liability of any kind for the content of any information transmitted to or received by any individual or entity in connection with such individual or entity's use of the "Ask the Doctor" Forum of the NPF website, and NPF does not endorse or recommend any such information.

ATTP Transforms Parkinson Care Delivery

Did you know that:

- it is estimated that 50 percent of persons living with Parkinson disease are being treated by their primary care physician?
- not all neurologists are up-to-date on Parkinson care?
- not all “front-line” providers fully understand Parkinson disease?
- prior to ATTP, there were few opportunities for health care providers to learn about Parkinson disease, or to experience the benefits of a team approach to patient care?

Recognizing that persons with a complex chronic illness like Parkinson disease need a system of care that is effective, timely, efficient, and safe, the National Parkinson Foundation created a two-pronged program, Allied Team Training for Parkinson (ATTP) – a unique, one-of-a-kind model interdisciplinary training program specifically designed to change the way Parkinson care is delivered.

“Our unique ATTP program is relevant to today’s needs. It addresses real concerns not being addressed as systematically in any other program of which we are aware,” said Ruth Hagestuen, R.N., M.A., ATTP project director.

Through this signature program, health care providers in the following six professions have the opportunity to receive in-depth knowledge on how to assess and treat persons with PD in an interdisciplinary setting:

- Occupational therapy
- Physical therapy
- Speech-language pathology
- Nursing
- Music therapy
- Social work

Plans are underway to expand the training to physicians and other professions such as pharmacists, dietitians and others, as funding permits.

The first part of the program is an intensive 4-1/2 day curriculum, leading to NPF certification, through which trainees practice integrated care planning in teams, using case study vignettes, role play, and videos of actual persons with Parkinson. Trainees also spend time learning state-of-the-art assessment and treatment techniques, and hearing about the impact of Parkinson disease on people’s lives directly from persons with young-onset PD and family caregivers.

Building on the knowledge base of the 4-1/2 day curriculum, the second part of the program involves follow-up consultation services to assist teams, on

site, as they work together to deliver state-of-the-art care designed to address the complex needs of persons impacted by Parkinson disease and their family members.

Since the program’s inception in 2002, ATTP has had a steady growth and is increasingly in demand across the country. To date, ATTP has completed ten trainings, graduating and certifying more than 453 practitioners and students. The most recent training was held June 21-25, 2006, in Portland, Oregon and more trainings are scheduled for the future:

Date	Location
October 11-15, 2006	New York City, NY Bellevue Hospital Parkinson Center
November 15-19, 2006	Phoenix, AZ Muhammad Ali Parkinson Center
March 21-25, 2007	Boca Raton, FL To be determined
June 20-24, 2007	Honolulu, HI Kuakini Medical Center

“ATTP has significantly impacted participants and changed their understanding of the impact of Parkinson disease, leaving them with a better understanding of their role and the role of other professions in providing care for persons with PD,” Hagestuen said. “Results demonstrate that ATTP produces not only significant knowledge gain, but a palpable excitement and renewed interest in working with persons with Parkinson.”

For more information, contact Ruth Hagestuen, R.N., M.A., at rh@parkinson.org, or contact Maite Moro for applicant information at mmoro@parkinson.org. ▲

NPF Provides Support for Texas Voice Project

People with Parkinson disease often focus so much on the physical symptoms of the disease, they don't realize how much they've lost their ability to communicate with others.

It can happen gradually... store clerks begin to express difficulty understanding them. Friends stop including them in conversations. Even family members begin to ignore them, making them feel isolated and withdrawn.

To change all that, a new pilot program in Dallas, Texas, called the Texas Voice Project for Parkinson Disease, Inc., is using the Lee Silverman Voice Treatment (LSVT), with outstanding results.

First developed by Dr. Lorraine Ramig in the late 1980s and named for the first patient who benefited from it, LSVT strengthens the muscles of the entire speech mechanism and teaches patients how to put forth more effort when they speak by learning to *"think LOUD."* For Parkinson patients to communicate effectively, they must feel as though they're speaking loudly, though their volume will sound normal to others.

Samantha Elandary, a speech pathologist and director of the new Texas Voice Project, pointed out that before

her LSVT training nine years ago, nothing worked for her Parkinson patients.

"It was so frustrating," she said. "You'd see people's lips move, but nothing came out." Since she began using the LSVT method, she has successfully helped over 150 Parkinson patients.

Determined to make this therapy available to an even wider group of Parkinson patients – regardless of their ability to pay – the National Parkinson Foundation is providing essential support for the program. Medicare, local fundraisers, and grateful patients are making up the difference.

The therapy, said NPF Chief Operating Officer Jose Garcia-Pedrosa, "is a precious tool that clearly has a physical and psychological impact."

Through the new Texas Voice Project, which held its kickoff celebration on May 20, 2006, speech language pathologists who are certified to offer LSVT provide a month of intensive therapy, followed by a maintenance program, designed especially by Elandary, that includes

(continued on page 30)



Left to right: Dr. Cynthia Fox, executive vice president, LSVT® Foundation; Mary Ann Sprinkle, director of development, NPF; Samantha Elandary, director, Texas Voice Project; and Jose Garcia-Pedrosa, chief operating officer, NPF



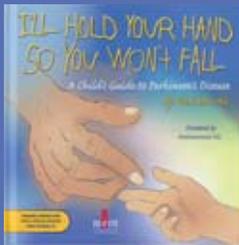
The Texas Voice Project held its kickoff celebration on May 20, 2006



Lois Williams and Samantha Elandary



Jim West and Mary Ann Sprinkle



Rasheda Ali, Daughter of Boxing Legend Muhammad Ali, Presents New Book

At the invitation of the National Parkinson Foundation Outreach Center of Lee County, Rasheda Ali visited Southwest Florida in April (Parkinson Awareness Month) where she met with fifth grade students at J. Colin English Elementary School, had lunch with them, and changed their lives forever. In discussing her new book, *I'll Hold Your Hand So You Won't Fall*, with the children, she was able to help them gain a better understanding of how they can improve the quality of life for their grandparents, neighbors and others they know with Parkinson disease.

A daughter of boxing legend Muhammad Ali, Rasheda wrote the new book to help her own children – Biaggio Walsh, 7, and Nico Walsh, 5 – gain a better understanding of the disease.

“My youngest one was four at the time when he asked, ‘Why is Papi shaking?’ Naturally, I’m thinking ‘Papi has Parkinson disease.’ But I really wanted to have a better answer for them,” Rasheda said.

The NPF Outreach Center of Lee County donated copies of Rasheda’s book, which had been purchased by the local Area on Aging, to area schools and to the Lee and Collier County Library Systems. The local outreach coordinator, Jeanne Csuy, suggested inviting Rasheda Ali to the school and helped land the school its celebrity author. The NPF Outreach Centers of Lee and Collier Counties also hosted a reception in her honor, and she was the featured speaker at an outreach center luncheon the following day. ▲



Clockwise: Rasheda Ali, daughter of boxing legend Muhammad Ali, presents her new book to the NPF Outreach Center of Lee County. NPF’s Chief Operating Officer, Jose Garcia-Pedrosa, was on hand to welcome Rasheda Ali. Jeanne Csuy, outreach coordinator, made the suggestion to invite Rasheda Ali to the school.

(continued from page 29)

individual follow-up visits, weekly support group meetings, a singing group and annual get-togethers.

One component of the maintenance program – a support group called The Loud Crowd™ – gives participants a chance to discuss common problems and to share their successes while using their new “loud” voices.

Richard Hacker, a 70-year-old retiree, reports that LSVT has “really given me confidence.” His voice had grown softer and softer to the point where people stopped paying attention to him. “You think people are being rude until you realize they can’t hear you,” he said in a May 9, 2006, article in the *Dallas Morning News*.

For Jim West, an 82-year-old Dallas-area singer and voiceover artist, LSVT has stabilized his voice and enabled him to continue singing and narrating films. “When someone gets their voice back, you see what it does for their self-respect. It gives you your life back.”

Elandary, who has worked with numerous Parkinson patients through the years, agrees that one’s ability to communicate through speech is vitally important.

“Since the muscles used for speaking are the same muscles used for swallowing and breathing, improving one’s speech and voice is about more than just being heard and understood,” she said.

“All the other problems of Parkinson disease – the tremors, the stiffness, the shuffling walk – overshadow the vocal disorders,” she added. “If we can help people regain or retain their voices, they can handle the rest better.”

For more information on the Texas Voice Project, call 214-862-0101, write to contact@texasvoiceproject.org, or visit www.parkinson.org.▲

Parkinson Profile – Nancy Grant

Nancy Grant has worn many “hats” in her 63 years. She was an international flight attendant for Delta Airlines for 30 years, and the owner of a successful art gallery and “tropical” department store in the Florida Keys for 15 years. She’s a wife, a stepmother, a sister and a friend to many.

But one thing she never counted on becoming was a person with Parkinson disease.

One morning, as Grant and her husband awoke at 4 a.m. to set up and work the Big Pine (Florida) Flea Market, she noticed that she was unusually tired. She couldn’t seem to get going.

Over time, the fatigue became overwhelming and she began to lose strength.

“When I brushed my teeth, I did not have any power in my hand,” she recalled. “It was like the battery went dead. I started having trouble in the shower handling the wash cloth and the soap.”

Then, she noticed that her handwriting, once big and bold, had become small and scribbly, like “chicken scratch,” she said.

Though she made a mental note to ask her doctor about these strange symptoms at her next examination, a friend’s concern motivated her into action.

“One of my friends would come into my shop and ask me, over and over, ‘Are you okay? You seem tired.’ Finally, I asked him, ‘Why are you asking me if I’m okay?’ And he replied, ‘Because you’re drooling!’”

That’s when she knew something was wrong. The next day, she saw her doctor, who referred her to a neurologist at nearby Mariner’s Hospital in Tavernier, Florida. When she was told she had Parkinson

disease, she was shocked and asked the neurologist to write the name of the disease on a piece of paper.

“I kept staring at that piece of paper in disbelief. I had not had a drink in 20 years, nor attended a meeting (for recovering alcoholics) in ten years, but that night, I desperately needed to attend a meeting. I felt like I was in someone else’s body.”

In the past, Grant had learned, through a 12-step program, how to avoid seeing herself as a victim. Now, with her Parkinson diagnosis, she knew it would take all her strength once again not to see herself as a victim. Going to that meeting gave her a sense of relief and the strength she needed, and she’s been making positive changes in her life ever since.

First, she sold her business – at a nice profit. Then, six months after being diagnosed, she “jumped” into retirement with a sky-diving adventure.

“I wanted to feel I had a sense



Nancy Grant gets ready for her sky-diving adventure with help from husband, Tom.



Sky-diving provided an “exhilarating rush” and a way for Nancy Grant to overcome her fears.

of control over my life,” she said. “This was something I had to do to overcome my own fears.”

Though she had never been sky-diving before, she couldn’t wait to try it. She was the only novice in the group on the day of her jump, but she followed directions well and had a smooth landing.

She liked it so much that she did it again, a year later, to mark the first-year anniversary of her retirement.

Although her husband, Tom – a private pilot and an artist – has never joined her in jumping out of a plane, he’s always there, on the ground, cheering her on, with her stepdaughter, April, and April’s husband, Jeffrey.

“I’m grateful I have a wonderful husband and family and that I’m not alone,” Grant said, adding that she keeps a “gratitude list” that helps her stay positive and motivated.

Although she takes life slower these days and paces herself, Grant is as determined as ever to live life to the fullest. She keeps active – swimming, walking, going to meetings, and helping others. And as soon as she gets the chance, she’ll go sky-diving again.

After all, she said, “You’ve got to push yourself to the limit.” ▲

Surrounded by Love

by **Carmelene Siani**,
Tucson, Arizona

I sat in the car behind the wheel watching my husband as he came out of the Circle K – slightly bent over, shuffling a bit, the Coke in his hand trembling. A big, tough-looking man wearing a tank top and baseball cap took hold of the door my shorter-than-he-ever-used-to-be husband was trying to push through and stood aside, gesturing with a nod that he should go on through, he'd hold the door.

One night, about a year after my husband was diagnosed, just as his symptoms were becoming noticeable to others, I was sitting on the edge of our bed in our bedroom when he came in from running to the Circle K to pick up a paper. He sat down on the bed



Carmelene Siani and her husband, Hallaj Bowman

next to me. What? The hardest thing about this disease is the pity, he said. What pity? The pity people give me. I see it in their eyes. What happened? Somebody asked if they could help me with the door when I was coming out. They had that look in their eyes. What look? Pity, he said.

I told my husband then that I thought he was misunderstanding people. I told him that having always

been a strong, healthy, capable man, he'd never been in a position in which people could see that he needed help. I told him that perhaps he was misreading the look in their eyes. I told him that perhaps he was confusing pity with love.

The other day at the Circle K, my husband saw that I had noticed what happened with the big, tough-looking guy holding the door for him. He saw that I had seen him look the stranger straight in the face. He saw that I had seen him tell the stranger, "thank you." When he got to the passenger side of the car, I reached over and opened the door for him from the inside. He sat himself down in the tortuously slow way that Parkinson's forces on him and put the Coke in the holder. I'm surrounded by love, he said.

After he and I had that conversation on the edge of the bed about seeing people as offering love instead of seeing them as offering pity, my husband changed. No more pity for him. It has always been my belief that if you offer people something tender and real, they will respond in kind – from their best selves. I have seen waiters help my husband on with his jacket, store clerks carry a single grocery bag out to the car, massage therapists offer to button his shirts – over and over, I have seen people reach out to him and over and over, I have seen him now let them do it.

Through it all, though, what has been the most moving aspect of the dynamic for me is that I have seen my husband allow others into his life in ways that help him and quite possibly helps them as well. I have seen Parkinson change my husband and more or less change the very world he lives in. He's right. Everywhere he goes, he's surrounded by love. ▲

SAVE THE DATE!

September 30, 2006

"The Parkinson Connection: An Interactive Forum for the Parkinson Community"

Novartis Pharmaceuticals Corporation and the National Parkinson Foundation invite you to join hundreds of people with Parkinson disease in this groundbreaking one-day event featuring the latest information on treatment options, tips for communicating with healthcare providers, exercise suggestions, and voice techniques.

Learn from leading Parkinson disease experts from around the country.

- **Matthew Stern, MD**, University of Pennsylvania
- **Mark Stacy, MD**, Duke University Medical Center
- **Becky Farley, PhD & Cynthia Fox, PhD**, University of Arizona

Log onto www.parkinson.org after July 1, 2006

Your NPF Literature/ Information Request

The National Parkinson Foundation offers many informational resources free of charge. You can access and download the following publications through our website, www.parkinson.org, or you may use this form to make your request and send it to us using the envelope attached inside this issue.

In English:

- ___ NPF Brochure: Your Guide to Parkinson Disease
- ___ NPF Brochure: Should You Volunteer? PD Research Studies
- ___ NPF Mission Statement
- ___ Parkinson Report (Quarterly)
- ___ Patient Request Card
- ___ Medical Alert Card

Patient Education Manuals:

- ___ What You and Your Family Should Know
- ___ Medications
- ___ Fitness Counts
- ___ Nutrition
- ___ Speech and Swallowing
- ___ Caring and Coping
- ___ Practical Pointers
- ___ Mind, Mood, and Memory
- ___ Guide to Deep Brain Stimulation Therapy

En Español:

- ___ Lo Que Usted y Su Familia Deben Saber
- ___ Medicamentos para la Enfermedad de Parkinson
- ___ Estar En Forma Cuenta
- ___ La Nutrición es Importante
- ___ Dificultades con el Habla y la Deglución (tragar)
- ___ El Cuidado y la Adaptación Necesaria
- ___ Consejos Prácticos

MY NAME	
HOME ADDRESS	
PERSON TO CALL	
ADDRESS	PHONE
PHYSICIAN	PHONE
ALLERGIES	
OTHER MEDICAL CONDITONS	

Medications and Diagnostic Tests That May Be Contraindicated in Parkinson Disease:

Antipsychotics: Drugs that belong to the class of medications known as "typical," "conventional" or "older-generation" antipsychotics block dopamine and several other receptors in the brain. Examples of these include haloperidol, thioridazine, etc. These medications should not be used if at all possible. Other "atypical" or "newer-generation" antipsychotics drugs have also been reported to worsen parkinsonism and are also best avoided, but if any are needed, quetiapine or clozapine have consistently shown to benefit Parkinson disease patients with minimal worsening.

Nausea/GI Drugs: Drugs such as prochlorperazine (Compazine), metoclopramide (Reglan), or promethazine (Phenergan) may block dopamine receptors and worsen PD resulting in the possibility of other movements disorders. Alternate drugs such as domperidone (Motilium), trimethobenzamide (Tigan), and ondansetron (Zofran) should be considered.

Central Nervous System Active Drugs: Drugs such as benzodiazepines, muscle relaxants, bladder control medications and other medications used for sleep and pain are frequently used in PD, but may lead to confusion, hallucinations and other symptoms. While not contraindicated in Parkinson disease, they should be used as necessary under a physician's guidance. While selective serotonin reuptake inhibitors (SSRIs such as fluoxetine, sertraline, paroxetine) have been reported to worsen parkinsonism, this is rare, and most neurologists will frequently use these medications for depression in PD. Only amoxapine, an older antidepressant, contains dopamine receptor blocking properties, and therefore should be avoided.

Medical Devices: Many Parkinson disease patients have deep brain stimulators implanted to aid in controlling symptoms. The "pacemaker(s)" is located in the chest region with a wire leading to the brain. The device may be switched off by utilizing a strong magnet held over the pacemaker(s) for 2-3 seconds. Patients may also have a remote control device that is capable of turning off the pacemakers(s) so that procedures such as EKGs can be performed without interference. MRIs should not be performed unless your hospital has MRI safe experience and a neurologist turns the device to 0.0 bolts. The MRI should never be performed below the head (neck, chest, abdomen, arms, legs), and in cases where the pacemaker(s) is placed in the abdomen, it is best to consult the implanting physician prior to consideration of any MRI study, or for any procedure requiring electrocautery, ultrasound or diathermy.

Literature Request Order Form

Name

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City

State

Zip

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E-mail address

Check one: Patient Caregiver Family Member

Other How long? _____

MEDICAL ALERT

I have

PARKINSON DISEASE

which could make me move slowly
and have difficulty standing or speaking.

I AM NOT INTOXICATED.

Please call my family or physician for help.



NATIONAL PARKINSON FOUNDATION

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Miami, Florida 33136-1494

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Fax: (305) 243-5595

www.parkinson.org

Important information for the treating physician regarding Parkinson disease.

Please note that Parkinson disease patients
can be treated with medications and
with brain pacemakers. See important
considerations listed in the back of this card.

Medical Alert Cards Now Available!

A new Medical Alert Card is
now available from the National
Parkinson Foundation!

Whether you simply cut
out this card, or contact us to
send you one, you'll appreciate
having this Medical Alert Card
to share with doctors, nurses,
hospital staff, other health care
professionals who provide
medical treatment.

This very important card lets
them know that you or a loved one
has Parkinson disease, so the

proper treatment can be provided.
The Medical Alert card is:

- **Convenient** – Simply fold it
down; it can be carried in your
wallet at all times.
- **Informational** – It lists
medications and diagnostic
tests that may be contraindi-
cated in Parkinson disease.
- **Life-Saving** – In case of an
emergency, the information
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save your life or the life of a
loved one.



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Fill in your personal
information and
medical conditions.



Fold it down and
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To request additional cards, use the "free print
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