

Progress in Cell Transplantation Therapy Research

By Danny Bega

Parkinson's disease results from the loss of dopamine-producing cells in a part of the brain called the substantia nigra. Current treatment for PD replenishes lost stores of dopamine, a neurotransmitter that helps facilitate communication for movement between different parts of the brain.

This dopamine treatment alleviates many of the symptoms but fails to correct the underlying degenerative process. Understandably, for many patients and their family members who seek a cure for PD, symptomatic treatment is not enough.

Patients often ask about fetal cell therapy for Parkinson's disease. The potential of transplanting cells into the brains of people with PD has become an area of great interest to both patients and researchers. The goal behind fetal cell therapy is to avoid constant medication (i.e., levodopa) for replenishing dopamine stores and instead to restore the brain's natural ability to release the neurotransmitter. Current research is aimed

at finding ways to regenerate dopamine-producing neurons as well as slow down dopaminergic cell loss. Scientists are studying the potential of cell transplantation as a means for the brain to self-generate dopamine. While still experimental, the research shows promise for future PD interventions.

Almost 30 years have passed since the first human fetal cell transplantation study in PD. Conducted at the University of Lund in Sweden, the innovative study enrolled 20 PD patients who received transplantation of fetal dopamine-producing cells directly into their brains. While the study proved that the procedure could be done, the benefit to participants was not convincing—except for two patients. The authors later published an update on these two, one of whom they followed for 15 years post-transplant and the other for 18 years. Both had been young-onset patients when they entered the study, and both remained free of medication and had minimal motor disease progression over

the extended period of observation. Since the natural tendency of PD is to progress gradually over a long period, these findings were surprising and exciting. But however tempting it is to attribute them to a disease-modifying or protective effect of the transplantation, it's not that simple. The two aforementioned Lund study patients—providing the longest follow-up data available on cell transplantation in PD—represent an anomaly in the existing data. There were striking differences in the short-term benefits of cell transplantation among the Lund study patients, and only a few could reap long-term benefits.

Two important transplant studies followed the Lund study; one demonstrated modest improvements in motor function at four years after surgery, and the other failed to show any benefit. Disappointingly, autopsies of patients who received the fetal tissue grafts showed that even the grafted neurons had accumulated abnormal proteins in PD-causing cells, suggesting that the disease

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Cell Transplantation Therapy

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continues not only to progress after transplantation but also to spread to transplanted cells.

The Lund study took place in the late 1980s, when in the United States the Reagan administration imposed a moratorium on federal funding of all medical research involving fetal tissue. US research into cell therapy remained dormant until the Clinton administration overturned the order in 1993 and Congress reinstated funding. Since then, a handful of studies have been published, and as a whole they have led to a great deal of academic controversy over fetal and stem cell transplantation.

WHAT DO WE KNOW?

Dopamine cell transplantation with fetal tissue grafts (as was performed in the Lund study) can replace dead neurons with new ones that reinnervate the movement pathways. Many researchers, however, think that this will not become a mainstream form of treatment for PD for several reasons, including the scarcity of available tissue and problems with standardizing grafts. Greater potential for transplanting large numbers of neurons into larger

numbers of patients is seen in the use of nonfetal cells, such as stem cells or fibroblasts, to develop dopamine-producing cells. Stem cells are a renewable source of tissue that can be coaxed to become different types of cells in the body. Embryonic stem cells can generate all of the body's major cell types (they are "pluripotent"), including dopamine-producing cells. Induced pluripotent stem cells, discovered in 2007, are mature cells, such as skin cells, that scientists turn into embryonic-like stem cells, which can then become other cell types. These cells may have the potential both as cell replacement treatment approaches in patients and as disease models for scientists to use in screening new drugs.

WHERE DO WE GO FROM HERE?

At this time there are a number of practical limitations to the widespread use of cell transplantation in PD; growth and functionality of the cells and implantation techniques need to be validated before the therapy can be useful. Other considerations include determining which candidates are even eligible for transplantation.

For a new therapy to be considered clinically useful, particularly when it is invasive, it must offer outcomes better than those of existing therapies and have low potential for adverse effects. Trials of cell transplant therapy have failed to demonstrate results that meet or exceed the motor benefits and side-effect profile of current therapies like deep-brain stimulation (DBS). PD is unique among neurodegenerative disorders in that life expectancy is relatively normal, and DBS, the available pharmacologic and surgical therapy, is extremely valuable in treating motor symptoms. A particular concern with cell transplants is the risk of developing intractable dyskinesias (abnormal involuntary movements), which in some studies affect more than 50 percent of participants. This risk must be minimized before transplantation can be practically implemented.

Clinically, it has become clear that subtypes of PD have variable responsiveness to medication, rates of progression, and extents of pathology in the brain. This may mean that certain factors, such as young age at disease onset and type of PD symptoms, may

be responsible for the different outcomes seen from patient to patient in the transplant studies. Practically, identifying factors in specific patients (like the two Lund study patients) that predict good clinical outcomes from grafting may yield valuable insight. A new multicenter grafting study sponsored by Transeuro, a European Union research consortium, is under way to address and reconcile many of the shortfalls of previous studies. Even if the symptomatic benefit of cell transplantation can be reproduced through high-caliber studies, disease-modulating effects, such as those apparently experienced by the two Lund study patients, must be demonstrated before the practical implementation of such a technique.

While it is clear that there is no fast track to the safe and thoughtful clinical implementation of cell transplantation therapy, the positive outcomes in a small number of patients give hope for the future of PD research. At the very least, the development of new PD cell models generated from stem cells should allow scientists to study and develop more targeted PD therapies.



Danny Bega, MD, is an instructor and movement disorders specialist at the Parkinson's Center.

Ongoing Programs

Parkinson's Disease Support Group

First Tuesday of the month, 10:30 a.m.-2 p.m.

Northwestern Memorial Hospital
251 E. Huron Street, Chicago
Feinberg Pavilion, third floor, room A
312-503-4397 or 312-503-3320

These informal groups—the support group for patients and a simultaneous session for caregivers—offer participants social interaction and discussion as well as professional presentations. Family members, visitors, and guests are welcome. Refreshments and parking validation are provided.

Art and Yoga Therapy

Second, third, and fourth Tuesdays, 1-3 p.m.

Northwestern Prentice Women's Hospital
250 E. Superior Street, Chicago, room Q

Art therapy, 1-2 p.m. Uses the creative process to enhance individual well-being. Focuses on the process, not the product; you do not have to be an artist to participate.

Yoga therapy, 2-3 p.m. Uses mindful movement for body awareness. Simple, effective exercises reduce mental, physical, and emotional stress. Beginners are welcome.

For more information on these programs or to be added to our email or mailing list, please contact either of the following:

Pamela R. Palmentera, LCSW, clinical social worker and center coordinator, 312-503-4397, ppalment@nmff.org

Trupti Patel, MPP, senior program associate, 312-503-3320, trupti@northwestern.edu



Self-Care for the Caregiver

By Pamela R. Palmentera

“Take care of yourself” often closes a conversation. We all know taking care of ourselves is important, especially when we face physical challenges or look after loved ones. But the more complicated life gets, the harder it is to take care of ourselves. Self-care might even feel derelict and indulgent when there’s a long to-do list. If we want to continue to operate at optimal level and don’t want to succumb to stress, however, we have no choice but to take care of ourselves.

Self-care promotes and enhances our personal resilience and helps us survive and thrive. The strategy involves looking at ourselves as whole human beings—biological, intellectual, and emotional. We take care of ourselves by paying attention to all these aspects.

A plethora of information is available about the right way to take care of ourselves. I offer no argument as to methodology—merely a reminder to pause at some points during the day to check in and touch base, examine your physical and emotional state, and then make conscious choices that enhance well-being. These might include

- Eating well. Don’t skip meals. Avoid sugary foods and drinks.
- Exercising. Even a little exercise will make a difference. A simple walk around the block can

do wonders. If you can walk with a loved one or someone you trust, even better.

- Finding time to rest.
- Sharing your emotions. Tumultuous emotions are an unavoidable part of life. Expressing your thoughts and feelings can be cathartic and enlightening, whether you use words, art, music, or another form of expression.
- Delegating whatever tasks you can to help reduce stress. Ask for help. Even let some things slide.
- Taking breaks or small breathers. Listen to music, watch a movie, go out to dinner, engage in some form of recreation or distraction.

Taking care of yourself is the first step in caring for someone else. I am reminded of the wisdom in the words of the *Tao Te Ching*:

Simplicity, patience, compassion.
These three are your greatest treasures.
Simple in actions and thoughts,
You return to the source of being.
Patient with both friends and enemies,
You accord with the way things are.
Compassionate toward yourself,
You reconcile all beings in the world.

Pamela R. Palmentera, LCSW, is the Parkinson’s Center’s coordinator and a clinical social worker.

RECRUITING FOR CLINICAL TRIALS

EARLY PARKINSON'S DISEASE

PPMI The objective is to identify clinical, imaging, and biologic markers of PD progression for use in clinical trials of disease-modifying therapies. The study is recruiting subjects with a loss of smell (hyposmia) and REM behavior disorder (RBD) who fit one of the following categories:

Genetic Cohort-PD

- Have at least two of the following: resting tremor, bradykinesia, rigidity or asymmetric resting tremor, asymmetric bradykinesia
- PD diagnosis for seven years or less
- Age 18 years or older
- Confirmation of LRRK2 or SNCA mutation
- Willingness to undergo genetic testing

Genetic Cohort-Unaffected

- Age 50 years or older with LRRK2 mutation or first-degree relative with LRRK2 mutation; or age 30 years or older with SNCA mutation or first-degree relative with SNCA mutation
- Willingness to undergo genetic testing

MODERATE TO ADVANCED PARKINSON'S DISEASE

Motor Fluctuations The primary objective is to establish the efficacy of istradefylline dosages of 20 and 40 milligrams a day on levodopa/carbidopa therapy for reducing the total hours per day of off time in patients with motor fluctuations and dyskinesia.

Fatigue The objective is to investigate the effect of selegiline, a selective and irreversible MAO-B inhibitor, on fatigue experienced by PD patients. The double-blind, randomized, placebo-controlled study lasts 12 weeks, plus a 1-week titration and a 1-week washout period. Funded by a 2011 Northwestern Parkinson's Disease and Movement Disorders Advisory Council Grants Initiative.

Gait Dysfunction and Freezing The objective is to explore the efficacy of amantadine for the treatment of gait dysfunction and freezing of gait with PD.

Yoga versus Resistance The objective is to explore the feasibility of yoga intervention and to collect pilot data comparing yoga's efficacy with traditional resistance training for patients with PD. Funded by the Northwestern Parkinson's Disease and Movement Disorders Advisory Council.

For more information about participating in these research studies at Northwestern Medicine, call 312-503-0755, email PDclinicaltrials@northwestern.edu, or visit www.parkinsons.northwestern.edu/clinical_trials.html.

Welcome, New Staff



Mahesh Padmanaban, a graduate of the West Virginia University School of Medicine, has

become a fellow in the Parkinson's Center. He completed his residency at the University of Chicago Medical Center. Interested in dystonia and Parkinson-spectrum disorders, Padmanaban hopes to continue his career in the field of movement disorders.

Thomas Bielawiec is a clinical research coordinator for the Parkinson's Center. He coordinates a clinical drug trial and the Parkinson's Progression Markers Initiative observational study. Bielawiec received a bachelor's degree from Northwestern, majoring in biology with a concentration in molecular biology and genetics. He was involved in molecular bioscience research investigating spindle assembly in *C. elegans*. Bielawiec hopes to eventually pursue a medical education.

Elise Johnson is a clinical research coordinator for the Parkinson's Center. She coordinates industry-sponsored and investigator-initiated clinical drug trials for advanced PD patients. She previously worked for a rare-disease neurologist at Massachusetts General Hospital, conducting clinical drug trials for adults with severe hereditary neuropathy and a gene therapy trial for children with adrenoleukodystrophy. Johnson graduated from Emory University with a bachelor's degree in neuroscience and behavioral biology.

Your Donations Support Cutting-Edge Research

Philanthropic partners of Northwestern Medicine's Parkinson's Disease and Movement Disorders Center help make possible cutting-edge research that may lead to the discovery of new possibilities in the treatment of Parkinson's disease.

The center's multidisciplinary neurologists and neurosurgeons are continuously engaging in research in order to extend the knowledge and treatment of movement disorders. Center director Tanya Simuni, for example, is conducting a five-year, phase III study of the efficacy of the drug isradipine as a neuroprotective agent for delaying PD progression. It is a monumental study involving 56 Parkinson's disease centers in

North America, and it has the potential to revolutionize the treatment of PD.

We are grateful for the generous efforts of all donors, volunteers, and thankful patients, many of whom are members of our advisory council. All gifts play a direct and significant role in the center's ability to pursue basic and clinical research and to offer a wide variety of services to patients and families.

If you have an interest in making a gift to support Parkinson's research or clinical care at Northwestern, please contact Leslie Post-Weissinger, philanthropy director, Northwestern Memorial Foundation, lpostwei@nmh.org or 312-926-0450.

RIC's PD-Specific Exercise Programs

The Rehabilitation Institute of Chicago's Adaptive Sports and Fitness Program helps people with physical disabilities reach their fullest potential through fitness, recreation, and competitive sports. Five specialized exercise programs at the RIC Adaptive Sports and Fitness Center, located in the heart of downtown Chicago at 541 North Fairbanks Court, serve people with Parkinson's disease. Two of the programs are also offered in Deerfield at Zion Lutheran Church, 10 Deerfield Road, and in Willowbrook at 6705 South Kingery Highway.

Integrated Exercise for Parkinson's Disease

(downtown, Deerfield, and Willowbrook)

Designed to help people with PD use exercise for symptom management. For all ability levels. Exercises target overall strength, flexibility, balance, and postural awareness.

Parkinson's Disease Amplitude-Based Training

(downtown, Deerfield, and Willowbrook)

Advanced-level group class with high-intensity, multi-directional exercises to enhance neuroplasticity and increase endurance, balance, and functionality of everyday movements.

Fall-Risk Screening and Conditioning (downtown)

Screening assesses level of risk for falling. Consists of a self-assessment, assessment of modifiable risk factors, and an objective evaluation of gait, balance, and strength using three major pieces of equipment.

Goldman Functional Fitness Program (downtown)

One-on-one specialized exercise programs with exercise physiologists to build on skills learned in physical therapy. Designed to help increase activity, continue to improve physical ability, and meet personalized fitness goals.



Personal Training (downtown)

Specialized exercise program to enhance personal fitness goals by working one on one with a physiologist who specializes in PD symptom-specific exercises. An in-depth assessment will be conducted to begin.

Anyone interested in participating in a specialized exercise program or becoming a fitness center member must have a physician complete a medical form. The form may be downloaded at the website below or obtained by contacting the center:

RIC Adaptive Sports and Fitness Center
541 North Fairbanks Court, mezzanine level
(accessible entrance at 303 East Ohio Street)
Chicago, Illinois 60611
phone 312-238-5001
fax 312-238-5017
www.ric.org/resources/sports-and-fitness/membership



OCTOBER 19, 2014 CHICAGO

Walk for Parkinson's | Fall 2014

PEOPLE WHO MOVE CHANGE THE WORLD.®

Register Today | www.MovingDayChicago.org

Moving Day® is a fun, inspiring fundraising event that unites families, friends and communities in the fight against Parkinson's disease. Join us by moving any way you can—by walking, running, stretching or taking part in other activities in our signature Movement Pavilion. Together we can raise awareness and celebrate the importance of movement for all of us.

A day to **move**. A day to **move** others. A day that **moves** you!

Sunday, October 19, 2014

LINCOLN PARK

Grove 2 | Stockton & Lasalle Drive

Registration 9:00 am

Opening Ceremonies 10:30 am

The event will include the walk, exhibits, music, food, family fun, and the "Movement Pavilion" encouraging a variety of physical activities.

Sign up for Moving Day® today and show your support!

In Collaboration with NPF Centers of Excellence:

Northwestern Parkinson's Disease & Movement Disorders Center

The National Parkinson Foundation's Moving Day®, headlined by Honorary National Chair Katie Couric, is a unique fundraising and awareness-raising event held in partnership with NPF chapters across the country.



Katie Couric is the Honorary National Chair of Moving Day® in memory of her father who had Parkinson's.

Thank you to our National Partners:



Annual Patient and Family Symposium

"Living Well with Parkinson's Disease"

Saturday, October 11 • 8 a.m.-12:30 p.m.

Northwestern Memorial Hospital

251 East Huron Street, Chicago, Conference Room A

8 a.m. REGISTRATION AND CONTINENTAL BREAKFAST

9 a.m. WELCOME

9:05 a.m. OPENING ADDRESS: "Living Well with Parkinson's Disease"

Paul Ruby, founder of the Paul Ruby Foundation and Parkinson's disease patient

9:25 a.m. "Humor and Parkinson's"

Alice Golan, comedian and songwriter

9:35 a.m. NEW TREATMENT PIPELINE: EARLY DISEASE

Tanya Simuni, MD, medical director and movement disorders neurologist at Northwestern Medicine's Parkinson's Center and Arthur C. Nielsen Professor of Neurology at the Feinberg School of Medicine

9:55 a.m. NEW TREATMENT PIPELINE: ADVANCED DISEASE

Cindy Zadikoff, MD, movement disorders neurologist at Northwestern Medicine's Parkinson's Center and associate professor of neurology at the Feinberg School of Medicine

10:15 a.m. BREAK

10:30 a.m. EXERCISE AND REHABILITATION

Christina Marciniak, MD, attending physician in the Movement Disorders Rehabilitation Program at the Rehabilitation Institute of Chicago and associate professor of physical medicine and rehabilitation and of neurology at the Feinberg School of Medicine

10:50 a.m. COMPLEMENTARY AND ALTERNATIVE MEDICINE

Danny Bega, MD, movement disorders specialist at Northwestern Medicine's Parkinson's Center and instructor at the Feinberg School of Medicine

11:10 a.m. PHYSICIAN PANEL: QUESTIONS AND ANSWERS

11:50 a.m. BREAKOUT SESSIONS

- Benefits of Occupational Therapy • Music Therapy
- Care and Caregiving • Tai Chi
- Deep Brain Stimulation • LVST (Speech Therapy) Big and Loud
- Rock Steady Boxing

To register, please call Northwestern Memorial Hospital's Health Resources and Physician Referral Service at 312-926-8400.

Participants in Spinning Class Report Gains

By Kathy Schulte

With studies showing that high-energy stationary biking—or “spinning”—improves movement for people with Parkinson’s disease, Northwestern Lake Forest Hospital’s Rehabilitative Services and Health and Fitness Center have teamed up to create Spinning for Parkinson’s. The class meets at 11 a.m. Tuesdays at the Lake Forest Health and Fitness Center at 1200 Westmoreland Road. Anyone with Parkinson’s and one family member may attend for free.

“It gives me a lot of energy,” says PD patient Martin Giarelli, who has been taking the class with his wife, Mary, every Tuesday morning since it started in March. “I can tell I am getting quicker in the mornings, and my balance has really improved.”

Jo Duffy also has been in the class since it began and reports improvement in her balance. Trainers Bo Wright and Kristina Wrezel “are fabulous and make the class fun,” Duffy says. Wright and Wrezel, specialists in exercise science, are dedicated to providing exercise training and opportunities to those who have been diagnosed with PD and to their families.

Besides improving movement, exercise beyond one’s comfort zone may help improve brain communication for movement, research has shown. With this level of exercise, improvement has been seen in the brain pathways that tell muscles to initiate and continue movement.

On Tuesday, October 21, there will be a half-hour discussion of tips for PD

exercise. Those who attend the 10:30 a.m. discussion are invited to stay on for the Spinning for Parkinson’s class at 11 a.m. To register, contact Anthony Simone, wellness manager, at 847-535-7140.

Kathy Schulte is a physical therapist and vestibular rehabilitation specialist at Northwestern Lake Forest Hospital Rehabilitative Services.



Lake Forest Health & Fitness Center

Spinning for Parkinson's

Studies show that forced stationary bicycle pedaling therapy at a high steady cadence (RPM) has recently been shown to significantly reduce the symptoms of Parkinson's disease and improve motor function.

Register at the front desk or contact Anthony Simone for more information at 847.535.7140

*Bring a family member for free

Lake Forest Health & Fitness Center | 1200 North Westmoreland Road | Lake Forest | Illinois 60045 | 847.535.7064 | lakeforesthfc.com

Like us on facebook!

Spin Class For Parkinson's

Tips for Hospital Stays

When entering the hospital

- Provide a list of your medications with exact times, frequencies, and dosages. Bring medications in original bottles.
- Let staff know that you understand on-off fluctuations and the importance of taking medications at specific time intervals.
- Know which drugs can worsen PD symptoms in case you are asked to take a new drug.
- If you are in a research study, provide information about the experimental drugs. Inform the study coordinator that you are in the hospital.
- Speak up when medications are wearing off.
- Do not take medication on your own.
- If you have a deep brain stimulation implant, let the staff know and bring instructions and anything related to it.
- Inform your neurologist that you are in the hospital, and give your neurologist's name and phone number to the hospital physician.

Be mobile

- Walk around as much as possible and perform range-of-motion exercises.

If you have difficulty swallowing

- Sit up while eating.
- Ask for a speech-swallow evaluation.
- Let the staff know if your medications need to be administered through a tube.

Know what factors may make your symptoms worse

- Not taking medications at specific times
- Dopamine-blocking drugs, such as Haldol, Risperdal, and Zyprexa
- Anxiety, stress, sleep deprivation
- Infection

Provide advance directives

- Request a National Parkinson Foundation "Aware in Care" hospitalization kit (free; see accompanying advertisement).

Center Offers NPF's "Aware in Care" Kits

Northwestern Medicine's Parkinson's Center is providing the National Parkinson Foundation's "Aware in Care" hospitalization kits free of charge to patients in our clinic and support groups.



NPF introduced the "Aware in Care" kits at the 2011 NPF Centers Leadership Conference. Intended to improve delivery of care, the kits help hospitalized PD patients share information about their symptoms and needs with hospital staff.

NPF produced the kits in response to alarming findings that during a hospital stay three out of four people with PD do not get their medications on time and that patients with PD suffer more avoidable complications than do other patients.

The kit includes the following:

- action plan with information about how to prepare for one's next hospital visit
- medical alert card with emergency contact information
- medications form and a magnet for displaying it in the hospital room
- PD ID bracelet
- PD fact sheet for the hospital chart and staff
- "I Have Parkinson's" reminder slips for the hospital care team
- thank-you card to give to hospital staff who provide high-quality care

Parkinson's Disease and Movement Disorders Center
710 North Lake Shore Drive, 11th floor
Chicago, Illinois 60611-3006
www.parkinsons.northwestern.edu



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CONTACT
312-503-4397 or 312-695-7950

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PDclinicaltrials@northwestern.edu

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Please contact us to be added to our mail or email lists or to update your address. We also welcome your comments and letters.

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Calendar

ANNUAL PATIENT AND FAMILY SYMPOSIUM

Saturday, October 11, 8 a.m.–12:30 p.m.
Northwestern Memorial Hospital
251 E. Huron Street, Chicago
Feinberg Pavilion, third floor, room A
312-926-8400

NATIONAL PARKINSON FOUNDATION'S

MOVING DAY CHICAGO (annual fundraising walk)

Sunday, October 19, 9 a.m.–1 p.m.
Grove 2, Lincoln Park, Stockton and LaSalle
Drives, Chicago (near the Lincoln Park Zoo)
movingdaychicago.org
312-505-7602

EARLY DIAGNOSIS AND YOUNG-ONSET MEETING

Saturday, October 25, 9–10:30 a.m.
Northwestern Memorial Hospital
251 E. Huron Street, Chicago
Feinberg Pavilion, third floor, room F
ppalment@nmff.org