A MOVEMENT DISORDER SOCIETY UPDATE

Moving Along

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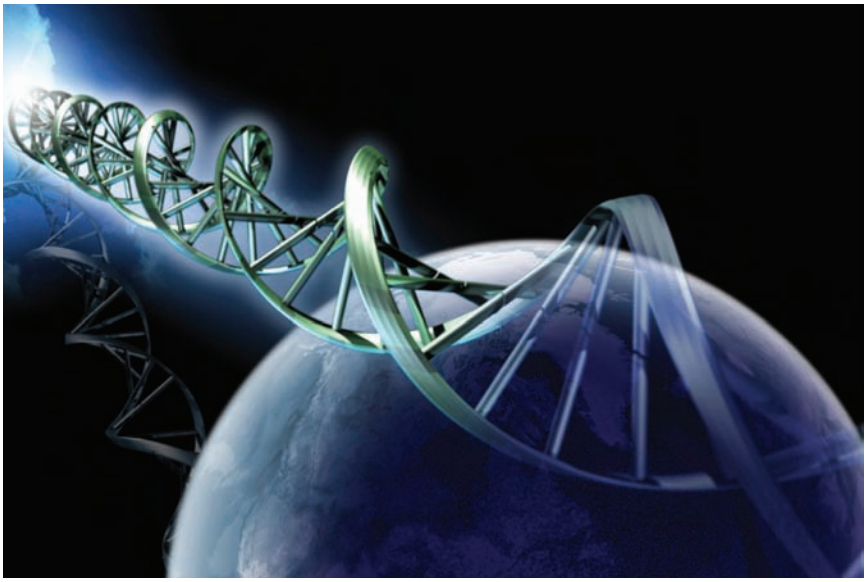
Genetics of Parkinson's Disease: Coming of Age

—Thomas Gasser, MD, Univserity of Tübingen, Hertie-Institute for Clinical Brain Research, Department of Neurodegenerative Diseases, Tübingen, Germany

Not much more than 10 years ago, reviewers and funding agencies alike were nearly unanimous in discouraging applicants to pursue research on a possible genetic basis of Parkinson's disease (PD). Epidemiology, twin studies and the everyday experience all seemed to argue along the same line: PD is a sporadic disorder and genetic causes have little, if anything at all, to do with it. Over the last few years, this picture has changed dramatically. A growing number of genes for rare (or not so rare) monogenic forms of Parkinson's disease have already been mapped and/or cloned, and more are certainly to follow. These recent discoveries have changed our view on PD in three important aspects:



1. **The genes causing monogenic forms of PD and their associated molecular pathways have provided a multitude of lines of investigation into the pathogenic cellular processes involved in nigral dysfunction and degeneration.**

The first "PD gene" to be discovered, was α-synuclein. A total of only three point mutations in this gene have been identified, which cause a severe form of familial PD, inherited in an autosomal-dominant fashion. More recently, another mutational mechanism has been found, also leading to rare cases of autosomal-dominantly inherited PD: the duplication or triplication of the entire gene, leading to an "overload" of the cell with the normal α-synuclein protein. Although all those mutations are very rare, their identification was extremely important, as it lead to the discovery that the encoded protein is the major fibrillar component of the Lewy body, the proteinaceous inclusion which has, since Friedrich Lewy's original description in 1917, been considered to be the pathologic hallmark of PD in both familial and sporadic cases.

The currently favored hypothesis, developed on the basis of these discoveries, states that the amino acid exchanges caused by point mutations as well as the overexpression caused by multiplications lead to an increased fibril- and/or aggregate formation, eventually causing the demise of the dopaminergic neurons, although the precise toxic mechanism has not yet been identified.

Three genes causing early-onset autosomal-recessive parkinsonism have been discovered subsequently: parkin, DJ-1 and PINK1, each pointing to another important cellular mechanism involved in nigral neurodegeneration: parkin is an enzyme of the group of ubiquitin-ligases, an important component of the proteasomal protein degradation machinery. This system is responsible for the degradation of proteins that are misfolded and therefore, potentially toxic to the cell. PINK1 is a mitochondrial protein kinase, and its deficiency is thought to be related to mitochondrial dysfunction, another important mechanism of cellular damage implicated in the pathogenesis of PD. DJ1, finally, is thought to act as a sensor for oxidative stress within the cell. The deleterious action of toxic oxygen radicals has long been suspected to be another crucial component of cellular damage in PD. Innumerable animal and cellular models have already been established on the basis of these discoveries in laboratories around the world, in a plethora of organisms, from yeast and drosophila to mice and rats, providing a multitude of experimental venues to study the multiple mechanisms that are probably involved in this complex disorder.

2. **It is becoming increasingly clear that while many genetic forms are exceedingly rare, others are sufficiently common to be of relevance in everyday clinical practice, and this is truly particular for certain populations.**

The most common autosomal-dominant form of PD discovered so far is caused by point mutations in the gene for leucine-rich repeat kinase 2 (LRRK2, the encoded protein has also been called "dardarin"). LRRK2 mutations have been found to be surprisingly common, accounting for 5% to 15% of familial, and 1% to 2% of sporadic cases of PD in most European populations, with an

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inside this issue

This issue of *Moving Along* provides us a lot of food for thought. Genetics are shaping our understanding of Movement Disorders and we wonder if recent discoveries in this field should start changing our clinical practice when evaluating patients with Parkinson's disease. In this winter/spring issue, two scholarly written articles address this topic. In the Cover Story, co-editor Dr. Thomas Gasser thoughtfully recapitulates how recent genetic discoveries have changed our view of Parkinson's disease. In the Public Policy section, Drs. John Hardy and Katrina Gwinn-Hardy meticulously discuss if the time has come to perform genetic testing for parkinsonism in our clinical practice.

With a lot of new knowledge on the causes of Parkinson's disease and the likelihood of having reached the limit of symptomatic therapy, we are ready for new therapeutic approaches. Drs. Byron Young and Mark Stacy academically debate whether GDNF intraparenchymal trials are to be continued. While we are for new biologic therapies, the jury is out if this is the way we should proceed.

This issue also brings you hot news regarding our successful 10th International Congress of Movement Disorders recently held in Kyoto, Japan. We congratulate Prof. Mizuno, the Congress Scientific Program Committee, and The *Movement* Disorder Society's leadership for the excellent program and organization.


Irene Litvan, MD


Thomas Gasser, MD

We have been asked to remain as co-editors of *Moving Along* for two more years and we happily accepted as it has been very rewarding to brainstorm on hot topics, controversies and advances in the field. For the next two years we hope to get your input on how you want us to proceed and have opened a "Letters to the Editor" section for your comments. We wish you the best for this New Year that is already in full force.

LETTERS TO THE EDITORS

Your Comments and Questions Are Always Welcome

Editorial Policy

As part of its democratic commitment, MDS welcomes the input of all its members about the features and articles that appear in this newsletter. Have a comment or question? Each issue will include responses in the "Letters to the Editor" section. All materials submitted become the property of MDS.

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Genetics of Parkinson's Disease: Coming of Age

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onset age spanning the range found also in typical PD, from the thirties to the eighties, with a mean of around 60.

It was particularly surprising to find out that some mutations are even much more prevalent in certain populations: One of them, the Gly2019Ser mutation alone, was detected on a founder haplotype across several European populations in up to 6% of dominant families and, even more striking, in up to about 40% in North African Arabs and Ashkenazi Jews. Many of the G2019S-patients in this population did not even have a family history of the disease, which is probably due to the incomplete, age dependent penetrance of the mutation. Very recently, it has been shown that about 10% of Chinese patients with PD carry another variant of the LRRK2-gene, G2385R, which is found in only 3% of controls, making this the most common risk factor for PD discovered so far. There may be other risk alleles of this gene in other populations that remain to be discovered. These numbers strongly indicate that genetic causes are not restricted to a small minority of PD patients. The consequences of this fact will demand completely novel strategies of

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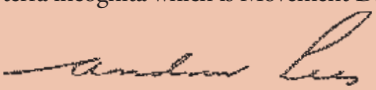
The last two years have been an interesting time for The *Movement* Disorder Society (MDS). The transition to annual International Congresses has gone well, and much to the surprise of many skeptics the pace of new research in Parkinson's disease and related Movement Disorders has avoided criticisms of stultification and repetition in our scientific programmes. It has also allowed us to experiment with new educational formats and provide more variety in the faculty. The move starting this year in Istanbul to a regular June date will also allow you to mark your diaries at least until 2012 with a fixed date for this premier fixture. As well as the phenomenal success of New Orleans and Kyoto, MDS supported the World Parkinson's Congress in Washington, D.C. last year which many of you attended and enjoyed.

The most gratifying developments during my Presidency have been the formation of the Asian and Oceanian Section of the Society, and the expansion of the MDS Visiting Professors programme. The MDS-AOS already has ambitious and exciting plans for raising interest in Movement Disorders in this complex and varied part of the world, and will kick off with its first regional meeting this year in Singapore. Sadnessses have been few, but for me the devastation of the Big Easy (New Orleans) by Hurricane Katrina after our meeting ranks highest. Many of you will have enjoyed the hospitality of the Creole culture and Cajun cooking and we can only hope that the rich cultural mosaic of the home of jazz will be given the support it needs to fight back. The loss of a number of friends and eminent colleagues including former MDS Treasurer Bill Koller has also been hard, but happy personal memories remain a lasting legacy through the awards given in Kyoto in his name for clinical research.

There is still much to do as our Society continues to grow and mature rapidly but it is in good hands with our new President. Tony Lang has many exciting projects including the development of the MDS Web site with webcasts, online videos and the first Podcasts describing highlights from Kyoto. I take this opportunity to wish Tony a smooth passage and thank him for his support during my Presidency. I would also like to conclude my valediction by thanking all my other fellow Officers for their hard work and wise advice which helped to keep my Presidential voyage on course. I also owe much to all the Past-Presidents who have chipped in with their collective wisdom at times of my need. Finally, I would like to remind you that the future of our Society will ultimately depend on our ability to enthuse the brightest and best young neurologists with our own fascination and excitement in the terra incognita which is Movement Disorders.



Andrew Lees, MD, FRCP
Past-President 2007-2008

It is a great honour for me to assume the position of President of The *Movement* Disorder Society for the next two years. I would like to express my tremendous gratitude to our Past-President Andrew Lees for his outstanding leadership over the past two years - I will be relying on him heavily during my Presidency for good counsel and assistance. I am looking forward to working closely with our other Officers and the International Executive Committee (IEC) members.

Annual Congresses

This is an extremely exciting time in our Society's history. We continue to grow and have now reached the largest membership to date of 2,400 members. The Society and our field have matured to the point of justifying Annual Congresses, and this year with the Istanbul International Congress, we will take up our regular time slot in June so mark your calendars for this meeting as well as Chicago - June 2008, Paris – June 2009 and Buenos Aires – June 2010.

We have just completed one of our most successful International Congresses ever in Kyoto, and I would like to strongly congratulate Yoshikuni Mizuno and his colleagues for their hard work in making this such a wonderful event. We are now looking forward to an equally successful meeting in Istanbul under the guidance of Murat Emre and his team. The Congress Scientific Program Committee under the direction of Eduardo Tolosa has developed an extremely exciting program which can be reviewed on the Society's Web site: www.movementdisorders.org/congress/congress07.

Sections

The establishment of MDS Regional Sections has been an important strength of the Society. These,

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Genetics of Parkinson's Disease: Coming of Age

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genetic counseling and genetic diagnosis in PD, with all its problems and promises (covered in the Public Policy article in this issue, by K. Gwinn-Hardy and J. Hardy).

3. There is increasing evidence that the genes that have been found mutated in monogenic variants of the disease may also play a role in the majority of patients without clear Mendelian inheritance. This effect is mediated by common variants (polymorphisms) that cause subtle alterations in expression of the gene and/or the cellular function of its encoded protein.

The G2385R variant of the LRRK2-gene is a striking example of a relatively "common" (3% population frequency in Chinese) polymorphism in a PD-gene, which clearly and substantially increases to the risk to develop the disease, without being a true disease-causing mutation in the classic sense (the exact risk for carriers of this variant to develop the disease during their lifetime is not known). Similarly, a number of reports now convincingly demonstrate that polymorphisms in the α-synuclein gene increase the risk for PD. It is therefore possible that there are several genetically determined paths that may "drive" a brain towards PD: a single, very deleterious mutation in one of the PD-genes may suffice in some cases, while two or (more likely) several less malignant variants in these genes may combine in other individuals, finally reaching a threshold and initiating the cascade of events that eventually leads to protein aggregation, cellular dysfunction and cell death. In this case, we may actually not be too far from being able to explain many, or maybe even the majority of PD cases in terms of the molecular etiology. It is then also conceivable that on the basis of the identified molecular pathways, we may find a combination of appropriate therapeutic interventions, specifically tailored towards the pattern of molecular defects in a particular case.

Sounds like science-fiction? But then what would anybody have called the astounding genetic discoveries of today, just ten years ago?

Table 1:

Locus / gene	Inheritance	Onset	Pathology	Map position	Gene	Ref.
PARK1	Dominant	40s	Nigral degeneration with Lewy-bodies	4q21	α-synuclein	(1, 2)
PARK2	Recessive	20 - 40	Nigral degeneration without Lewy-bodies	6q25	Parkin	(3)
PARK3	Dominant	60s	Nigral degeneration with Lewy-bodies, Plaques and tangles in some	2p13	?	(4)
PARK4	Dominant	30s	Nigral degeneration with Lewy-bodies, vacuoles in neurons of the hippocampus	4q21	α-synuclein triplications and duplications	(5)
PARK5	Dominant	~ 50	No pathology reported	4p14	ubiquitine C-terminal hydrolase L1	(6)
PARK6	Recessive	30 - 40	No pathology reported	1p35-37	PINK1	(7)
PARK7	Recessive	30 - 40	No pathology reported	1p38	DJ-1	(8)
PARK8	Dominant	~ 60	Variable α-synuclein and tau pathology	12cen	LRRK2	(9, 10)
PARK9	Recessive	30	No pathology reported	1q36	ATP13A2	(11)
PARK10	Dominant (?)	50-60	No pathology reported	1p32	?	(12)
PARK11	Dominant (?)	late	No pathology reported	2q34	?	(13)

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along with the growth of our educational programs, visiting professorships and other important programs, advance the interests of our membership in different parts of the world. Encouraged by the tremendous success of the MDS-European Section, the MDS-Asian & Oceanian Section (MDS-AOS) was born last year. The MDS-AOS Officers and Asian & Oceanian Section Executive Committee members are looking forward to their inaugural congress, which will be held in Singapore from October 20-22, 2007. Additional information regarding the 1st Asian and Oceanian Parkinson's Disease and Movement Disorders Congress can be found on their Web site: www.aopmc.com.sg.

Education

The MDS leadership has prioritized three important items for ongoing active development. Education is seen as one of our highest priorities. The Education Committee, under the guidance of Cindy Comella as Chair, continues to develop educational programs, enduring materials and other items for the benefit of our membership. Education will also be emphasized at our annual International Congresses and a number of sessions in the International Congress will be designated and highlighted for their educational value.

Web site

The second important priority is the MDS Web site, under the supervision of Olivier Rascol, Philip Thompson, Matthew Stern and the Web Site Committee. The Web site will be actively expanded and developed to provide a great deal more value to our Society's members. We will be enhancing the role of the Web site in providing education materials originating from our annual International Congress. An example of this that is already available are the excellent Podcasts that highlight several components of the Kyoto meeting and can be found on the Society's Web site: www.movementdisorders.org/congress/congress06/.

Journal

A third ongoing priority is our flagship journal, *Movement Disorders*. A remarkable testament to the activity of our field and the tremendous success of our journal has been the recent expansion to 16 issues per year. Our Editors, Günther Deuschl and Christopher Goetz, and their Subspecialty Editors and Editorial Board will continue to explore new ways of keeping our journal as vibrant, dynamic and responsive to the needs and interests of its readership as possible.

The *Movement* Disorder Society is thriving. Through our International Congresses, Journal, Committees and Working Groups we are aggressively pursuing our mandates of educating physicians throughout the world in all aspects of Movement Disorders, encouraging scientific developments in our field and improving the care of patients suffering from the many neurological diseases that result in Movement Disorders. The *Movement* Disorder Society can only continue to succeed in addressing these goals with the active participation of its membership. Get involved in Society business. Attend the annual International Congresses and participate actively. Share your thoughts, concerns, suggestions, etc. with myself, or any of our Officers, IEC members or Regional Section Executive Committee members. I look forward to working for you and with you in my capacity as President over the next two years, and expect that with the support and involvement of a dedicated membership we can rise to even greater heights.

Finally, on behalf of all of our members and particularly all of the Officers who have had the good fortune and pleasure of working with Caley Kleczka, I would like to express our deepest gratitude for her extremely hard work and tremendous dedication to the Society in her position as Executive Director over the past five years. Unfortunately, Caley formally resigned her position in February, but has kindly agreed to continue to provide critical support and assistance as we transition to a new Executive Director. I look forward to working with Kay Whalen and her excellent staff at EDI in the MDS Secretariat over what I hope will be an exciting and productive two-year term as your President.

Anthony E. Lang, MD, FRCPC
MDS President 2007-2008

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MDS Commemorates Success of the 10th International Congress

Kyoto, Japan, was the site for The *Movement* Disorder Society's (MDS) 10th International Congress of Parkinson's Disease and Movement Disorders, held October 28 – November 2, 2006 at the Kyoto International Conference Hall. Located in the serene Northern hills of Kyoto, the venue proved to be a desirable location for the 3,000 delegates who participated in this past International Congress.

Due to high demand for Industry supported Seminars, the 10th International Congress commenced with an additional day of Opening Seminars on Saturday, October 28. In the evening, delegates gathered for the traditional Opening Ceremony. During the Welcome Reception that followed, delegates enjoyed a Koto Performance, a traditional Japanese instrument, while sampling Western and Japanese cuisine.

Prof. Andrew Lees presents Prof. Eduardo Tolosa with the President's Distinguished Service Award during the Opening Ceremony

Several awards were also announced and distributed at the 10th International Congress. Mark Hallett received the C. David Marsden Lecture Award for his work with Myoclonus and Tulips and Ira Shoulson received the Stanley Fahn Lectureship Award for his work relating to the challenges and prospects for neuroprotection in Parkinson's disease. Other award recipients included Andre Troiano who received the Junior Award in the Clinical Research category and Akiko Imamura who received the Junior Award in the Basic Science category. Patrick McGeer and Niall Quinn received the Honorary Membership Awards and Eduardo Tolosa received the President's Distinguished Service Award. Additionally, ten William Koller Memorial Awards and thirty-five Travel Grants were distributed. Please see page 7 for more information on these awards.

A traditional Japanese Awa dance performs during the Gala Dinner

The Scientific Program continued throughout the week with 218 faculty participating in a broad array of Plenary Sessions, Parallel Sessions, Skills Workshops and Video Sessions. The increasingly popular session, Lessons My Patients Taught Me, provided valuable insight and a personal point of view of what difficult, unusual or even average cases can teach prominent Movement Disorder specialists.

New to this year's International Congress were Meet the Expert Sessions, Young Scientists Best Posters Presentations and Teaching Courses. The ever-popular Controversies Session concluded the International Congress on Thursday, November 2. Additionally, the 10th International Congress was pleased to showcase over 1,300 posters from authors world-wide.

MDS was glad to officially launch the Asian and Oceanian Section (MDS-AOS) at the 10th International Congress. It was created not only to further the goals and objectives of the MDS regional sections, but also to strive to increase the interest, education and participation of neurologists, Movement Disorder specialists, non-Movement Disorder specialists, trainees, allied health professionals and scientists in the Asian and Oceanic regions. Information was provided at the MDS-AOS exhibit booth and proved to be an area of interest as it was a common gathering place for delegates.

10th International Congress attendees participate in a Teaching Course

The Gala Dinner on Wednesday, November 1, proved to be a memorable event for delegates. A Marimba performance by Mr. Tetusya Okudaira, followed by a traditional Japanese Awa Dance, fashioned an upbeat and interactive environment for the evening.

Nineteen companies exhibited at this year's International Congress, including pharmaceutical companies, patient organizations and medical publishers. Supporters of the 10th International Congress, who greatly contributed to the success of this event, also exhibited.

Delegates share their research on posters while others view the booths in the International Congress Exhibit Hall

MDS is proud to announce that their first series of Podcasts were launched during the 10th International Congress. These downloadable, pre-recorded audio files allow those interested to hear highlights from the 10th International Congress. To access or download MDS Podcasts, visit our Web site at www.movementdisorders.org/congress/congress06/.

The *Movement* Disorder Society would like to extend their gratitude to faculty, supporters, exhibitors and delegates for their contributions in making the 10th International Congress a colossal success.

2006 MDS Awards Announced

During the 10th International Congress of Parkinson's Disease and Movement Disorders, held October 28-November 2, in Kyoto, Japan, the Society was proud to honor the following 2006 MDS awards recipients:

President's Distinguished Service Award

The President's Distinguished Service Award is given in recognition of long and distinguished service to The *Movement* Disorder Society. The recipient may only receive this award once in their lifetime.

Eduardo Tolosa
Barcelona, Spain

Honorary Member Award

The Honorary Membership Awards recognize individuals who have made extraordinary contributions to the field of Movement Disorders or otherwise to The *Movement* Disorder Society. The criteria for evaluation of Honorary Member Award nominees included the following: age, career situation, commitment to MDS, and quality of scientific contribution. Candidates for Honorary Membership may be nominated by any Regular Member or Junior Member, and are entitled to lifetime membership.

Patrick McGeer
Vancouver, BC, Canada

Niall P. Quinn
London, United Kingdom

William Koller Memorial Fund Award

The William Koller Memorial Fund Awards were given in recognition of a significant contribution to clinical research in the field of Movement Disorders. Recipients were eligible based on the criteria that they possess a clinical degree and are the first author of their abstract.

Kailash P. Bhatia
London, United Kingdom

Sanjay Bidichandani
Oklahoma City, OK, USA

K. Ray Chaudhuri
London, United Kingdom

Chadwick Christine
San Francisco, CA, USA

Donald Grosset
Glasgow, United Kingdom

Katherine Grosset
Glasgow, United Kingdom

Susan Hayflick
Portland, OR, USA

Gary Hotton
London, United Kingdom

Susanne Schneider
London, United Kingdom

Barbara Tilley
Charleston, SC, USA

Junior Award

Two Junior Award recipients were selected based on their significant contribution to clinical and basic science research in the field of Movement Disorders. The recipients were eligible based on the criteria that they are forty years of age or less, or within five years of completion of training and are the first author of the abstract.

Akiko Imamura,
Basic Science Research
Jacksonville, FL, USA

Andre R. Troiano,
Clinical Research
Vancouver, BC, Canada

Travel Grant Awards

The Movement Disorder Society's 10th International Congress Travel Grants were offered as partial support of delegates to facilitate their travel to and participation in the 10th International Congress. Candidates provided a letter of application stating their age, current position and financial need, as well as a copy of the abstract(s) they had submitted to the meeting. Preference was given to residents and trainees with five or less years experience as a healthcare professional or scientist.

Annu Aggarwal
Mumbai, India

Bhooma Aravamuthan
Bethesda, MD, USA

Mislav Budisic
Zagreb, Croatia

Anna Budzianowska
Szczecin, Poland

Andrea Carmine Belin
Stockholm, Sweden

Zuzana Chovancova
Olomouc, Czech Republic

Paulien de Vries
Groningen, Netherlands

Giorgio Fabiani
Curitiba, Brazil

Felix Geser
Philadelphia, PA, USA

Marcel Ivanov
Iasi, Romania

Natasa Klepac
Zagreb, Croatia

Norbert Kovacs
Pecs, Hungary

Renju Kuriakose
Ernakulam, India

Leonides Laguna Salvia
Hoguin, Cuba

Celia Larramendy
Buenos Aires, Argentina

Edilberto Martinez-Gongora
Hoguin, Cuba

Ashkan Mowla
Shiraz, Iran

Amit Nayak
Sagar, India

Igor Nestrasil
Prague, Czech Republic

Martin Nevrly
Olomouc, Czech Republic

Dominic Paviour
London, United Kingdom

Santiago Perez Lloret
Buenos Aires, Argentina

Igor Petrov
Skopje, Macedonia

Ilse S. Pienaar
Cape Town, South Africa

Sasa Radovanovic
Belgrade, Serbia and Montenegro

Mona Ragothaman
Bangalore, India

Julian Rodrigues
Perth, Australia

Susanne A. Schneider
London, United Kingdom

John Paul Shotbolt II
London, United Kingdom

Achal Srivastava
New Delhi, India

Dorina Jurie Tiple
Rome, Italy

Saumya Udupa
Bangalore, India

Bart van Nuenen
Nymegan, Netherlands

Hana Vranova
Olomouc, Czech Republic

Subhashie Wijemanne
Houston, TX, USA

11th International Congress Announcements

The 11th International Congress of Parkinson's Disease and Movement Disorders will gather delegates and faculty from around the world in a city where the East meets the West. The Imperial City of Istanbul is awaiting your arrival.

Dates

June 3-7, 2007 in Istanbul, Turkey

Location

All scientific sessions will take place at the Istanbul Convention and Exhibition Centre (ICEC). The ICEC is located in the heart of Istanbul, with many housing options nearby. Attendees can fly into the Istanbul Ataturk Airport or the Istanbul Sabiha Gokcen International Airport. The Havas bus service has frequently scheduled trips between the airport and the city. The service between terminals is free. You can also use a (metered) taxi to get to the city.

Abstracts

The Call for Abstracts for the 11th International Congress is now closed. We are pleased to have received over 900 abstracts, which is a great number given that the Kyoto International Congress was just months before this. All submitted abstracts were reviewed for consideration and acceptance by the Abstract Review Committee.

Scientific Program

The 2007 Scientific Program will incorporate educational courses, Opening Seminars, Plenary and Parallel Sessions, Meet the Expert Sessions, Skills Workshops, Video Sessions, Oral Platform Presentations, Controversies, Highlights of Poster Sessions and new to this year's program are the How-To-Do-It sessions. To view all faculty and Scientific Program session information, please visit the Web site to download a PDF file of the program at www.movementdisorders.org/congress/congress07/program.php.

Hotels

MDS has reserved a number of rooms at multiple hotels in Istanbul, Turkey. Please visit www.mds2007.com to reserve your hotel room. Full details, including hotel descriptions, location and distances to ICEC can be found on this Web link.

Important Dates

April 9, 2007
Advance Group registration deadline

April 23, 2007
Advance Individual registration deadline

Sunday, June 3-Thursday, June 7, 2007
11th International Congress of Parkinson's Disease and Movement Disorders

New 2006-2009 MDS Strategic Plan Approved

The 2006-2009 MDS Strategic Plan was approved by the International Executive Committee (IEC) in August 2006. The new Strategic Plan serves the Society's mission through practical application of its principles.

MDS Mission

The objective and mission of the Society shall be to advance the neurological sciences pertaining to Movement Disorders; to operate exclusively for scientific, scholarly and educational purposes; to encourage research; to provide forums, such as medical journals, scientific symposia and International Congresses, for sharing ideas and for advancing the related clinical and scientific disciplines; to encourage interest and participation in the activities of the Society among healthcare and allied professionals and scientists; and to collaborate with other related professional and lay organizations.

The 2006-2009 Strategic Plan includes several important changes and will provide continuity for the Society's future plans. The key objectives of the Plan are:

- Congress, Education and Industrial Relations
- Membership
- Journal
- Organization/Finances
- Outreach

Through the Society's many initiatives and activities, the MDS leadership, committees, task forces, regional sections, and members continue to provide support in carrying out this new Plan. The 2006-2009 Strategic Plan is also available on the MDS Web site at www.movementdisorders.org.

2006-2009 Strategic Plan

Priority I: Congress, Education and Industrial Relations

Goals:

- Expand educational program
- Expand educational role of International Congress
- Establish MDS's capacity to generate enduring educational materials
- Enhance MDS's ability to function as an in-house medical education arm
- Establish premier role of MDS in fields of RLS, Parkinson's dementia and other key topics in Movement Disorders
- Actively explore collaborative efforts towards a joint congress with other related organizations
- Identify new revenue streams to support the Society's educational activities and other initiatives that address the needs of members and the Movement Disorders community
- Integrate Supported Meetings into the Society's educational program

Priority II: Membership

Goals:

- Expand upon existing membership and create new member benefits
- Increase membership in Europe and North America
- Increase membership from underrepresented regions
- Establish affiliations of national Movement Disorder and basal ganglia groups
- Establish corporate membership
- Establish and/or enhance allied health membership in the Society

Priority III: Journal

Goals:

- Assess success/future needs of the journal
- Assess current online structure and search functionality of the Web-based journal
- Utilize the journal for education
- Increase impact factor

Priority IV: Organization/Finances

Goals:

- Increase IEC involvement in governance and administration of the Society
- Clarify and communicate the internal leadership structure of MDS
- Develop future generation of leadership
- Maintain and create new regional sections
- Establish relationships with existing international Movement Disorders research groups

Priority V: Outreach

Goals:

- Increase awareness of the Society and Movement Disorders subspecialty
- Continue to explore potential for collaborations with related organizations

The official launch of the Asian and Oceanian Section of The Movement Disorder Society (MDS-AOS) took place in Kyoto during the 10th International Congress of Parkinson's Disease and Movement Disorders. Prior to the official launch the results of the first MDS-AOS elections were announced. The first annual Asian & Oceanian Section Business Meeting was held by the AOS Officers and Executive Committee with welcome assistance from Professors Andrew Lees and Anthony Lang. We congratulate all of the founding members who helped establish the AOS and we hope it will be able to promote and expand the objectives of MDS in the Asian and Oceanian region.

Dr. Louis Tan and his colleagues are currently working very hard to organize the first Asian and Oceanian Parkinson's Disease and Movement Disorders Congress (AOPMC) which will be held in Singapore on 20 – 22 October 2007 at the Suntec International Convention and Exhibition Centre (www.aopmc.com.sg). This meeting is directed toward all healthcare professionals interested in Movement Disorders. A number of different presentation formats will be used including didactic lectures, workshops, video presentations, platform and poster sessions, as well as industry supported kick-off seminars which will be held on a date preceding the congress, 20 October 2007. The AOPMC will run concurrently with a patient and carer meeting, the 6th International Asia & Pacific Parkinson's Association Congress, which coincidentally is celebrating their Association's 10 year anniversary.

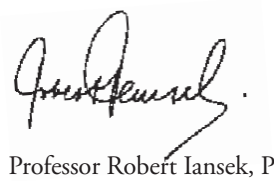
Professor Shu-Leong Ho in conjunction with Professor Shengdi Chen will run a pre-meeting course in Shanghai, Peoples Republic of China, on the 17 - 18 October 2007 on 'Evidence Based Management in Parkinson Disease'. This meeting will be supported by an Educational Grant from MDS. We are most grateful to Professors Ho and Chen for organizing this meeting which we hope will be one of many that has been developed previously for North America and Europe, but we have never had an opportunity to run within our region.

We are also currently in preliminary discussions for the preparation for the 2nd AOPMC meeting which is being organized in India. Professor Madhuri Behari is currently involved in undertaking the preliminary work for that meeting which will be held in New Delhi possibly in February 2009.

The AOS Officers and Executive Committee members will, in the next few months, look at ways of determining the educational needs of our region, focussing on all members of the healthcare team in order for us to tailor education according to the specific needs of each country, its medical infrastructure and its support services.

We are all very excited by this opportunity to represent MDS in the Asian and Oceanian region, and look forward to participating more and more in MDS activities.

Kind regards,



Professor Robert Iansek, PhD, FRACP
Chairman, MDS-AOS

Participants of the AOS General Assembly Meeting in Kyoto, Japan. From left to right: Victor Fung, Tim Anderson, Nobutaka Hattori, Young-Ho Sohn, Sheng-Di Chen, Louis Tan, Eng-King Tan, Bhim Singhal, Shu-Leong Ho, Robin Wu, Andrew Lees, Santhi Puvanarajah, Robert Iansek, Madhuri Behari, Anthony Lang, Lillian Lee, Jithanorm Suwantamee, Philip Thompson, Yoshikuni Mizuno, Caley Kleczka.

MDS-Asian & Oceanian Section (MDS-AOS)

Officers and Executive Committee Members 2007-2008

Name	Position
Robert Iansek	Chairman
Bhim Singhal	Chairman-Elect
Louis Tan	Secretary
Tim J. Anderson	Secretary-Elect
Mohit Bhatt	Treasurer
Mitsutoshi Yamamoto	Treasurer-Elect
Philip Thompson	Past-Chairman
Madhuri Behari	Executive Committee Member
Shengdi Chen	Executive Committee Member
Victor Fung	Executive Committee Member
Nobutaka Hattori	Executive Committee Member
Lillian Lee	Executive Committee Member
Santhi Puvanarajah	Executive Committee Member
Eng-King Tan	Executive Committee Member
Ruey-Meei Wu	Executive Committee Member

As I have officially handed over the Chairmanship of the European Section to Wolfgang Oertel, it is satisfying to review the progress the Section has achieved in the objectives we set for the two-year term, 2005-2006.

Ensure that all European countries served by the MDS-ES/European Federation of Neurological Societies (EFNS) Scientist Panel on PD and Other Movement Disorders have one liaison person to MDS. In April 2006, MDS-ES and EFNS wrote to the national neurological societies in Europe represented within the EFNS, proposing that one person act as liaison to both MDS (via MDS-ES) and EFNS. In light of responses received, we are working with Regina Katzenschlager, Chair of the MDS Liaison/PR Committee to establish the individual liaisons.

Propose that all European countries served by MDS-ES/EFNS should have a Movement Disorders special interest group or basal ganglia club. We identified 11 countries - Austria, Bulgaria, Denmark, Germany, Hungary, Iceland, Italy, Norway, Sweden, Switzerland and Turkey with formal or informal Movement Disorders groups. Ireland and Belgium/Netherlands, are considering the creation of national/regional groups and seven countries - Czech Republic, Estonia, Finland, Greece, Poland, Ukraine and UK – reported a Movement Disorders section within the national neurological society. If you can add to this information, please let us know!

Aim for ten countries in Europe to have a Movement Disorders special interest group or basal ganglia club affiliated to MDS-ES by December 2006. Current affiliates are the All Russian Society of Neurologists; DISMOV-SIN – Italy; SWEMODIS – Sweden; DANMODIS – Denmark. We received requests for details about affiliation from Movement Disorder groups in Ireland and the Netherlands.

Aim to recruit 200 Waived Dues members from HINARI countries in Europe. Waived Dues memberships have not been taken up as enthusiastically as we had hoped in Europe, in spite of considerable promotion by MDS-ES Visiting Professors and Invited Lecturers. Perhaps in countries where there is little sub-specialisation within neurology, neurologists are unlikely to take up membership of one specialist organization?

Increase outreach to Eastern Europe. We welcomed Mira Kapisyzi as an ex-officio MDS-ES Executive Committee member for the 2005-2006 term, and she has offered valuable insights into the educational needs of our Eastern European members in underserved countries. Neurologists from Georgia, Azerbaijan and Armenia attended the MDS-ES Teaching Course in Tbilisi, Georgia in 2005. Our Invited Lectureships at EFNS Regional Workshops in 2006 have taken MDS-ES speakers to Novosibirsk, Russia; Ekaterinburg, Russia; and Bucharest, Romania. Ipsen's support towards travel costs in 2006 was much appreciated.

MDS-ES leaders met the EFNS leadership in Glasgow to review our collaborative agreement, which runs until 2008. Both parties remain delighted with the collaboration, and our Movement Disorders programs at the annual EFNS Congress continue to be well received.

An important aim from the 2005 MDS Strategic Planning Meeting in Dublin was to establish outreach to our non-neurological colleagues. An exciting collaboration was initiated with the European Union Geriatric Medicine Society (EUGMS), when MDS members Birgit Högl, Doug McMahon and David Burn were our faculty for an MDS-ES sponsored symposium on Movement Disorders at the EUGMS 2006 Congress. GSK kindly provided support for the air fares of our faculty.

The European Section has been actively promoting The Movement Disorder Society throughout Europe. We are expanding our outreach to neurologists in developing countries in harmony with the EFNS, to general neurologists and young neurologists in training through the EFNS Congresses and outreaching to the geriatricians who share the care of Movement Disorders patients.

The MDS-ES Officers and ES-EC have worked hard to ensure the success of these initiatives, and I thank them very much for their major contribution. Special thanks go to Eduardo Tolosa, Thomas Gasser and François Tison, who retired as Section Past-Chairman, Secretary and Treasurer respectively at the end of 2006, and Carlo Colosimo, Murat Emre, Paul Krack, and Ivan Rektor, outgoing ES-EC members. It is also a pleasure to thank all the MDS-ES Invited Lecturers who have worked so hard to promote our Society.

Prof. Niall Quinn
2007-2008 Past-Chairman, MDS-ES Section

Should GDNF Intraparenchymal trials be Continued? YES

—Don M. Gash, PhD, University of Kentucky Chandler Medical Center, Morris K. Udall Parkinson's Disease Research Center for Excellence, Department of Anatomy and Neurobiology, Neurology and Neurosurgery, Lexington, KY, USA
—Greg A. Gerhardt, PhD, University of Kentucky Chandler Medical Center, Morris K. Udall Parkinson's Disease Research Center for Excellence, Department of Anatomy and Neurobiology, Neurology and Neurosurgery, Lexington, KY, USA
—John T. Slevin, MD, University of Kentucky Chandler Medical Center, Morris K. Udall Parkinson's Disease Research Center for Excellence, Department of Anatomy and Neurobiology, Neurology and Neurosurgery, Lexington, KY, USA
—Byron Young, MD, University of Kentucky Chandler Medical Center, Morris K. Udall Parkinson's Disease Research Center for Excellence, Department of Anatomy and Neurobiology, Neurology and Neurosurgery, Lexington, KY, USA

Can a drug that failed to demonstrate efficacy in two double-blinded clinical trials, with patients showing placebo responses in the drug effect range and reported to stimulate autoimmune responses possibly revolutionize the treatment of PD? Such was levodopa's record in the mid 1960's, the gold standard for current therapy.

"……the Phase-II Intraputamenal-GDNF trial has generated valuable data and important questions that can only be answered by testing and retesting in additional clinical trials and pre-clinical studies."

Some "great drugs," as George Cotzias, the father of levodopa therapy, cogently wrote,[1] are the "consequences of making, testing, rephrasing and retesting scientific hypotheses." Now, we are challenged with the enigma of glial cell line-derived neurotrophic factor (GDNF). Why was it not efficacious in a recent double-blinded, placebo controlled Phase-II trial?

In two preceding phase I trials,[2,3] all 15 patients were reported to significantly benefit from continuous GDNF infusion into the putamen. Postmortem examination of a patient dying from a heart attack with pronounced clinical benefits from three years of GDNF therapy, revealed regeneration of the nigrostriatal dopaminergic system,[4] consistent with similar responses found in numerous animal studies. Yet, the recent Phase-II trial[5] did not cross the prospectively defined primary efficacy hurdle. Placing the study in perspective, as with some of the early findings on levodopa efficacy, the results from a single trial do not mean that GDNF has no efficacy, or that the benefits observed in the Phase-I trials were placebo effects, or that the Phase-II trial "failed". The relatively small number of patients given intraputamenally infused GDNF to-date, the variables of dose, delivery mode, clinical trial design and analysis make it premature to draw conclusions about whether genuine clinical benefits can be distinguished from non-specific or placebo phenomena. Rather, as in the development of other drugs and therapies, the Phase-II Intraputamenal-GDNF trial has generated valuable data and important questions that can only be answered by testing and retesting in additional clinical trials and pre-clinical studies.

While pre-clinical research is underway, several safety concerns are blocking new clinical trials. Amgen has reported that high levels of GDNF can produce brain damage – specifically, cerebellar lesions in rhesus monkeys. Unfortunately, the complete results from the toxicology study in which the lesions were reported have not been made public. What has been revealed suggests that the study may have been seriously flawed, with many animals having to be euthanized because of surgical complications. Trophic factor-induced cerebellar lesions are not consistent with any known properties of GDNF and have not been independently replicated. Most importantly, there is no evidence of GDNF-induced cerebellar injury in patients. The other concern is the presence of GDNF antibodies in some patients. So far, patient response to neutralizing GDNF antibodies has been similar to that of neutralizing antibodies to beta interferon. Up to 45% of the patients treated with beta interferon developed antibodies, without clinical manifestations. One reason is that other related proteins in the body can substitute for beta interferon. GDNF also has closely related proteins that can substitute for it. An example is neurturin, which is found in overlapping brain areas with GDNF. Clinical manifestations to GDNF antibodies have not been documented in patients receiving GDNF therapy. Thus, while safety concerns have been raised, they are hypothetical and not supported by patient data.

Therefore, we believe that it is time to proceed with properly designed, adequately powered, multicenter Phase-II studies building upon the knowledge and insights gained from the completed clinical trials. Trophic factor therapy has the potential to revolutionize the treatment of PD by slowing neurodegenerative processes and promoting the restoration of injured neurons and neural circuitry. As history shows, only through resuming clinical testing can we determine if this promise can be realized.

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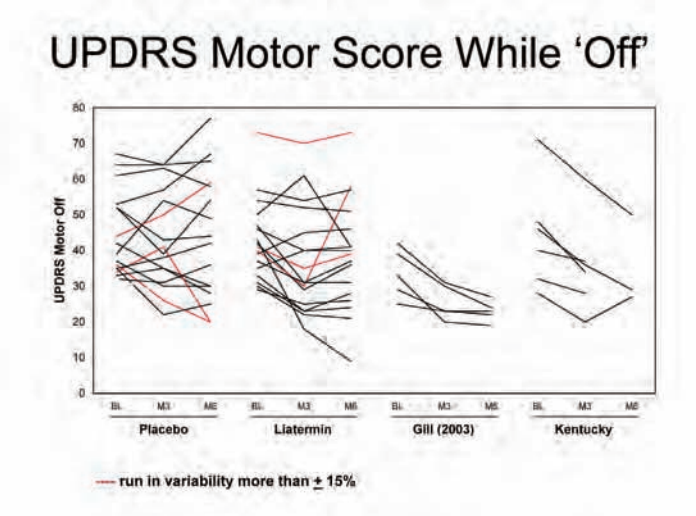
2. Gill SS, Patel NK, Hotton GR, et al. Direct brain infusion of glial cell line-derived neurotrophic factor in Parkinson disease. Nat Med. 2003;9:589-595.
3. Slevin JT, Gerhardt GA, Smith CD, Gash DM, Kryscio R, Young AB. Unilateral Intraputamenal GDNF Improves Bilateral Motor Functions in Patients with Parkinson's disease. J of Neurosurgery 2005; 102:216-222.
4. Love S, Plaha P, Patel NK, Hotton GR, Brooks DJ, Gill SS. Glial cell line-derived neurotrophic factor induces neuronal sprouting in human brain. Nat Med. 2005; 11:703-704.
5. Peck P. Amgen decision to halt GDNF clinical trials and withdraw the drug triggers protests from researchers and patients. Neurology Today 2005;5 (4):4,7,24.

Should GDNF Intraparenchymal Trials be Continued? NO

—Mark Stacy, MD, Duke University, Division of Neurology, Durham, NC, USA

The central issue in the glial cell line-derived neurotrophic factor (GDNF) program is whether a randomized placebo-controlled trial demonstrates primary outcome variable efficacy. By agreeing to participate in this trial, it seems reasonable to assume that each investigator recognized that placebo-controlled data is necessary to confirm open trial findings.

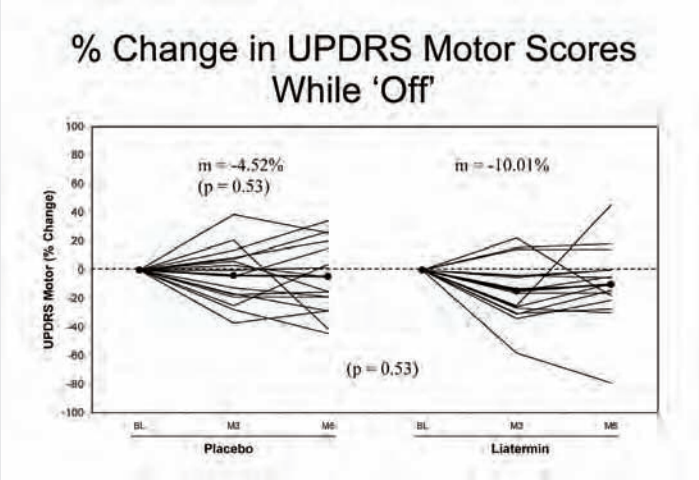
In 2003, a single center open-label trial of continuous intraputamenal infusion (Ipu) of 30 µg/day in five subjects reported a 39% improvement in UPDRS motor score and significant increase in putamenal ^{18}F-dopa uptake on PET after 12 months of therapy. A second open unilateral Ipu trial in 10 subjects noted > 30% bilateral benefit in both on- and off-medication scores at 24 weeks. [Figure 1; Columns 3,4] These encouraging reports prompted a double-blind trial in which 34 subjects were randomized 1:1 to receive bilateral Ipu at 15 µg/day or placebo. The primary endpoint was the change in UPDRS motor score in the off condition at six months. Secondary endpoints included other UPDRS scores, dyskinesia ratings, patient diaries, timed walking, Purdue Pegboard, levodopa dosage and ^{18}F dopa uptake. Guided by the open label data, the sample size was powered for a 90% chance of detecting a 25% difference between the groups. No statistical differences were seen in any clinical outcome variables, even when the data were reassessed by moderate and severe impairment. However, a 32.5% difference favoring GDNF in ^{18}F-dopa influx was observed. Adverse events included parasthesias, headache, upper respiratory infection and three subjects developed neutralizing antibodies. (Pending manuscript acceptance, these are previously presented abstract data.)



The controversy concerning the Amgen GDNF (Liatermin®) clinical trial remains puzzling. The www.gdnf4parkinsons.org Web site has been instrumental in garnering support for program renewal, even though most of the 16 subject testimonials recount open-label experiences. Although the media strongly advocates resuming Ipu, no story has mentioned that only one subject demonstrated remarkable (80%) improvement in the blinded phase. In retrospect, investigator opinions may reflect this chance of randomization, given that in two sites only one of seven subjects received the active drug.

> *"....it remains difficult to endorse pleas to continue the current Ipu protocol without critically addressing issues of study design, subject selection, randomization, catheter placement, port size, dosage, statistical analysis and the significance of neutralizing antibodies."*

At this time blinded, GDNF therapy falls far short of efficacy in any clinical measure [Figure 1]. While some disagree with the decision to stop this clinical program, it remains difficult to endorse pleas to continue the current Ipu protocol without critically addressing issues of study design, subject selection, randomization, catheter placement, port size, dosage, statistical analysis and the significance of neutralizing antibodies. These potential questions are not trivial, and it seems prudent to assess the past before leaping back into human trials with a failed protocol.



Consider these prophetic words from Professor Patrik Brundin in an October 2002, Brain editorial: "… the path to a new clinical therapy is typically painstakingly long and difficult to navigate. ...[it] may be tortuous, filled with detours that set the field back, as well as shortcuts and parallel tracks that yield different strategies, which develop at their own speed. The development of glial cell line-derived neurotrophic factor … provides an example of such an interesting journey."

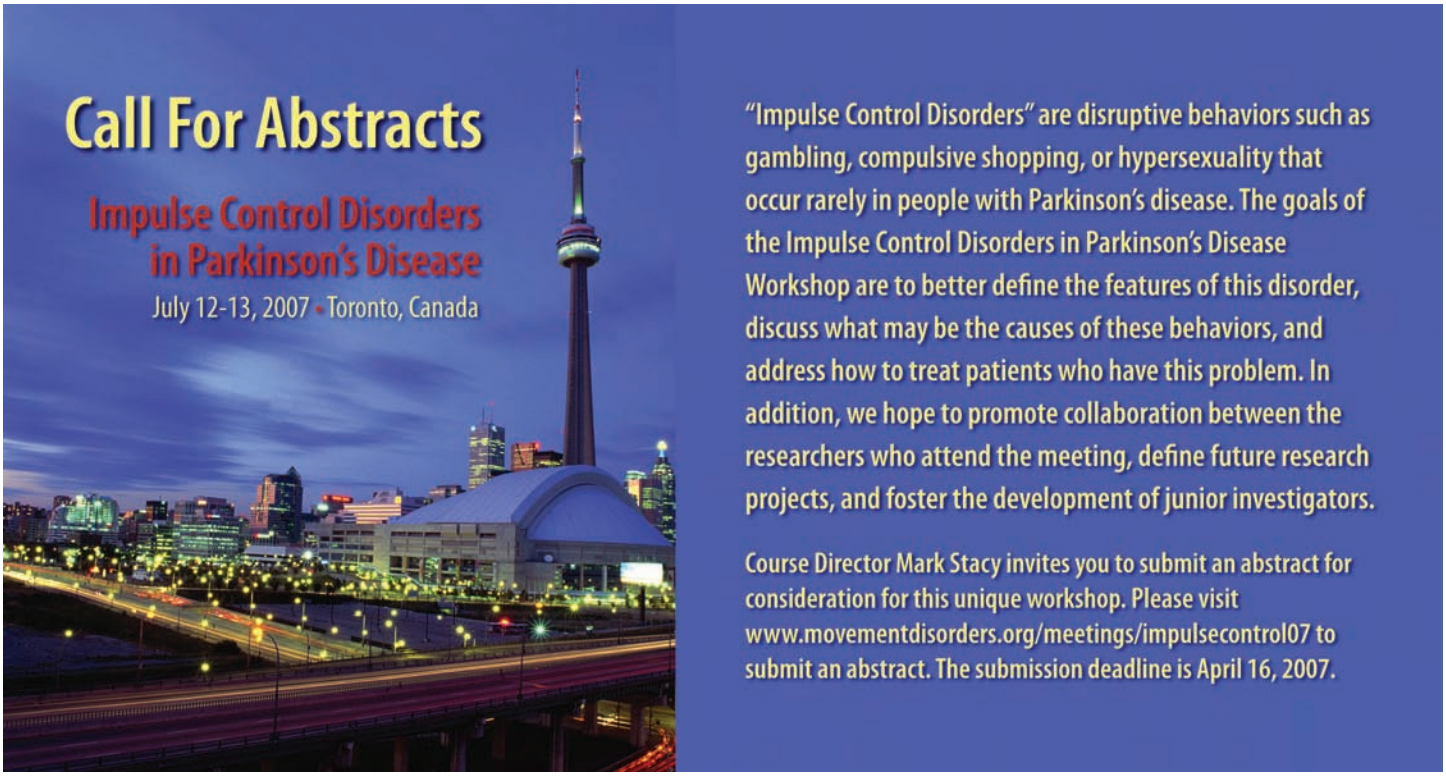
Genetic Testing for Parkinsonism?

—John Hardy, PhD, NIA and NINDS, NIH, Bethesda, Maryland, USA
—Katrina Gwinn-Hardy MD, NIA and NINDS, NIH, Bethesda, Maryland, USA

The finding of many genes involved in Parkinson's disease (see Cover story by Thomas Gasser) immediately brings up the issue of genetic testing for the disease: is diagnostic testing appropriate? And is presymptomatic testing also appropriate? Currently, this is a very complex issue without a simple answer. A high proportion (estimated at up to 50%) of cases with onset before the age of 40 are believed to have recessive inheritance of parkin, DJ-1 or PINK1, however, it is not clear that the screening of such cases for mutations would be of clinical utility. The presence or absence of any of these would not alter the clinical management of the case, nor would it have quantifiable implications for the children of the patient, since the likelihood would be that they would be heterozygotes and thus at comparatively low risk. The only relatives whose risk status would be considerably altered would be sibs of the proband who, in the case of a recessive disease, would be at ¼ a priori risk. While conceivably a couple would want testing for the purpose of family planning, it is unlikely that the unaffected parent would be a heterozygous mutation carrier except in the case of consanguineous marriages. In addition, for boring technical reasons, screening for mutations in recessive diseases is a non-trivial problem because some mutations are difficult to find. Thus, all three outcomes of a genetic test (two mutations in trans, one mutation or no finding) are not simply interpretable. For the moment, it is difficult to think of any utility for clinical genetic testing for the recessive genes in Parkinson's disease.

Some pedigrees with autosomal dominant inheritance in which mutations in either α-synuclein or LRRK2 have been found, have been offered the Huntington's protocol, and certainly, many of the synuclein kindreds have a fulminant course of disease, similar to the severity and rate of decline of Huntington's itself. However, LRRK2 mutations have genetic features for which an approach by clinicians and genetic counselors remains to be developed. These include that they are common, but not completely penetrant, and appear to be associated with a rather benign disease and slower course than average Parkinson's diseases cases and with less prevalent dementia. This combination of factors is difficult to legislate, since screening for the most common mutations is relatively simple and could be applied to all Parkinson's disease cases. Finding a mutation, in such a case may be associated with a benign outcome for the case, but will, of course, imply that the patients' children are at moderately increased risk of disease (much less than 50% because it seems that the disease is less than 50% penetrant even by age 80). The large number of cases who would be reasonably eligible for screening probably means that it is impractical to apply the Huntington's protocol before genetic testing, but equally clear, the children of mutation positive cases will need some counseling.

And one final note… in autosomal dominant Asian and African families (especially) with "Parkinson's disease", clinicians should consider SCA2 and SCA3 testing even in the absence of ataxic signs.



Two Dopamine Transporter Imaging in Neurological Practice Workshops held in Copenhagen, Denmark and Barcelona, Spain

The *Movement* Disorder Society European Section's Dopamine Transporter Imaging in Neurological Practice workshop was held on December 5, 2006 at the Bispebjerg University Hospital in Copenhagen, Denmark. Course Director Dr. Lene Werdelin (Copenhagen) led the workshop, which included presentations from Drs. Jan Booij (Amsterdam), Lars Friberg (Copenhagen), Annemette Løkkegaard (Copenhagen), Markus Nowak Lonsdale (Copenhagen) and Christoph Scherfler (Innsbruck).

The most recent offering of the workshop was held at the Hospital Clinic in Barcelona, Spain on February 23, 2007. Prof. Eduardo Tolosa (Barcelona) and Dr. Francisco Lomeña (Barcelona) served as Workshop Directors, while Andrew Lees (London), Maria Jose Marti (Barcelona), Javier Pavia (Barcelona), Werner Poewe (Innsbruck), Philippe Remy (Orsay, France), Domenec Ros (Barcelona) and Francesc Valldeoriola (Barcelona) also presented during the course.

These workshops introduced participants to the basic aspects of dopamine transporter function in neuroimaging, as well as the role of dopamine transporter single photon emission computed tomography (SPECT) imaging in the investigation of parkinsonism syndromes and in the diagnosis of atypical tremors, drug-induced and psychogenic parkinsonism. The cost-effectiveness of dopamine transporter imaging was discussed as well.

Aside from formal presentations at the Copenhagen workshop, participants were divided into small groups and given a chance to discuss unique case presentations, including an introduction to the SPECT imaging equipment. The fully subscribed audience consisted mostly of neurologists and neurological residents from Denmark and The Netherlands, but also included participants from Bulgaria, Sweden, Norway, Spain and the United Kingdom.

Participants at the Barcelona workshop were treated to a tour of the Nuclear Medicine Department of the Hospital Clinic during the afternoon session. These participants were mainly neurologists, nuclear medicine and neurology residents from Barcelona, but also included participants from the United Kingdom, Italy, Romania, France, Greece, Portugal, the Philippines, Austria, Norway, the United States, the Czech Republic and Chile.

Participants listen to a didactic lecture during the DTI course in Copanhagen

These courses were made possible by an educational grant from GE Healthcare.

Third International Symposium on Neuroacanthocytosis: The Asian Perspective

—Ruth H Walker, MB, ChB, PhD, Veterans Affairs Medical Center, Neurology, Bronx, NY, and Mount Sinai School of Medicine, New York, NY, USA
—Adrian Danek, MD, Ludwig-Maximilians-Universtät München, Neurogische Klinik und Poliklinik, Germany
—Akira Sano, MD, PhD, Kagoshima University, Department of Psychiatry, Kagoshima, Japan
—Shinji Saiki, MD, Cambridge Institute for Medical Research, University of Cambridge, Department of Medical Genetics, Cambridge, UK

The Third International Symposium on Neuroacanthocytosis was held at Library Hall of Kyoto Prefectural University of Medicine on October 28, 2006 and was supported by The *Movement* Disorder Society, Nippon Boehringer Ingelheim, The Mary Kinross Charitable Trust, Mr. and Mrs. Carl H Pforzheimer, The Advocacy for Neuroacanthocytosis Patients, and John Grooms. This meeting was a satellite meeting of the 10th International Congress of The Movement Disorder Society and provided an important opportunity to collaborate with Japanese researchers and clinicians, as there appears to be a relatively high incidence of chorea-acanthocytosis in Japan.

This meeting was aimed at integrating Asian thinking and experience into the European and North American work on chorea-acanthocytosis (ChAc) and McLeod syndrome (MLS), the core neuroacanthocytosis (NA) syndromes. It was proposed by Prof. Akira Sano (Kagoshima) and organized by Shinji Saiki (Cambridge), Ruth Walker (New York) and Adrian Danek (Munich). The meeting brought together clinicians and basic scientists from a variety of disciplines, including neurologists, psychiatrists, haematologists, neuropathologists, biochemists, and molecular biologists from Asia, Australia, Europe and North America. Taking place in Kyoto, the meeting featured many Japanese presenters, who have made important contributions to the field over the past quarter century. The meeting program consisted of 18 invited lecturers plus one poster session covering the molecular features, animal models, and clinical and neuropathological features of the neuroacanthocytosis syndromes.

The first session of the Symposium was an introduction: Overview of the neuroacanthocytosis syndromes (Ruth Walker) in Japan (Genjiro Hirose). The second and third session included basic research concerning VPS13A protein function (Antonio Velayos-Baeza and Clotilde Levecque), XK and Kell proteins (Soohee Lee), red blood cell (RBC) shapes (Gordon Stewart), membrane anomalies (Giel Bosman), and biochemical features in MLS (Lucia de Franceschi).

At the poster session, Kageyama and collaborators (Kagoshima, Japan) presented a case of ChAc with cardiomyopathy. Dr. Kawakami et. al. reported a case of McLeod syndrome which neuropathologically mimicked muscular dystrophy. Dr. Pang Ying Shih from Taiwan described some success in the treatment of involuntary trunk movements with the anti-convulsant, levetiracetam. Dr. Sonia Gandhi from London is tracing Richard Hardie's 1991 cohort of NA cases in the UK. Benedikt Bader from the Munich group showed data on detection of the chorein protein in brain tissue.

Afternoon sessions focused on animal models (Masayuki Nakamura: ChAc; Mac Ho: MLS) as well as clinical aspects of NA syndromes (Yoshihiko Tani: MLS detected by Japanese blood centers; Hans Jung: MLS update; Akira Sano: Psychiatric morbidity; Fusako Yokochi: Neurosurgery; Shinji Saiki: Muscular aspects of ChAc; Mikihiro Kihara: autonomic dysfunction of ChAc; Benedikt Bader: Neuropathology of ChAc; Felix Geser: Neuropathology of MLS). In this session, neurologist Adrian Danek from Munich presented plans to build a database for the ready exchange of anonymous patient information in ChAc and MLS, to facilitate research and drug tests. Using the model established by the European Huntington Disease Project, this could be ready in early 2007 – given sufficient input from a working group of colleagues. We believe that this would lead to the future therapeutic strategies in NA syndromes.

Glenn Irvine closed the meeting by encouraging international cooperation in the campaign to understand neuroacanthocytosis and support patients. Information for families and patients through The Advocacy for Neuroacanthocytosis Patients can be found at www.naadovocacy.org.

This meeting resulted in the development of new collaborations between North American and European and Japanese researchers and clinicians. Plans are in progress to publish the abstracts of the presentations in a journal, and the proceedings as a book in Neuroacanthocytosis Syndromes, Volume II, to be published by Springer.

Announcements

Join the International RLS Study Group

We are inviting individuals with a special interest in Movement Disorders to join the International Restless Legs Syndrome Study Group (IRLSSG).

The IRLSSG is responsible for:

- Developing the criteria for the essential clinical features of Restless Legs Syndrome (RLS).
- Developing and validating a severity rating scale for RLS.
- Defining the clinical criteria for measuring Periodic Limb Movements in Sleep.

IRLSSG members are currently carrying out joint linkage studies in an attempt to find the gene(s) responsible for RLS symptoms. The IRLSSG has advised pharmaceutical companies on the experimental design of therapeutic trials, and IRLSSG members have participated in several large industry-sponsored RLS treatment trials.

There are two types of membership:

1. VOTING MEMBERS
   a) Individuals with a doctoral degree or equivalent who are currently working in areas related to RLS research or clinical practice.
   b) Students or para-professionals (including study coordinators and technicians) who provide evidence of significant contributions to the field within the past five years (such as working with an RLS support group) or one or more publications in the field.
2. NON-VOTING MEMBERS
   Students or para-professionals who have not published or made significant contributions to the field may apply for non-voting membership.

   Excluded from membership are individuals working full time for for-profit organizations with potential conflicts of interest, such as pharmaceutical companies.

   Membership is free. To apply, please submit a letter of intent and attached curriculum vitae to Dr. Marco Zucconi at zucconi.marco@hsr.it.

The Progressive Supranuclear Palsy (PSP Europe) Association

Research Fellowship Grant Announcements for 2007

The PSP (Europe) Association announces that funding for research fellowships is available. Applicants should apply in the first instance to the Sara Koe PSP Research Centre, 1 Wakefield Street, London WC1N 1PJ or by email to s.stoneham@ion.ucl.ac.uk. Submit a brief proposal giving an outline of their research project with an estimate of costs to cover salary and, if deemed necessary, laboratory consumables. Following peer review successful applicants will be asked to complete a full grant application. Preference will be given to 2 year research fellows.

Progressive Supranuclear Palsy Study

The University of Louisville Movement Disorder Program, is seeking patients with progressive supranuclear palsy for a multi-center study to identify environmental and genetic risk factors associated with the disease. Subjects will be provided with a physical and neuropsychological examination, will be asked to provide a blood sample for DNA testing and will take part in a detailed phone interview. This study is sponsored by the National Institutes of Health (NIH). Subjects can be seen at eight medical centers throughout the United States. For more information please call 1-866- PSP- 0448 (1-866-777-0448).

MDS Accepting Applications for the Visiting Professor Program

The *Movement* Disorder Society (MDS) is currently accepting applications for countries interested in hosting a Visiting Professor in the MDS-sponsored Visiting Professor Program. The MDS Visiting Professor Program provides educational opportunities in Movement Disorders to regions of the world that are under-represented in MDS and do not have regular access to educational programs in Movement Disorders. For more information or applications for this program, please click on the following link, www.movementdisorders.org/education/visitingprofessor.shtml or contact Crystal Henderson, MDS Education Program Manager, at +1 414-276-2145.

Job Openings

Movement Disorders Specialist at Penn State Milton S. Hershey Medical Center

The Department of Neurology at Penn State Milton S. Hershey Medical Center is recruiting for a full-time Movement Disorders Specialist. The position is at the Assistant/Associate Professor level. This is an exciting opportunity for an individual with expertise in movement disorders to join a growing comprehensive clinical and research program. Candidates should be board certified or board eligible in neurology and have completed fellowship training in movement disorders, or have comparable experience. Applicants should submit a letter of interest with a C.V. to David Good, MD, Professor and Chair, Department of Neurology-H037, Penn State University College of Medicine, 500 University Drive, Hershey, PA 17033, e-mail dgood@psu.edu. Women and minorities are encouraged to apply. Job Requisition #18056.

Movement Disorders Neurologist at Evanston Northwestern Healthcare

The Department of Neurology and the Division of Movement Disorders at Evanston Northwestern Healthcare is seeking a third neurologist with subspecialty interest and training in movement disorders to support a growing program.

This position is full-time in a hospital-based practice, Evanston Northwestern Healthcare Faculty Practice Associates. Evanston Northwestern Healthcare operates the Evanston, Glenbrook, and Highland Park Hospitals.

Applicants will be eligible for faculty appointment at the Instructor or Assistant Professor level, non-tenure track, at the Feinberg School of Medicine, Northwestern University. The proposed starting date is negotiable. Salary is competitive. Applicants must be certified by the ABPN, or in process of certification.

Continued from page 19...

Applications being accepted starting October 1st, 2006. Send C.V. to Thomas P. Bleck, M.D., Chairman, Department of Neurology, Evanston Northwestern Healthcare, 2650 N. Ridge Ave., Evanston, IL 60201.

Evanston Northwestern Healthcare and Northwestern University are Affirmative Action/Equal Opportunity Employers. Hiring is contingent upon eligibility to work in the United States. Women and minorities are encouraged to apply. Close date July 2007.

Movement Disorders fellowship at the Keck/USC School of Medicine

The Division of Movement Disorders at the Keck/USC school of Medicine is offering a 1-2 year movement disorders fellowship to start July 1, 2007. The fellowship offers a comprehensive clinical opportunity to work in a large specialty clinic with 5 faculty members. The fellow will become proficient in the care of Parkinson's Disease patients, dystonia patients including an extensive botulinum toxin clinic, and will have an opportunity to work in our DBS/surgical program. There will also be an opportunity to participate in a large, thriving clinical trials program for PD and dystonias. If desired, a second year of fellowship to include a rich basic research experience in our lab is available. We have a well developed neuroplasticity lab evaluating non-human primate and rodent models of MPTP-parkinsonism.

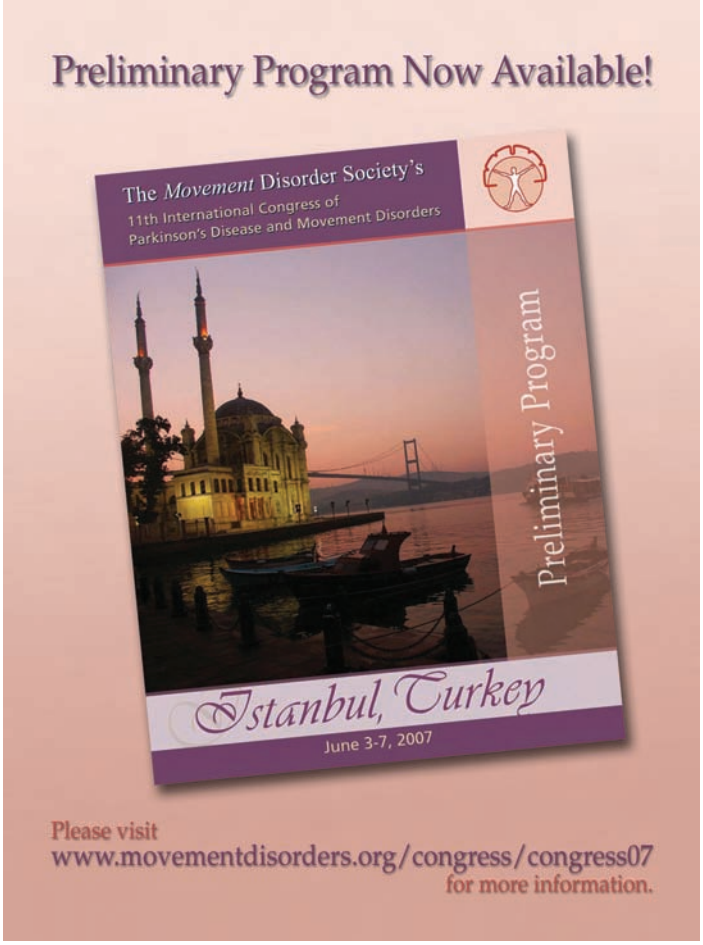
All interested candidates should email Dr. Mark Lew for further details and an application. mlew@surgery.usc.edu

Pediatric Clinical Neurologist at Texas A&M University

Scott & White/ Texas A&M College of Medicine Movement Disorders, The Scott &White Department of Neurology and The Texas A&M University System Health Science Center College of Medicine is seeking outstanding adult and pediatric Clinical Neurologists with fellowship training in movement disorders to expand its clinical neuroscience program. The department (currently consisting of 5 adult and 1 pediatric neurologists) functions as a consultative service and is involved in medical student and resident education. Academic appointment and rank is commensurate with experience and qualifications. Clinical research opportunities are available for interested candidates.

Scott & White is the largest multi-specialty practice in Texas, with more than 530 physicians and research scientists who care for patients at Scott & White Memorial Hospital in Temple and within the 15 regional clinic system networked throughout Central Texas. Over $250 million in expansions are currently underway, including two new hospitals and three regional clinics. Led by physicians with a commitment to patient care, education and research, Scott & White is listed among the "Top 100 Hospitals" in America and serves as the clinical educational site for The Texas A&M University System Health Science Center College of Medicine. Additionally, the 180,000-member Scott & White Health Plan is the #1 health plan in Texas.

Scott & White offers a very generous salary, retirement plan, three weeks CME, and a comprehensive benefit and vacation package. For additional information, please call or send your CV to: Dr. Richard Lenehan, MD; Chairman, Department of Neurology; c/o Jason Culp, Physician Recruiter, Scott & White Clinic, 2401 S. 31st, Temple, TX 76508. (800) 725-3627 jculp@swmail.sw.org Scott & White is an equal opportunity employer. For more information on Scott & White, please visit our web site at: www.sw.org



May 10, 2007
Language, Cognition and Parkinson's Disease: A Multidisciplinary Meeting. University of Groningen, The Netherlands. Contact: Femke Wehrens, TEL: +31-(0)503635870, E-mail: e.j.h.m.wehrens@rug.nl; Web site: www.let.rug.nl/parkinson

***May 10-12, 2007**
GeNeMove Symposium: Hereditary Movement Disorders. Bonn, Germany. Contact: Thomas Klockgether, University of Hospital Bonn, Department of Neurology, Germany; TEL: +49-228-5736; FAX: +49-228-5024; E-mail: klockgether@uni-bonn.de; Web site: www.genemove.de/html/symposium/sympengl; Symposium Program: http://www.movementdisorders.org/meetings/hereditaryataxias0507.pdf

May 30 – June 2, 2007
Dopamine 50 Years. Göteborg, Sweden. Contact: Congress Secretariat, Congrex Sweden, Ref. Dopamine 2007, P.O. Box 5078, 402 22 Göteborg, Sweden; TEL: +46-31-708-60-00; FAX: +46-31-708-60-25; E-mail: DA50@congrex.com; Web site: http://www.congrex.se/dopamine50years/ Second Announcement: http://www.movementdisorders.org/meetings/dopamine50years.pdf

***June 3-7, 2007**
11th International Congress of Parkinson's Disease and Movement Disorders. Istanbul, Turkey. Offered by The Movement Disorder Society. Contact: The Movement Disorder Society, 555 E. Wells Street, Suite 1100, Milwaukee, WI 53202 USA; TEL: +1 414-276-2145; FAX: +1 414-276-3349; E-mail: congress@movementdisorders.org; Web site: www.movementdisorders.org

June 8-9, 2007
Update on Dystonia: from basic science to therapeutic strategies. Villa Mondragone, Rome, Italy. Contact: Antonio Pisani, MD, University of Rome Tor Vergata, via Montpellier, Rome 00133, Italy; TEL: +39-06-72596010; FAX: +39-06-72596006; E-mail: pisani@uniroma2.it; Web site: http://dystonia2007.uniroma2.it/

June 16-20, 2007
17th Meeting of the European Neurological Society. Rhodes, Greece. Contact: Administrative Secretariat ENS, AKM Congress Service, Clarastrasse 57, Basel, 4005 Switzerland; TEL: +41-61-686-77-11; Fax: +41-61-686-77-88; E-mail: ensinfo@akm.ch; Web site: www.ensinfo.com

***June 27, 2007**
1997 - 2007, 10 Years of Alpha-Synuclein in Parkinson's disease. Athens, Greece. Contact: Leonides Stefanis, University of Athens Medical School, Athens, Greece; TEL: +30-210-659-7214; FAX: +30-210-659-7545; E-mail: lstefanis@bioacademy.gr ; Web site: www.bioacademy.gr

***July 8-9, 2007**
New Frontiers in Basic and Clinical research in Parkinson's Disease and Other Synucleinopathies. Queensland, Australia. Contact: Kay Double, Prince of Wales Medical Research Institute, Barker Street, Randwick, NSW 2031, Australia; TEL: +61-0-9399-1056; FAX: +61-2-9399-1105; E-mail: k.double@unsw.edu.au ; Web site: www.powmri.edu.au

July 10-11, 2007
Movement Disorders: Focus on the Thalamus and Basal Ganglia. Sydney Australia. Contact: Dr. Mick Gould, Convention Associates, 13th Jeffrey Street, Mt. Waverley VIC 3149 Australia; TEL: +61-3-9887-8007; FAX: +61-3-9887-8773; E-mail: convention@optusnet.com.au; Web site: www.ibrosatellite.com

***July 12-13, 2007**
Impulse Control Disorders in Parkinson's Disease Workshop. Toronto, ON, Canada. Contact: Larissa Sevcik Program Manager, The Movement Disorder Society, 555 East Wells Street, Suite 1100 Milwaukee, WI 53202, USA; TEL: +1 414-276-2145; FAX: +1 414-276-3349; E-mail: lsevcik@movementdisorders.org; Web site: www.movementdisorders.org/meetings/impulsecontrol07

July 14-18, 2007
International Society for Posture and Gait Research. Burlington, VT, USA. Contact: John Jeka, University of Maryland, Department of Kinesiology, Neuroscience and Biomedical Engineering, College Park, MD 20742-2611 USA; TEL: +1 301-405-2512; FAX: +1 301-405-5578; E-mail: jjeka@umd.edu; Web site: www.ispgr.org

***July 18-20, 2007**
Motor Control. Darwin, Australia. Contact: Michael Ridding, The University of Adelaide, Adelaide, SA 5005 Australia; TEL: +61-8830-37592; FAX: +61-8830-33356; E-mail: Michael.ridding@adelaide.edu.au

***July 30-August 2, 2007**
17th Annual Course: A Comprehensive Review of Movement Disorders for the Clinical Practitioner. St. Regis Resort, Aspen, CO, USA. Contact: Center for Continuing Medical Education, Columbia University College of Physicians & Surgeons, 630 West 168th Street, Unit 39, New York, NY, 10032, USA; TEL: +1-212-305-3334; FAX: +1-212-781-6047; E-mail: cme@columbia.edu; Web site: http://ColumbiaCME.org

September 6-9, 2007
1st World Congress on Controversies in Neurology (CONy). Berlin, Germany. Contact: ComtecMed Medical Congresses, P.O. Box 68, Tel Aviv, 61000, Israel. TEL: +972-3-5666166; FAX: +1 972-3-5666177; E-mail: cony@comtecmed.com; Web site: www.comtecmed.com/cony

September 15-20, 2007
American Association of Neurological Surgeons Annual Meeting. San Diego, CA, USA. Contact: American Association of Neurological Surgeons, 5550 Meadowbrook Drive, Rolling Meadows, IL 60088 USA; TEL: +1 847-378-0500 or +1 888-566-2267; FAX: +1 847-378-0600; E-mail: info@aans.org; Web site: www.neurosurgery.org/aans/meetings

October 7, 2007
21st Annual Symposium on the Etiology, Pathogenesis and Treatment of Parkinson's Disease and Other Movement Disorders. Marriott Wardman Park Hotel, Washington D.C., USA. Contact: Roseanna Battista; TEL: +1 585-275-1642; E-mail: Roseanna.Battista@ctcc.rochester.edu

October 10-13, 2007
Second Joint Meeting of the European Federation of Autonomic Societies & American Autonomic Society Meeting. Palais Ferstl, Vienna, Austria. Contact: Bianca Theuer, Vienna Medical Academy, Alser Str. 4, Vienna 1090, Austria; TEL: 43-1-4051383-12; FAX: 43-1-4078274; E-mail: efas2007@efasweb.com; Web site: www.efasweb.com/2007

***October 11-13, 2007**
Abnormal Plasticity in Basal Gangila: From Dyskinesia to Deviant Behavior. Quebec City, Quebec, Canada. Contact: Emmanuelle Pourcher, Quebec Memory and Motor Skills Disorder Clinic, 65 Sainte-Anne, 3rd Floor, Quebec City, Quebec, Canada; TEL: +418-692-2227; FAX: +418-692-3338; E-mail: psa@rig.qc.ca

October 12-13, 2007
4th International Meeting of the Brain Stem Society. Johannes Gutenberg University, Mainz, Germany. Contact: PD Dr. Juergen Marx, BSS Meeting 2007, Department of Neurology, University of Mainz, Lagenbeckstr. 1, Mainz, Germany; TEL: +49-6131-177194; FAX: +49-6131-175697; E-mail: marx@neurologie.klinik.uni-mainz.de; Web site: http://www-klinik.uni-mainz.de/Neurologie/aktuelles/VorprogrammBrainStemMeeting.pdf

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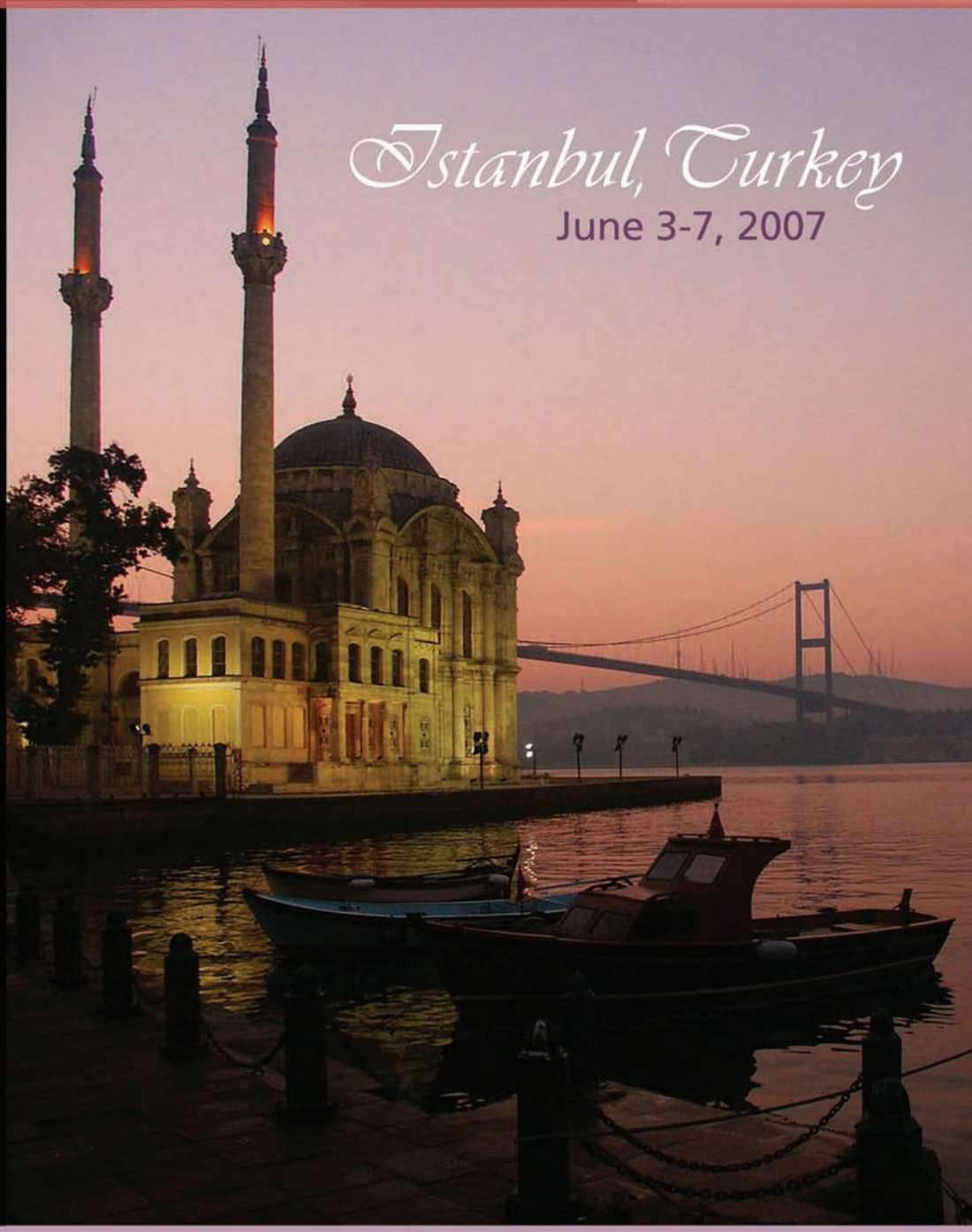
The *Movement* Disorder Society's

11th International Congress of Parkinson's Disease and Movement Disorders

The purpose of the MDS International Congress is to offer a forum for clinical and basic discussion on a variety of Movement Disorder topics, including presentations of current research and available treatments. The target audience includes clinicians, researchers, post-doctoral fellows, residents and medical school students with an interest in the current research and approaches for the diagnosis and treatment of Movement Disorders.



Istanbul, Turkey

June 3-7, 2007

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