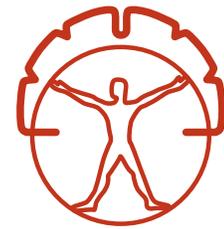


MOVING ALONG

Editor, Antonio Strafella, MD, PhD, FRCPC



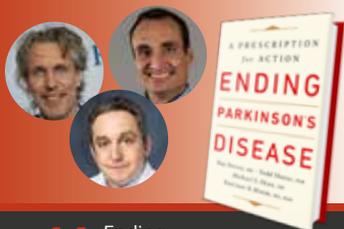
International Parkinson and
Movement Disorder Society



10 Telemedicine and
Movement Disorders: The
Impact of the Coronavirus
Pandemic

move together to end
parkinson's
disease

15 MDS Partners with World
Federation of Neurology
for World Brain Day on
July 22, 2020



16 Ending
Parkinson's Disease:
A Prescription for Action
- An Interview with the
Authors



19 Multiple System Atrophy:
Recent Developments and
Future Perspectives



Highlights and Hot Topics from the 3rd PAS Congress

Read more on page 6



International Parkinson and Movement Disorder Society

OFFICERS (2019-2021)

President

Claudia Trenkwalder, MD

President-Elect

Francisco Cardoso, MD, PhD, FAAN

Secretary

Bastiaan Bloem, MD, PhD

Secretary-Elect

Charles Adler, MD, PhD

Treasurer

Louis CS Tan, FRCP

Treasurer-Elect

Irene Litvan, MD

Past-President

Christopher Goetz, MD

INTERNATIONAL EXECUTIVE COMMITTEE

Shengdi Chen, MD, PhD

Mark Edwards, MBBS, BSc, FRCP, PhD

Cristian Falup-Pecurariu, MD

Joaquim Ferreira, MD, PhD

Marina de Koning-Tijssen, MD, PhD

Alice Nieuwboer, PhD

D. James Surmeier, PhD

Pille Taba, MD, PhD, FEAN

Mayela Rodriguez-Violante, MD, MSc

Ruey-Meei Wu, MD, PhD

International Parkinson and Movement Disorder Society
International Secretariat
555 East Wells Street, Suite 1100
Milwaukee, Wisconsin 53202-3823
USA

Tel: +1 414-276-2145

Fax: +1 414-276-3349

info@movementdisorders.org

www.movementdisorders.org



MDS-0620-398

Table of Contents

- 3 Editorial: Antonio Strafella, MD
- 4 President's Corner: Claudia Trenkwalder, MD
- 6 3rd Pan American Parkinson's Disease and Movement Disorders Congress
- 7 3rd PAS Congress Hot Topics in Movement Disorders: The Pan American Perspective
- 10 Telemedicine and Movement Disorders: The Impact of the Coronavirus Pandemic
- 12 The Experience of Being a Patient and Physician During COVID-19
- 14 2021 MDS Leadership Nominations Process
- 15 MDS Partners with World Federation of Neurology for World Brain Day on July 22, 2020
- 16 Ending Parkinson's Disease: A Prescription for Action - An Interview with the Authors
- 18 The Next Frontier for Parkinson's Disease and Movement Disorders: The MENASA Region
- 19 Multiple System Atrophy: Recent Developments and Future Perspectives
- 21 Discriminating Alpha-Synuclein Strains in Parkinson's Disease in Multiple System Atrophy
- 23 Changing the Model for How Parkinson's Disease is Treated: The Patient is the Sun - An Interview with Michael Okun, MD
- 25 MDS-AOS Rare Movement Disorders Course
- 28 MDSICON2020 - 5th Annual Conference of Movement Disorders Society of India

Letters to the Editor *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.

Address your communications to:

Editor: *Moving Along*
International Parkinson and Movement Disorder Society
555 East Wells Street, Suite 1100
Milwaukee, WI 53202-3823 USA
Tel: +1 414-276-2145
Fax: +1 414-276-3349
info@movementdisorders.org

Editorial

On behalf of the *Moving Along* Editorial Board, we hope that you and your family members continue to be healthy and safe during this challenging time of the coronavirus (COVID-19) pandemic. We would like to thank the entire MDS community for the enthusiasm demonstrated in contributing new exciting content for this new issue of *Moving Along* during this struggling time. The Editorial Board greatly appreciates your participation and has worked tirelessly to pull together all of this material.

As you may imagine, some articles in this issue feature the topic of COVID-19. One of the "Early View" articles, presented also on the MDS website and social media channels, focuses on the timely topic of the impact of telemedicine during this pandemic. On a more personal level, a young MDS member presents her own direct experience, first as patient, and then as neurologist.

The new series of interviews with our members provides an opportunity to hear directly from the authors about a recent published book on "*Ending Parkinson's Disease – a Prescription for Action*". The second issue of 2020 also takes a look at the latest events and highlights from our Society, with several MDS activities occurring worldwide. For the first time, we have highlighted activities from the Middle East Working Group, as well as great scientific articles with recent discoveries. Lastly, the "President's Corner", by Prof. Claudia Trenkwalder, continues to introduce young members to our MDS community.

We would like to thank the MDS Officers, International Executive Committee, Regional Section leadership, and all of the MDS staff for their amazing support in making this possible. We hope you enjoy this and the future issues of *Moving Along*.

Warm regards,



Antonio Strafella, MD, PhD, FRCPC
Moving Along Editor, 2019-2021



2019-2021 Moving Along Editorial Board



Bettina Balint, MD



Margherita Fabbri, MD



Anhar Hassan, MD



Carlos Juri, MD, PhD



Prashanth Kukkle, DM



Jee-Young Lee, MD, PhD



Daniel Martinez-Ramirez,
MD

President's Corner

MDS continues to adapt to the changing global climate in 2020. Due to the impact of COVID-19, we are replacing the in-person 2020 International Congress of Parkinson's Disease and Movement Disorders in Philadelphia with a complete virtual meeting this September. The MDS Leadership believes this is the best decision to protect the health and safety of our members and attendees. We are making plans to provide the same great educational and scientific experience MDS is known for, including the full program with plenary sessions, teaching courses, parallel sessions and workshops, e-poster presentations and even networking opportunities to keep you connected with colleagues from all over the world - only in a virtual format, which will be free to all registered delegates. Although we will not meet together this September, I am proud to see the MDS community come together virtually to achieve our mission. More details regarding the MDS Virtual Congress will be released in the coming weeks.



In addition, the Society has been working diligently to provide other new virtual forms of education, including a free OnDemand Series of webinars, podcasts and blogs with topics relevant to the current pandemic. We also continue to provide the latest references and resources related to COVID-19 and Movement Disorders on a special corner of the [MDS website](#). It is an entirely new world for everyone - and we do not know how long it will last, but we see it as a chance to move forward the best we can.

To include more basic scientists in our society, the MDS Leadership has approved a new Basic Science member category. Pending a final vote and approval by the MDS membership this year, this new member type will be offered beginning in 2021. In an effort to best serve the needs of these researchers, we are currently seeking new members for our Basic Science Special Interest Group, chaired by Prof. Per Svenningsson, with a mandate to establish a group of research-oriented neurologists and neuroscientists with interest in fundamental mechanisms underlying movement disorders. If you are interested in serving in this role, please contact the Secretariat at info@movementdisorders.org.

In our continued collaborations with other societies, MDS has partnered with The World Federation of Neurology (WFN) to raise awareness for World Brain Day on July 22, 2020. This day is dedicated to awareness, advocacy and fostering brain health worldwide, and the WFN's chosen theme this year is Parkinson's disease. As an MDS member, I invite you to join WFN and MDS to "Move Together to End Parkinson's". More information on how you can help in this initiative can be found on page 15.

Finally, I want to continue my introduction of two more members of the Young Members Steering Committee (See page 5). It is my hope that the younger generation of MDS will continue to enhance the field and help the Society advance our mission through their contributions.

Sincerely,

A handwritten signature in black ink, appearing to read 'Claudia Trenkwalder'.

Claudia Trenkwalder, MD
MDS President, 2019-2021

President's Corner, continued from p. 4



Michele Matarazzo, MD
Madrid, Spain & Vancouver, BC, Canada

I am currently working at the HM CINAC, a Neuroscience research centre in the HM Puerta del Sur University Hospital in Madrid, Spain. I have the privilege to combine clinical activity, working as a movement disorders specialist, and research activity, focused mostly on Parkinson's

disease and other related disorders. I am also a visiting scientist in the Pacific Parkinson's Research Centre in the University of British Columbia in Vancouver, Canada, which is where I completed my fellowship in movement disorders, and where I happily go back to every few months to advance in some ongoing research projects (and to enjoy some trails in the beautiful nature of British Columbia). My research is mainly focused on the use of molecular imaging to better understand the brain mechanisms underlying Parkinson's disease and other movement disorders. I am also interested in new technologies and their use as a tool for the clinicians to improve the management of diseases and help patients in the diagnosis, monitoring and treatment of patients with movement disorders.

I have been a member of MDS since the last year of my residency, back in 2014, and I got progressively more involved over the years. I am proud to serve as a member of the Steering Committee of the Young Members Group, which allows me to connect with other young colleagues around the world, and contribute to the expanding MDS educational activities. Along with my colleague Sara Schafer, I created the podcast channel of the Society, the MDS Podcast, which is released on a monthly basis featuring interviews with authors of articles published in the two Society journals. The MDS Podcast is still a newborn, but we hope to make it grow big and strong, and hopefully it will be one of the novel formats to educate and reach movement disorders specialists and researchers, adapting to new ways of communicating and sharing science in a world that is changing rapidly.

As the leading society in the field, MDS has been helping to create a strong movement disorders scientific community, which stimulates collaboration and therefore advances in the understanding and treatment of our patients. The main challenge we must face in the close future is to improve the crosstalk between basic science and clinical research, and MDS will be key to catalyze the translation from lab to patients in the upcoming years and decades. MDS is also a place where I have met many colleagues that have become friends over the years. Sharing with them some of my passions, such as jazz music or traveling and recently some advice for my upcoming fatherhood, is an important part of being a member of MDS, and hopefully will continue to be in the future.



Roopa Rajan, MD, DM
New Delhi, India

I am Roopa Rajan and I am an Assistant Professor of Neurology at the All India Institute of Medical Sciences, New Delhi, India. I am a movement disorders neurologist and completed all my medical training in India, including a post-doctoral fellowship in Movement Disorders

under Prof. Asha Kishore at the Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, India. I currently work in one of the largest public-funded, tertiary care, teaching hospitals in India, where I am committed to providing state-of-the-art, comprehensive and individualized care including botulinum toxin injections and Deep Brain Stimulation for movement disorders. As a clinician-researcher, I am driven by the need to seek pathophysiologically targeted solutions to clinical problems. My research focuses on the electrophysiology of dystonia and tremor, and the genetics of movement disorders in Indian patients. At our lab, we host a clinical registry and biorepository for Indian patients with movement disorders (focusing on dystonia) and collaborate widely with other clinical centers, geneticists, data scientists and other basic science researchers both within and outside of India.

I developed a passion for movement disorders during my neurology residency and my involvement with MDS dates back to that time in 2014. I came across the MDS website while scouting the internet for movement disorders educational resources and made the best use of the eLearning materials, video libraries and rating scale training programs to prepare for fellowship interviews. MDS has been an important part of my professional journey since then, providing immense opportunities to learn, contribute and collaborate. I am part of the MDS LEAP class of 2019 and a Steering Committee member of the MDS Young Members group. I am also part of the Task Force on the Management of Movement Disorders: Interdisciplinary and Integrated Care and the Tremor Study Group.

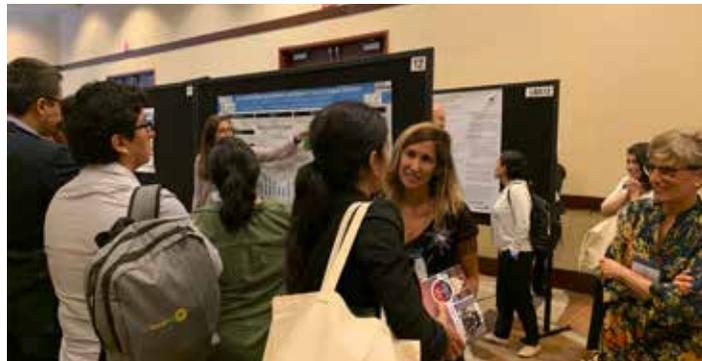
What I love about MDS is its accessibility and global outreach and the opportunities it provides for promoting not only scientific knowledge, but also mentorship and leadership to a global audience. In a sense, I feel that MDS has been a virtual mentor to me during my career development, allowing me to engage with a host of supportive senior faculty and peer group mentors. I am glad to have had opportunities to give back to this network by being involved in eLearning module development, as junior faculty for SYNERGIES, and through research collaborations. I hope that the Society would continue to spread its wings to underserved areas of the world and I wish to contribute my efforts in this regard.

Outside the professional realm, I am an avid reader, these days alternating between readings of children's literature with my six-year-old and ancient history and historical fiction when I can grab some time for myself.

3rd Pan American Parkinson's Disease and Movement Disorders Congress – Miami, FL, USA, February 14-16, 2020

— Francisco Cardoso, MD, PhD, Chair, PAS Congress Scientific Program Committee

The 3rd Pan American Parkinson's Disease and Movement Disorders Congress took place in Miami, FL, USA, February 14-16, 2020. The meeting had 637 attendees from 29 countries, including delegates from outside the American Continent. There were 62 faculty participating in six Plenary Sessions, six Parallel Sessions, three Skills Workshops, three Video Sessions, Challenging Case MDS-PAS Rounds, 206 abstracts, 12 Late-Breaking Abstracts and four Guided Poster Tours. The PAS also awarded 30 Fellows Scholarships and 20 Travel Grants. During the Opening Ceremony of every PAS Congress, the MDS-PAS Leadership Award is presented. This year, the PAS Congress Scientific Program Committee honored Dr. Christopher Goetz, in recognition as an outstanding leader and contributor in the field of Movement Disorders within the MDS Pan American Section. During his term as President of MDS, Dr. Goetz provided unfailing support of PAS, actively promoting the participation of representatives of its diverse sectors. As Chair of the PAS Congress Scientific Program Committee, I would like to acknowledge the support of our sponsors as well as of Cynthia Comella, Chair of the PAS Section. This was decisive to the success of the 3rd PAS Congress.



Left to right: Cynthia Comella, Christopher Goetz, Francisco Cardoso

This edition of the PAS Congress reinforced the character of the previous editions. There was an intimate atmosphere allowing interaction and networking among the participants. Senior members of our Society, like Dr. Stanley Fahn, one of our founding fathers, were easily approached by young attendees in search of discussion of cases, professional advice or even a selfie. The talks, both in the plenary sessions, as well as in the parallel activities in the afternoons, had a very high level, enthusiastic feedback from the audience. The theme was Therapeutics of Movement Disorders in the Americas. The PAS Congress Scientific Program Committee strived to include faculty in a gender and geographic balanced manner. The outcome was highly successful, with presenters providing a view of how management of movement disorders is done in different parts of the Americas.

At the time of the 3rd PAS Congress, no one knew that we were at the brink of the COVID-19 pandemic that may change in an irreversible way how to organize Congresses. The very casual in-person interactions so representative of the Miami atmosphere seem to belong to a bygone era. MDS hopes that we all remain safe and healthy and capable of repeating this wonderful experience in Miami in 2022!

3rd PAS Congress Hot Topics in Movement Disorders: The Pan American Perspective

Leaky Gut and Neurotoxins as Drivers of Parkinson's Disease Onset

— Kathleen Shannon, MD, Detling Professor and Chair, Department of Neurology, University of Wisconsin School of Medicine and Public Health, Madison, WI, USA



Interest in the role of gut-derived sterile inflammation in the pathogenesis of Parkinson's disease (PD) relates to a number of observations: Intestinal symptoms occur frequently as part of the PD prodrome;¹ there is an overlap of genetic risk between PD and inflammatory bowel disease;² inflammatory bowel disease is associated with an increased risk of PD;³ and the increased risk is

reduced by therapies targeting peripheral tumor necrosis factor, a cytokine, suggesting a role for the systemic innate immune system.³ Moreover, lipopolysaccharide (LPS), a gram-negative bacterial neurotoxin for which the only exposure in man is through the intestinal tract can be used to model PD in animals.⁴

It has been proposed that gut-derived sterile inflammation could drive PD pathogenesis either through synuclein aggregation in the enteric nervous system that then spreads in a prion-like fashion accessing the medulla through the vagus nerve,^{5,6} or that systemic inflammation affects blood brain barrier function, and that central nervous system inflammatory mechanisms drive neurodegeneration.⁷

We have performed a series of clinical and preclinical studies to determine the potential role of gut-derived sterile inflammation in early and more advanced PD. Our clinical cohort included nine untreated and 29 treated PD subjects and healthy control (HC) subjects. We examined samples of feces and distal colon biopsies using 16S ribosomal RNA high-throughput amplicon sequencing of the V4 variable region of the microbial genome. Treated and untreated PD subjects showed increased representation of pro-inflammatory and decreased representation of anti-inflammatory short-chain fatty acid producing bacterial populations in the colonic intestinal lumen (dysbiosis).⁸ PD subjects showed increased urinary excretion of an oral load of the poorly absorbed sugar sucralose, suggesting significantly increased intestinal permeability ("leaky gut"). This was associated with increased CD3+ T cells and increased expression of cytokines and toll-like receptor 4 (TLR4) in the intestinal wall.^{9,10} PD subjects showed interruption of zona occludens 1 (ZO-1), a tight junction protein critical for maintenance of the intestinal barrier.¹⁰ LPS binding protein levels were decreased in PD serum, a marker of exposure to the bacterial endotoxin LPS.

In an alpha-synuclein overexpression mouse PD model, germ free mice are partially protected from the experimental PD pathology and behavioral phenotype compared to mice with normal intestinal microbial populations. Abnormal pathology and behavior are more severe when the gut microbiome in germ free mice is reconstituted using stool from PD subjects versus HC, suggesting an inflammatory microbiome can

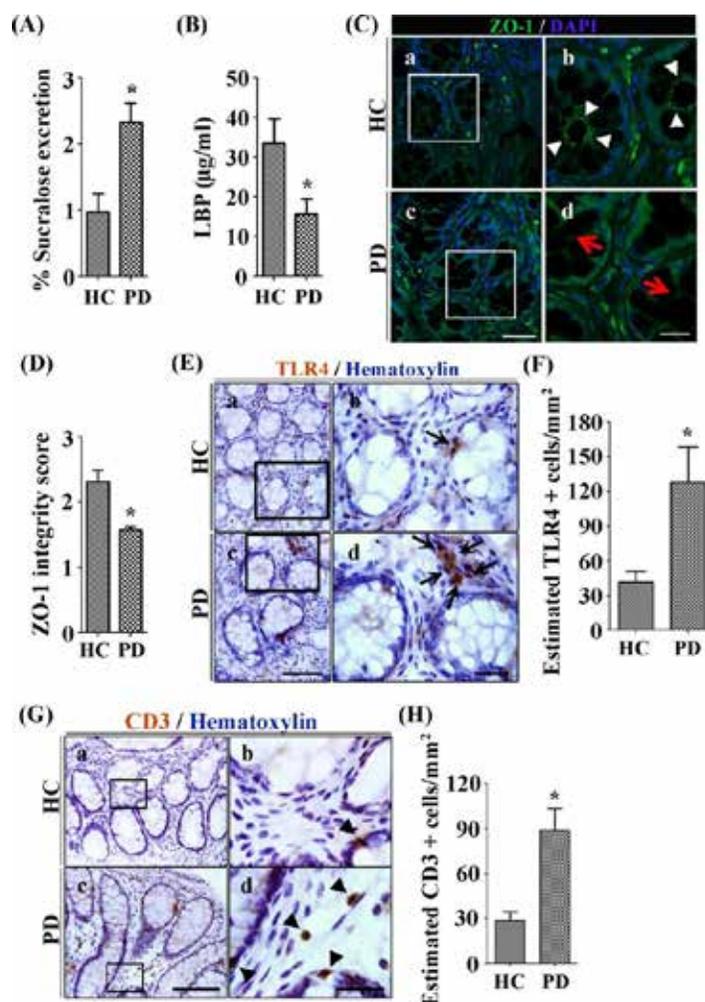


Figure legend

Markers of gut-derived sterile inflammation in subjects with Parkinson's disease. (A) Urinary excretion of sucralose over 24 hours as percent of ingested sugar is increased in PD compared to HC; (B) plasma levels of LPS binding protein are lower in PD than in HC; (C) Immunofluorescence staining of ZO-1 in colonic mucosa in HC (a,b) and PD (c,d); (D) integrity scoring for ZO-1 tight junction protein in HC and PD; (E) TLR4 immunostaining in lamina propria of HC (a,b) and PD (c,d); (F) estimated numbers of TLR4+ cells/mm³ in HC and PD; (G) CD3+ T cells in colonic mucosa of HC (a,g) and PD (c,d); (H) CD3+ cells in lamina propria of colonic samples in HC and PD. Scale bars: C(c)=50 µm and C(d)=20 µm, E(c)=75 µm and E(d)=25 µm, G(c)=40 µm and G(d)=25 µm. *P<0.05; **p<0.001, ***p<0.0001. Data represent mean±SEM.

HC= healthy controls; PD=Parkinson's disease, LBP=lipopolysaccharide binding protein, ZO-1=zonula occludens tight junction protein 1, TLR4=toll-like receptor 4, CD3=cluster differentiation 3.

The figure credit is reproduced with permission from Perez-Pardo P, Dodiya HB, Engen PA, et al. Role of TLR4 in the gut-brain axis in Parkinson's disease: a translational study from men to mice. *Gut* 2019;68(5):829-843.

3rd PAS Congress Hot Topics in Movement Disorders: The Pan American Perspective, *continued from p. 7*

drive central nervous system PD pathology.¹¹ In another mouse model, the astrocyte activation and loss of dopaminergic cells in substantia nigra produced by oral rotenone is accompanied by loss of ZO-1 integrity and increased inflammation in the intestinal wall, as seen in human PD subjects. TLR4 knockout reduces the neuropathological and behavioral phenotype and is associated with less severe intestinal inflammation.¹⁰

These findings are intriguing and suggest that systemic inflammation, and especially gut-derived sterile inflammation could play an important role in the genesis or progression of PD. While animal studies suggests a proinflammatory fecal bacterial profile, and gut leakiness with systemic inflammation are associated with the development of typical nigral synucleinopathy and experimental parkinsonism, definitive evidence of causation in man remains elusive. The pivotal question is whether changes in critical gut functions are a cause or result of the neurological illness. The relevance of these findings must be borne out by further investigation, especially work focused on identifying and studying systemic drivers of pathology in prodromal PD populations prior to the development of any CNS pathology.

References

1. Ross GW, Abbott RD, Petrovitch H, Tanner CM, White LR. Pre-motor features of Parkinson's disease: the Honolulu-Asia Aging Study experience. *Parkinsonism Relat Disord* 2012;18 Suppl 1:S199-202.
2. Liu Z, Lenardo MJ. The role of LRRK2 in inflammatory bowel disease. *Cell Res* 2012;22(7):1092-1094.
3. Peter I, Dubinsky M, Bressman S, et al. Anti-Tumor Necrosis Factor Therapy and Incidence of Parkinson Disease Among Patients With Inflammatory Bowel Disease. *JAMA Neurol* 2018;75(8):939-946.
4. Liu M, Bing G. Lipopolysaccharide animal models for Parkinson's disease. *Parkinsons Dis* 2011;2011:327089.
5. Chen Y, Shao Q, Yuan YH, Chen NH. Prion-like propagation of alpha-synuclein in the gut-brain axis. *Brain Res Bull* 2018;140:341-346.
6. Lema Tome CM, Tyson T, Rey NL, Grathwohl S, Britschgi M, Brundin P. Inflammation and alpha-synuclein's prion-like behavior in Parkinson's disease--is there a link? *Mol Neurobiol* 2013;47(2):561-574.
7. Houser MC, Tansey MG. The gut-brain axis: is intestinal inflammation a silent driver of Parkinson's disease pathogenesis? *NPJ Parkinsons Dis* 2017;3:3.
8. Keshavarzian A, Green SJ, Engen PA, et al. Colonic bacterial composition in Parkinson's disease. *Mov Disord* 2015;30(10):1351-1360.
9. Forsyth CB, Shannon KM, Kordower JH, et al. Increased intestinal permeability correlates with sigmoid mucosa alpha-synuclein staining and endotoxin exposure markers in early Parkinson's disease. *PLoS One* 2011;6(12):e28032.
10. Perez-Pardo P, Dodiya HB, Engen PA, et al. Role of TLR4 in the gut-brain axis in Parkinson's disease: a translational study from men to mice. *Gut* 2019;68(5):829-843.
11. Sampson TR, Debelius JW, Thron T, et al. Gut Microbiota Regulate Motor Deficits and Neuroinflammation in a Model of Parkinson's Disease. *Cell* 2016;167(6):1469-1480 e1412.

3rd PAS Congress Hot Topics in Movement Disorders: The Pan American Perspective, continued from p. 8

Genome Editing as a Therapy for Movement Disorders: Promising Perspectives with Many Challenges Ahead

— Patricia de Carvalho Aguiar, MD, PhD, Hospital Israelita Albert Einstein, Sao Paulo, Brazil, Department of Neurology and Neurosurgery- Universidade Federal de Sao Paulo, Sao Paulo, Brazil



Genome editing consists of custom-engineered genomic modifications, such as single nucleotide replacements, insertions or deletions. We have been editing the genome for decades, in order to create *in vitro* or *in vivo* disease models. Major genome editing technologies involve programmable nucleases capable of performing double-strand DNA breaks at specific sites. In the

last decade, a system named Clustered Regularly Interspaced Short Palindromic Repeat/CRISPR Associated Protein 9 (CRISPR/Cas9) took the world by storm and has revolutionized the field, bringing genome editing to the therapeutic level.¹ It has a wide range of applications, not only in the medical field but also in agriculture, environment, and in the biotechnology industry.²

Potentially, every movement disorder caused by a nuclear DNA mutation can benefit from genomic editing. Monogenic diseases, especially those with a single type of mutation, such as Huntington's disease or DYT-TOR1A dystonia, are ideal candidates for this kind of intervention, as a single drug targeting a specific mutation could benefit most patients.³ Several studies using cell or animal-based models showed promising results for Parkinson's disease, Dystonia, Ataxias, and Huntington's disease.⁴⁻⁸ In one of the many examples of the power of this technique, Yang *et al.* (2017) used CRISPR/CAS9 editing in the HD140Q-KI Huntington's disease mouse model, observing a significant decrease in the nuclear accumulation and aggregation of mutant Huntingtin, as well as improved phenotype, even in aging mice.⁷ Although the most obvious targets of genome editing are mutant genes, CRISPR/CAS9 has the potential to be applied for gene expression regulation, expanding the application of this technology to a vast number of non-inherited conditions, such as sporadic Parkinson's disease.

In order to apply CRISPR/CAS9 at the therapeutic level, we must overcome technical and ethical challenges. Most systems for getting CRISPR into the brain are delivered by viral vectors, and the continuous expression of CAS9 has the potential to cause permanent damage to the DNA.⁹ Synthetic delivery systems, aiming for safe induction of permanent

effects, must be developed. Moreover, if we aim for a wide clinical application, synthetic systems are usually easier to scale up. Off-target and unintended consequences, including malignancy, are a big concern. The specificity and efficiency of targeted editing are highly dependent on the guide-RNA design. However, *in silico* prediction algorithms are not error-free, and only whole-genome sequencing can guarantee there are no off-targets.

Ethical concerns are perhaps the most challenging of all, and some are intertwined with economic matters, with societal implications: who gets access to it, how to make it more widely available and what will be the costs for the healthcare system? Germline editing is a significant concern, not only due to unpredictable inheritable changes but also for the risk of its uncontrolled use for non-therapeutic genetic enhancement.¹⁰

These are exciting times; we have a powerful tool to treat diseases until now incurable but must face the many challenges and use it wisely.

References

1. Kotagama OW, Jayasinghe CD, Abeysinghe T. Era of Genomic Medicine: A Narrative Review on CRISPR Technology as a Potential Therapeutic Tool for Human Diseases. *Biomed Res Int* 2019;2019:1369682.
2. Knott GJ, Doudna JA. CRISPR-Cas guides the future of genetic engineering. *Science* 2018;361(6405):866-869.
3. Im W, Moon J, Kim M. Applications of CRISPR/Cas9 for Gene Editing in Hereditary Movement Disorders. *J Mov Disord* 2016;9(3):136-43.
4. Reinhardt P *et al.* Genetic correction of a LRRK2 mutation in human iPSCs links parkinsonian neurodegeneration to ERK-dependent changes in gene expression. *Cell Stem Cell* 2013;3:354-67.
5. Rakovic A *et al.* Genome editing in induced pluripotent stem cells rescues TAF1 levels in X-linked dystonia-parkinsonism. *Mov Disord* 2018;33(7):1108-1118.
6. Shin JW *et al.* Permanent inactivation of Huntington's disease mutation by personalized allele-specific CRISPR/Cas9. *Hum Mol Genet* 2016;25(20):4566-4576.
7. Yang S *et al.* CRISPR/Cas9-mediated gene editing ameliorates neurotoxicity in mouse model of Huntington's disease. *J Clin Invest* 2017;127(7):2719-2724.
8. Ouyang S *et al.* CRISPR/Cas9-Targeted Deletion of Polyglutamine in Spinocerebellar Ataxia Type 3-Derived Induced Pluripotent Stem Cells. *Stem Cells Dev* 2018;27(11):756-770.
9. Wilbie D, Walther J, Mastrobattista E. Delivery Aspects of CRISPR/Cas for *in Vivo* Genome Editing. *Acc Chem Res* 2019;52(6):1555-1564.
10. Daley GQ, Lovell-Badge R, Steffann J. After the Storm - A Responsible Path for Genome Editing. *N Engl J Med* 2019;380(10):897-899.

Telemedicine and Movement Disorders: The Impact of the Coronavirus Pandemic

— Esther Cubo, MD, PhD, FAAN, Hospital Universitario Burgos, Spain; Anhar Hassan, M.B., B.Ch., Mayo Clinic, Rochester, MN, USA; Zoltan Mari, MD, Cleveland Clinic Lou Ruvo Center for Brain Health, Cleveland, OH, USA on behalf of the MDS Telemedicine Study Group



Esther Cubo



Anhar Hassan



Zoltan Mari

Since the emergence of the COVID-19 pandemic, many countries have taken radical measures to slow down infection rates. These range from social distancing to a lock-down of non-essential business and marked restrictions on social and economic life.¹ While these measures are necessary to contain the pandemic, they come with particular concerns around the increased vulnerability of the many patients living with chronic diseases, including neurodegenerative diseases like Parkinson's disease (PD) and other movement disorders.^{1,2}

Changes in healthcare have been to limit access to clinics and neurology wards to protect fragile PD and other movement disorder patients from infection exposure. In some regions, the shortage of medical staff has required movement disorders neurologists to provide care for COVID-19 patients instead.³ During this time of crisis, many patients with PD and other movement disorders are likely to benefit from restored access to subspecialty care via telemedicine, whether this is videoconferencing or simply telephone consultations. Also, even after the immediate threats of the current COVID-19 outbreak have been brought under control, we may likely be facing a need for continued restrictions on public and social life for the foreseeable future, as COVID-19 re-emergence or other outbreaks remain possible. It is too early to know how COVID-19, either directly or indirectly (via social and healthcare restriction measures), will impact patients with PD and other movement disorders in the long-term.² The observation of new-onset anosmia with COVID-19 is intriguing, given this is a common feature of prodromal PD. However thus far, coronaviruses have not been linked to specific long-term neurological sequelae.^{2,4,5}

Since the crisis, use of telemedicine for the delivery of urgent and ongoing healthcare has speedily scaled upwards.¹ Many neurologists and other healthcare professionals are using a variety of telemedicine healthcare tools at their disposal to continue delivering patient care. These include phone calls, use of email or text message, and video visits. Telemedicine can be used for routine follow-up, urgent and research visits, new subspecialty consultations, psychotherapy, genetic counseling, social services, rehabilitation, education, and can produce

care outcomes comparable to traditional visits. The merits and benefits of telemedicine are supported by a small but growing body of evidence.⁶⁻⁹ However, telemedicine has yet to be established universally for virtual management of device-aided therapies in PD and other movement disorders, which will require the additional technological implementation of a secure remote digital interface within Deep Brain Stimulation and infusion pump devices.^{10,11}

In order to assist MDS members, the Telemedicine Study Group has created a [“step-by-step” guide](#), including specific requirements for reimbursement and regulation, incorporating the latest information available in several countries and global regions. The Telemedicine Study Group has posted an [educational webinar](#) to reflect recent telemedicine changes related to the unfolding COVID-19 pandemic, and how to set up a successful Movement Disorders telemedicine practice. The Telemedicine Study Group also has developed a network of regional experts covering the globe to continue to provide updated information as telemedicine guidelines continue to evolve. In this regard, a [web form](#) to post questions is available on the MDS website. Continuously updated regulatory information and guidelines, and a robust question and answer section addressing all relevant questions posted by MDS members is available on the [MDS website](#). We hope to hear about the hands-on experience with telemedicine from many colleagues in the field, as this will help to further shape optimal delivery of telemedicine services for both patients and healthcare workers, and holds great promise of becoming a routine part our work-life in the future.

MDS Telemedicine Resources

- [Telemedicine in Movement Disorders Practice: A Step-by-Step Guide](#)
- [Free MDS OnDemand Webinar: Telemedicine for Movement Disorders during the COVID-19 crisis: How does this affect us?](#)
- [Submit Questions to the Telemedicine Study Group](#)
- [MDS COVID-19 Pandemic: MDS Statement, References and Resources](#)
- [Implementation of Telemedicine for Urgent and Ongoing Healthcare for Patients With Parkinson's Disease During the COVID-19 Pandemic: New Expectations for the Future \(Cubo E, et al. J Parkinsons Dis. 2020.PMID: 32417800\)](#)

References

1. Helmich RC, Bloem BR. The Impact of the COVID-19 Pandemic on Parkinson's Disease: Hidden Sorrows and Emerging Opportunities. *J Parkinsons Dis.* 2020;10:351-354.
2. Papa S.M, Brundin P, Fung V.S.C, Kang U.J, Burn D.J, Colosimo C, Chiang H.L., Alcalay R.N., Trenkwalder C., the MDS-Scientific Issues Committee. Impact of the COVID-19 Pandemic on Parkinson's Disease and Movement Disorders. *Mov Disord Clin Pract* 2020; <https://doi.org/10.1002/mdc3.12953>

Telemedicine and Movement Disorders: The Impact of the Coronavirus Pandemic, *continued from p. 10*

3. Fasano A, Antonini A, Katzenschlager R, Krack P, Odin P, Evans AH, Foltynie T, Volkman J, Merello M. Review Management of Advanced Therapies in Parkinson's Disease Patients in times of Humanitarian crisis: the COVID-19 experience. *Mov Disord Clin Pract* 2020; <https://doi.org/10.1002/mdc3.12965>
4. Rey NL, Wesson DW, Brundin P. The olfactory bulb as the entry site for prion-like propagation in neurodegenerative diseases. *Neurobiol Dis* 2018; 109(Pt. B): 226–248.
5. Tulisiak CT, Mercado G, Peelaerts W, Brundin L, Brundin P. Can infections trigger alpha-synucleinopathies? *Prog Mol Biol Transl Sci* 2019; 168: 299–322.
6. Srinivasan R, Ben-Pazi H, Dekker M, Cubo E, Bloem B, Moukheiber E, Gonzalez-Santos J, Guttman M. Telemedicine for Hyperkinetic Movement Disorders. *Tremor Other Hyperkinet Mov (N Y)*. 2020 Feb 17;10. doi: 10.7916/tohm.v0.698.
7. Ben-Pazi H, Browne P, Chan P, Cubo E, Guttman M, Hassan A, Hatcher-Martin J, Mari Z, Moukheiber E, Okubadejo NU, Shalash A; International Parkinson and Movement Disorder Society Telemedicine Task Force. The Promise of Telemedicine for Movement Disorders: An Interdisciplinary Approach. *Curr Neurol Neurosci Rep*. 2018 Apr 13;18:26. doi:10.1007/s11910-018-0834-6.
8. Schneider RB, Biglan KM. The promise of telemedicine for chronic neurological disorders: the example of Parkinson's disease. *Lancet Neurol* 2017;16:541-551.
9. Achey M, Aldred JL, Aljehani N, et al. The past, present, and future of telemedicine for Parkinson's disease. *Mov Disord* 2014;29:871-883.
10. Zhang C, Zhang y, Zhan S, Li D, Jin H, Denys D, Sun B. Telemedical Deep Brain Stimulation: Merits and Limitations. *Stereotact Funct Neurosurg* 2018;96:272-273.
11. Zhang C, Li D, Zeljic K, Tan H, Ning Y, Sun B. A Remote and Wireless Deep Brain Stimulation Programming System. <https://doi.org/10.1111/ner.12448>.

SAVE THE DATE



International Parkinson and
Movement Disorder Society

MDS *Virtual* Congress 2020

SEPTEMBER 12–SEPTEMBER 16
www.mdscongress.org



The Experience of Being a Patient and Physician During COVID-19

— Margherita Fabbri, a member of the Moving Along Editorial Board, interviewed Miryam Carecchio, who currently serves on the MDS Young Members Group Steering Committee, about her personal experience with COVID-19 in Italy



Margherita: Miryam, thank you for taking the time for an interview for *Moving Along* in this difficult and grim time. We really appreciate your contribution and we believe your experience could be useful for our readers. We know that you recently got the COVID-19 infection and you luckily recovered. We would like to discuss with you what this experience has meant for you as both physician and patient.

Where do you currently work and when did you get the infection?

Miryam: I currently work at Padua University Hospital as Assistant Professor of Neurology. It is likely I got the infection at the end of February, and I tested positive on a nasopharyngeal swab on March 5, 2020, at the beginning of the Italian epidemics.

Margherita: Which were the first symptoms that you felt and the feelings you had?

Miryam: I totally lost the sense of smell and taste, without a cold, nasal congestion or sore throat. I also had diffuse muscle pain and dry cough; the latter lasted one month; as for hyposmia and ageusia, unfortunately, I have only partially recovered so far. At first, I was surprised to test positive, since my symptoms were mild and I could work normally; then I felt scared, because symptoms can potentially evolve to pneumonia and respiratory failure and I had no way to predict my clinical course. Eventually, I felt guilty. I was afraid I could have infected others. At the beginning of March, the use of PPE was still very limited in hospitals.



Margherita: What did you usually do during your quarantine? What was the hardest aspect of your quarantine?

Miryam: I spent 20 days in isolation at home. I received dozens of messages, emails, calls from friends and colleagues who never made me feel alone. I read, wrote, and above all, I had time to think; about myself, my past and future, projects, dreams, and also a few regrets.

Margherita: Before coming back to work, have you been tested for COVID-19 antibodies?

Miryam: I went back to work after I tested negative on two consecutive swabs; I had antibodies tested later, and I had a positive IgG anti-Sars-Cov-2 titre and a negative IgM one.

Margherita: We know that, after recovering you donated your plasma; is plasma infusion considered a valuable therapeutic treatment for COVID-19-infected patients?

Miryam: I was one of the first donors in Italy and I was very happy to help during the emergency. Different centres are evaluating the efficacy of plasma in advanced COVID-19 cases and it seems to be very effective; however, no definite official efficacy data are available, but this therapeutic option is certainly very promising.

Margherita: How has the organization of your ward/hospital changed during the last two months? Are you currently doing telemedicine?

Miryam: In my hospital, all medical and paramedical staff has constantly been tested, and in case of a positive worker, all his/her contact got tested within 24 hours. After my swab turned out to be positive, 200 people were tested in the hospital. This allowed an immediate isolation of positive cases and limitation of virus spreading. COVID patients were all cured in specific areas of the hospital, whereas the neurology ward remained COVID-free. COVID patients were seen by neurologists in COVID areas, if needed.

All outpatient clinics were cancelled in March and April and only urgent consultations were guaranteed. Now, we have restarted seeing patients who have more urgent need of consultation, and we also reach them by call and by web-based platforms. Although, I do think that movement disorders are hard to manage if you do not perform a live examination. Old school!

The Experience of Being a Patient and Physician During COVID-19, continued on p.13

The Experience of Being a Patient and Physician During COVID-19, *continued from p. 12*

Margherita: Did this experience change your mind? What have you learned?

Miryam: I have learned, once again, that everything can change in a second in our life, and I have realized how lucky I was not to get a severe form of the disease. Some young colleagues had pneumonia and respiratory distress, and they went through much more difficult times than I did. Above all, I experienced fragility. This is something all doctors should go through in life, to deeply understand how our patients often feel when they get seen by us. We are simply used to be on the “right” side, but all of a sudden, every doctor can become a patient.

Margherita: How will this pandemic change our healthcare system and society?

Miryam: We have learned that a community-based approach is more effective to contain the infection than a hospital-based one. General practitioners had a key role in the management of patients in isolation, but they were not always and promptly given appropriate resources to face the pandemic. I think it will be crucial to reinforce the network of family doctors in the future, to invest more money on our NHS, and, above all, to get more permanent medical staff in every hospital. Having said that, I feel enormously proud of our NHS staff. They literally saved our country; over 150 doctors died from COVID-19, and we will never forget their sacrifice.

2021 MDS Leadership Nominations Process

— Cynthia Comella, MD, FAAN, FASM, FANA, Professor Emeritus, Neurological Sciences, Rush University Medical Center, Chicago, IL, USA, Chair, MDS Nominating Committee (2019-2021)



As Chair of the 2019-2021 MDS Nominating Committee, I am honored to take this opportunity to provide you general information on the MDS nominations process and invite you to take an active role in the selection of the next leaders for MDS.

The MDS President appoints the Nominating Committee by taking into account the international scope of the Society and ensuring there is broad representation on the Committee. The 2019-2021 Nominating Committee members are:

Susan Fox, Canada
Oscar Gershanik, Argentina
Christopher Goetz, USA
Beomseok (BJ) Jeon, South Korea
Christine Klein, Germany
Janis Miyasaki, Canada
Werner Poewe, Austria
Raymond Rosales, Philippines
Pille Taba, Estonia

The MDS Bylaws charges the Nominating Committee to prepare a slate of Officers and International Executive Committee (IEC) members for the Society every two years. The Nominating Committee takes this process very seriously and strives to nominate the best leaders to advance the mission of the Society. After the Nominating Committee prepares the slate, the members have the opportunity to review the nominees and then submit their votes via proxy ballot or in-person at the annual Business Meeting during the International Congress. The next election will take place at the International Congress in Copenhagen, Denmark on Tuesday, September 21, 2021.

One of the ways that you, as an MDS Member, can be involved is through submitting candidates for the Nominating Committee to consider. MDS puts out a call to the membership asking for candidate names that fit the criteria to serve in our leadership positions. This call will be emailed to all members in July 2020 as well as be included on the 'Get Involved' webpage on the MDS website. If you are interested in submitting your name or your colleague's name for consideration as an Officer or IEC member, please be sure to respond to that call with the requested information.

The criteria used for the selection of candidates has been carefully refined over the past years. Generally, we are seeking a mixture of the following attributes as candidates:

- Long volunteer experience within MDS. Typically, the higher the position, the more extensive the experience should be (i.e. Previous service as an MDS Officer (Secretary or Treasurer) for Presidential consideration)
- Ability to work in teams
- Scientific and/or clinical reputation
- Organized working style, being responsive to requests
- Ability to represent the Society
- Representation of different disciplines (Neurology, Neurosurgery, basic sciences)
- Diversity: gender, geographic distribution

After we have received the list of candidates from the membership, the Nominating Committee evaluates the candidates based upon the defined criteria. The Nominating Committee's goal is to prepare a diverse slate that is poised to work well as a team and bring forward their individual expertise to advance MDS and provide the best experience for our membership.

We look forward and welcome your active participation in this process through submitting candidate names for consideration, reviewing the slate and bios that have been prepared, and finally participating in the final voting process. Together we will select the next Leaders of the Society!

To learn more about the 2021 Nominations process and submit candidate profiles, please visit the [MDS website](#).

MDS Partners with World Federation of Neurology for World Brain Day on July 22, 2020

— Tissa Wijeratne, MD, Department of Neurology, Western Health, Melbourne, Australia; Chair, World Brain Day

— William Carroll, MD, Department of Neurology, Sir Charles Gairdner Hospital, Nedlands, Australia; President, World Federation of Neurology

— Wolfgang Grisold, MD, Ludwig Boltzmann Institute for Experimental and Clinical Traumatology, Vienna, Austria; Secretary General, World Federation of Neurology

— Claudia Trenkwalder, MD, University Medical Center Goettingen, Kassel, Germany; President, International Parkinson and Movement Disorder Society

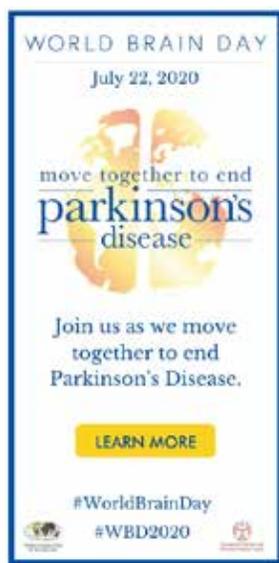
The Global Burden of Disease Study 2016 Parkinson's disease (PD) collaborators described the global burden of Parkinson's disease between 1996 and 2016 to identify trends and to enable necessary public health, scientific, and medical responses in 2018[1]. Over the past generation, the global burden of PD has more than doubled, with potential longer disease duration and environmental factors[1]. We can expect that the trend will continue in the next few decades with the possibility of 12 million patients with Parkinson's disease worldwide by about 2050 [2].

Right now, the comorbid diagnosis itself has not emerged as a specific risk factor for poor outcomes of COVID-19[3]. However, unforeseen impacts (potential medication supply issues, disruption to research and clinical trials) and emerging opportunities (telemedicine, how the pandemic influences the course of PD, taking advantage of technology such as wearables) have become visible during this pandemic [3, 4].

In this context, the World Federation of Neurology's World Brain Day campaign is crucial for neurology, healthcare professionals and above all for patients, families and carers. Held each year on July 22, World Brain Day is dedicated to awareness, advocacy and fostering brain health worldwide. For World Brain Day 2020, the WFN chose Parkinson's disease as its theme and is partnering with MDS to raise awareness and advocate for improved patient care, education, and additional research for those living with Parkinson's disease and their caregivers.

Launched in 2014, World Brain Day has been planned jointly by the WFN and other international societies such as International League Against Epilepsy, World Stroke Organisation, and the International Headache Society. Each year a topic is chosen to drive home the importance of brain health and promoting better neurological care globally. For 2020, the WFN and MDS co-developed five key educational messages for members and others to share leading up to and on World Brain Day:

- **Prevalence:** Parkinson's disease is a chronic, neurodegenerative brain disease that impacts more than 7 million people worldwide and continues to increase.
- **Disability:** Parkinson's disease is a whole-body disease that affects movement and almost all aspects of brain function, with symptoms worsening over time.



- **Standard of Care:** Access to quality neurological care, life-changing treatments and essential medication are unavailable in many parts of the world.
- **Research:** Additional resources are needed to help unlock the cause, onset, progression and treatment of this disease across all ages.
- **Advocacy:** Let's work together to diagnose earlier, treat more effectively, and improve the lives of both those living with Parkinson's disease, and their caregivers.

As in [preceding years](#), the aim of World Brain Day 2020 is to inform not only member societies but also the public on critical neurological issues. Members of the WFN and its partner organizations are encouraged to help amplify the key messages above by utilizing the resources available on the [World Brain Day webpage](#):

- **Toolbox:** Press release, World Brain Day logo, Banner Ads for websites and publications, and Social Media graphics and sample posts for Facebook, Twitter, Instagram and LinkedIn
- **PowerPoint:** A slide deck containing facts and figures on Parkinson's disease
- **Poster:** A save the date poster featuring the World Brain Day logo, tagline and website URL
- **Webinar:** A live webinar on July 22 featuring a panel of speakers discussing Parkinson's disease, including MDS President Claudia Trenkwalder, MD

MDS Members are invited to join the WFN and MDS to "Move Together to End Parkinson's". Consider how you may help spread the news through mainstream media, social media platforms, virtual educational and advocacy activities, and more. The educational and promotional materials from the WFN-MDS collaboration are designed to help you be the best advocates for your patients.

A live webinar will take place on July 22, 2020 with ample opportunity for questions and answers. Details will be available on the [World Brain Day webpage](#). Contact World Brain Day Chair Prof. Tissa Wijeratne for ongoing support.

References

1. Collaborators, G.B.D.P.s.D., *Global, regional, and national burden of Parkinson's disease, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016*. *Lancet Neurol*, 2018. 17(11): p. 939-953.
2. Rocca, W.A., *The burden of Parkinson's disease: a worldwide perspective*. *Lancet Neurol*, 2018. 17(11): p. 928-929.
3. Papa, SM, et al., *Impact of the COVID-19 Pandemic on Parkinson's Disease and Movement Disorders*. *Mov Disord*, 2020.
4. Helmich, R.C. and B.R. Bloem, *The Impact of the COVID-19 Pandemic on Parkinson's Disease: Hidden Sorrows and Emerging Opportunities*. *J Parkinsons Dis*, 2020. 10(2): p. 351-354.

Ending Parkinson's Disease: A Prescription for Action - An Interview with the Authors

— Bas Bloem, MD, PhD, FRCPE, Director, Radboudumc Center of Expertise for Parkinson & Movement Disorders, The Netherlands

— Ray Dorsey, MD, Professor of Neurology, Director of the Center for Human Experimental Therapeutics at University of Rochester, Rochester, NY, USA

— Michael Okun, MD, Adelaide Lackner Professor and Chair of Neurology, Executive Director, Norman Fixel Institute for Neurological Diseases, University of Florida Health, Gainesville, FL, USA



Bas Bloem



Ray Dorsey



Michael Okun

The *Moving Along* Editorial Board members had the opportunity to preview the new book, *Ending Parkinson's Disease: A Prescription for Action*, and compiled the following questions for the authors.

How did you come together, as authors, to write this book? What inspired you to write it?

The book's genesis was the World Without Parkinson's event, celebrating the bicentennial of Dr. James Parkinson's description of the disease. From that event, Bas and Ray wrote a piece in *JAMA Neurology* called (courtesy of Michael) "The Parkinson Pandemic," which was well received by the community. With the participation and encouragement of Todd Sherer, the CEO of the Michael J Fox Foundation, we decided to write the book. We drew parallels to how society previously addressed polio, HIV, and breast cancer and sought to apply those lessons to the fight to end Parkinson's disease.

What is this book aiming to achieve?

We hope to lay out the path necessary to prevent and end Parkinson's disease. As a community of researchers and clinicians dedicated to individuals affected by Parkinson's disease, we should be judged by how well we respond to the challenge. That challenge is to decrease the number of people developing the disease (through prevention) and to reduce the burden for those who are already affected (through better care and treatment).

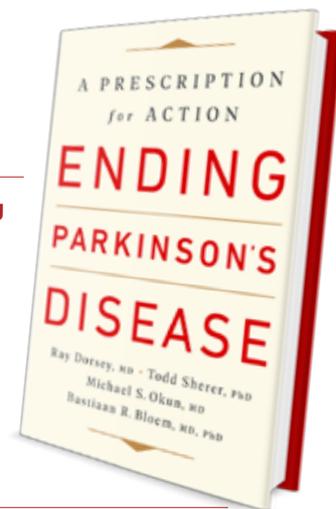
Besides Parkinson's disease patients, what other audience is the book is targeting?

Ideally, the book is a roadmap for patients, their families and friends, clinicians, scientists, politicians, industry, payers and activists. Even Parkinson's specialists will discover many under- and untold stories in the book and will encounter new perspectives from the stories of 40+ individuals affected by the disease. Finally, the book should be

a wonderful introduction to the field for students, residents, and fellows.

How did you decide on the title "Ending Parkinson's Disease: A Prescription for Action"?

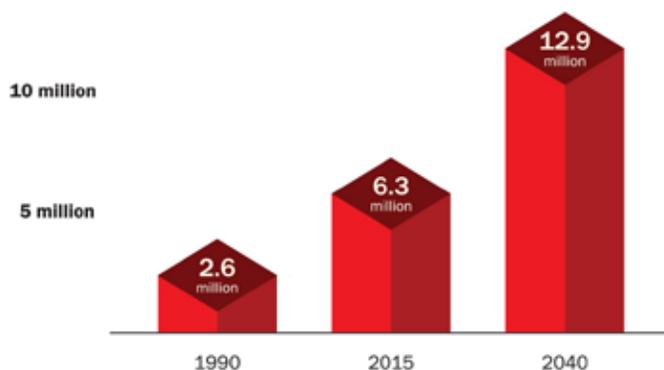
Our great editor, Colleen Lawrie at Public Affairs, pushed for a hopeful and bold title. The subtitle includes a prescription, which is broader and contains a call to action for all of us.



Can you elaborate on the concept and definition of Parkinson's disease as a pandemic? Can this terminology create more confusion?

The word "pandemic" derives from Greek roots (e.g., pan is all, demos is people). It was first used in the 19th century, and the original definition was not limited to infectious diseases. We recognize now that the modern word almost exclusively uses the word for infectious outbreaks, such as the unfolding COVID-19 pandemic.

But when you consider it, Parkinson's disease fulfills all other criteria to qualify as a pandemic. First, Parkinson's disease is the world's fastest growing neurological disorder, even faster than Alzheimer's. The number of people with the condition has more than doubled globally in the last 25 years, and absent change will double again in the coming generation. Second, rates of the disease, adjusted for age, are increasing in virtually every part of the world and have doubled in China. Third, no one is immune to the condition: Parkinson's disease affects both men and women, from all backgrounds, and although the incidence rises with age,



Ending Parkinson's Disease: A Prescription for Action - An Interview with the Authors, continued on p. 17

Ending Parkinson's Disease: A Prescription for Action - An Interview with the Authors, continued from p. 16

even young people can be affected. Finally, as with any other pandemic, the Parkinson's one has a tremendous impact, both on affected individuals and on society.

As such, even though Parkinson's disease is a non-infectious disease, it does constitute a real pandemic. Importantly, our goal was to raise awareness and open the dialogue, and obviously not to create a new controversy. What is undeniable is the rise of Parkinson's disease and its toll on individuals, families, and societies around the world. We want people to focus on these issues.

How can the #ParkinsonPACT be implemented, when there is so much that we do not know or understand about Parkinson's disease?

We know quite a bit about Parkinson's disease. Twenty years ago, Dr. Caroline Tanner and colleagues demonstrated that environmental factors contributed to the majority of cases. Numerous studies in several parts of the world conducted by many members of the MDS have linked certain pesticides and some industrial solvents to Parkinson's disease. Yet, many of these factors are still in use and contaminate the air we breathe, the food we eat, and the water we drink. We did not know critical elements of the PACT to treat polio or HIV when we started down that road. We now realize that Parkinson's disease is no different and that the #ParkinsonPACT can benefit from the lessons learned in the fields of polio and HIV.

There is no doubt that today we can be bold, charismatic, and disruptive by creating a "PACT" to Prevent as many cases of Parkinson's disease as possible, to Advocate for better policies, to Care as best as we can for all affected, and to Treat the condition optimally with existing and novel therapies. We have the ability to execute such a plan... Now we just need the will!

Can you elaborate more on the role exercise may have in prevention of Parkinson's disease, based on two studies published in 2018?

Two large studies of U.S. military veterans (n=7,000) and participants in a cancer prevention study (n=140,000) demonstrated that vigorous exercise (3.5 to 4 hours/week of running or swimming) in your 40s and 50s may possibly reduce your subsequent risk of developing Parkinson's disease a decade later by 20% or more. These results need replication, and there are many unanswered and critical questions the field should and will answer.

How can ECHO or telemedicine improve Parkinson's disease care in rural areas and lower income countries? Please extend as well to current experience with the COVID-19 pandemic.

We are learning a lot from the COVID-19 pandemic. One lesson is that we can use telemedicine globally to bring care into the homes of most anyone with Parkinson's disease (and many other movement disorders). Project ECHO, developed at the University of New Mexico, uses video

conferencing to connect specialists to remote general practitioners to enhance their ability to care for patients with complex diseases in their communities. Developed initially for hepatitis C, it can be applied to Parkinson's disease and other movement disorders. The silver lining of COVID-19 is that it has finally opened the door for telemedicine for Parkinson's disease on a global scale. We can now provide more care in the home, where it is often most wanted and needed.

What kind of additional resources would be required to face this "pandemic"?

We are going to need more resources, including money. The large investments the NIH (currently \$3 billion/year) and other funders made to fight HIV changed the course of the disease and prevented millions from ever developing the disease. Last year, the NIH spent \$224 million on Parkinson's disease. That is not going to be enough to alter the course of a disease that now affects over a million Americans. We need to lobby for a 10-fold per year increase. Beyond funding, MDS can play a crucial role in its ongoing effort to globally train and educate more professionals, so more individuals with Parkinson's disease and their families can receive expert care.

Is there really hope on the horizon?

There is always hope, but hope must be created by our energy, enthusiasm and perseverance. In the 1950s, millions of Americans mailed dimes to the White House and ultimately raised millions of dollars to develop a vaccine for polio, which previously closed swimming pools, houses of worship, and community centers. In the 1980s, an unknown virus caused a rapidly fatal disease. In the absence of a federal response, a group of HIV activists in New York adopted a motto of "Silence=Death." They blocked the streets of New York, shut down the New York Stock Exchange, occupied the FDA, and operated their own shadow healthcare system. Fifteen years later, protease inhibitors were developed. Because of these efforts, individuals infected with HIV now have a near normal life expectancy. Today, we are acting again to address the COVID-19 pandemic. If we confront Parkinson's disease with the same vigor, we will can pave the road toward ending this debilitating disease.

Should Movement Disorder Specialists start taking a different clinical approach when addressing Parkinson's disease?

We should all recognize that our current investment in and approach to Parkinson's disease is not working. The *Movement Disorder Society* was founded in 1985. Since that time, the number of people with Parkinson's disease has more than tripled. We have advanced knowledge and improved care, but we have had not any major therapeutic breakthroughs this century. We need a prescription for action to change the course of this disease. We outline this path in *Ending Parkinson's Disease* (#ParkinsonPACT), and we hope that our generation and that this Society can address one of the great global health challenges of our time.

The Next Frontier for Parkinson's Disease and Movement Disorders: The MENASA Region

— Shivam Om Mittal, MD, Consultant Neurologist, Cleveland Clinic Abu Dhabi, Abu Dhabi, UAE; Mehri Salari, MBBS, Shahid Beheshti University of Medical Science, Tehran, Iran; Zakiyah Aldajani, MBBS, Neurology Unit, King Fahad Military Medical Complex, Dhahran, Saudi Arabia; Jawad A. Bajwa, MD, National Neuroscience Institute, King Fahad Medical City, Riyadh, Saudi Arabia on behalf of the MDS Middle East Working Group

Very little is known about the richness and diversity of Parkinson's disease (PD) and movement disorders in the Middle East, North Africa and South Asia (MENASA) region. The MENASA region provides tremendous opportunities but with significant challenges to the development of clinical and research programs for PD and movement disorders. This region constitutes one-third of the global population which encompasses very few economically rich countries, but mostly low and middle-income countries. Western countries relish the rich presence of movement disorder specialists in addition to a vast array of clinical, educational and research programs, but these opportunities are currently lacking in MENASA. Expertly trained specialists, however, now are returning to the MENASA region after training and are today in the position to develop programs based on successes elsewhere but uniquely tailored to the MENASA region.

The International Parkinson and Movement Disorders Society (MDS) created the Task Force for the Middle East in 2016 to explore the region's challenges, limitations and set the foundation for the growth of PD and movement disorders. Since the MDS Task Force creation, noticeable changes were observed in educational activities, membership growth and raising awareness. To assess the region's needs, the Task Force conducted a survey in 2016. It was the first survey that shed light into the unmet needs in providing care for people with PD in the MENASA countries, the scarce of the movement disorders' specialists, educational opportunities, research, as well as the high cost of treatment, the lack of general health infrastructure, resources and health insurance coverage were described as the main barriers to provide care for people with PD in the MENASA countries. The data suggested that there is a great need to increase the awareness of PD and to provide educational opportunities within this field in the MENASA countries.

In 2019, the Task Force was transformed into a permanent body, the Middle East Working Group (MEWG). The group's mandate is to develop education, foster collaboration with other regional societies through affiliate memberships to build strategic partnerships, develop guidelines and increase membership.

Since the 1st Middle East camp in April, 2014, the MEWG members have organized 16 courses in the form of live courses for medical and allied professionals, young neurologists and also outreach programs such as Developing World Education Program (DWEPE), Ambassador and Virtual Professor programs; other work includes patient education leaflet translations into Arabic, Persian, Bangla and Urdu. The members also have been involved with the translation and validation of MDS-UPDRS and MDS-UDysRS rating scales into Arabic across ten of the regional countries which will expand to other regional languages in the future. The MEWG also published its first consensus paper on PD highlighting needs, challenges and limitations in providing care for people with PD in MENASA.

So far the work done by the former Middle East Task Force and the present MEWG has helped fill up the gaps in educational support and has promoted collaboration. The past educational activities in different countries of the region and the publications by the group attest to the productivity of the group. The future awaits and the target goal for 2020 and 2021 is exploring in depth the region's needs, challenges and limitations.

The group's long-term goal is to make advancements in science of PD and movement disorders through regional collaboration and support, education and raising awareness especially among the young neurologists of the region.

Although much effort is required there is an extraordinary passion among our members in working together towards a better future. We appreciate the MDS leadership support to our efforts, as MENASA is the next frontier in PD and movement disorders.

References:

1. Khalil H, Chahine L, Siddiqui J, Aldajani Z, Bajwa JA. Parkinson's disease in the MENASA countries. *Lancet Neurol.* 2020;19(4):293-294. doi:10.1016/S1474-4422(20)30026-0
2. Khalil H, Chahine LM, Siddiqui J, et al. Parkinson's Disease in the Middle East, North Africa, and South Asia: Consensus from the International Parkinson and Movement Disorder Society Task Force for the Middle East. *J Parkinsons Dis.* 2020;10(2):729-741. doi:10.3233/JPD-191751
3. Khalil H, Bajwa JA. Barriers and Facilitators in Physical Rehabilitation for Parkinson's Disease in the Arabian World. *Mov Disord Clin Pract.* 2015;2(3):227-229. Published 2015 Jun 30. doi:10.1002/mdc3.12200
4. MDS Middle East Working Group: <https://www.movementdisorders.org/MDS-AOS/Middle-East-Working-Group.htm>



Members of the MDS Middle East Working Group in Nice, France, 2019

Multiple System Atrophy: Recent Developments and Future Perspectives

— *Wassilios G Meissner, MD, PhD, French Reference Center for MSA, Institute of Neurodegenerative Diseases, University Hospital and University Bordeaux, France*
— *Olivier Rascol, MD, PhD, French Reference Center for MSA, Departments of Clinical Pharmacology and Neurosciences, University Hospital of Toulouse, France*



Wassilios G. Meissner



Olivier Rascol

In a recent review, we have discussed significant developments in multiple system atrophy (MSA), with emphasis on pathogenesis, diagnosis, prognosis and treatment development. We have further highlighted some unsolved questions and perspectives.¹

The pathologic hallmark of MSA is the accumulation of aggregated α -synuclein in oligodendrocytes forming glial cytoplasmic inclusions (GCI), which qualifies MSA as synucleinopathy. There has been significant progress in our understanding of the role and origin of α -synuclein in MSA. Recent findings have challenged prior evidence and suggest that oligodendrocytes may be the principal source of α -synuclein in GCI. Additional mechanisms are likely involved as illustrated by the demonstration of cell-to-cell transfer of α -synuclein from neurons to oligodendrocytes in preclinical studies and the abundant presence of soluble α -synuclein oligomers in neurons in post-mortem brains of MSA patients. The hypothesis that α -synuclein aggregates may act as prions has also gained increasing attention. Hitherto, no study undoubtedly supports the claim that MSA is a prion disease and key issues remain to be addressed in the future.

There have been significant advances in brain imaging during the last decade. In this regard, brain MRI studies using machine-learning or multimodal techniques have shown promising results regarding the differential diagnosis between MSA and Parkinson's disease (PD), and have also informed about the progression of imaging abnormalities in MSA. The results are heralding the use of automated algorithms in clinical routine for the diagnosis of MSA in the near future. Additional progress will very likely increase diagnostic accuracy and lead to additional refinements of MSA diagnosis criteria. Beyond MRI, abnormal findings on [¹⁸F]fluorodeoxyglucose PET and dopamine transporter SPECT belong to the additional features of current diagnosis criteria. Noteworthy, the MSA-related metabolic pattern distinguishes MSA with high sensitivity and specificity from PD and progressive supranuclear palsy, and seems to allow the early identification of patients with rapid eye movement related sleep behavioral disorder who convert to a diagnosis of MSA.

The development of fluid biomarkers for the diagnosis and prognosis is still in early days. Differences in blood and cerebrospinal fluid (CSF) levels of α -synuclein, markers of axonal degeneration and catecholamines have been observed in some studies between MSA, healthy controls and relevant differential diagnoses. Noteworthy, two recent studies have found distinct α -synuclein seeding activities in CSF samples of MSA patients compared to other synucleinopathies.^{2,3} These findings not only corroborate the idea that pathologic α -synuclein species are distinct in MSA, but also pave the way for the development of a diagnostic test.

Available symptomatic treatment options for MSA have not significantly changed over the past decade and disease-modification remains an urgent unmet need. All randomized controlled disease-modification trials except one have failed (see table). α -synuclein is currently the main target for the development of possible disease-modifying treatments for MSA. Specific active immunotherapy with Affitopes PD01A/PD03A and the aggregation inhibitor anle 138b (NCT04208152) have recently entered clinical development. In addition, a single-center futility trial with sirolimus is ongoing (NCT03589976). Sirolimus is believed to increase the degradation of α -synuclein through enhanced autophagy.

Finally, efforts should be continued to implement large international research networks and harmonize care practices. The MDS-sponsored MSA Study Group, the European MSA Study Group, the European Reference Network for Rare Neurological Disorders (ERN-RND), other regional MSA networks outside Europe and the MSA Coalition are major stakeholders for this endeavor.

References

1. Meissner WG, Fernagut PO, Dehay B, et al. Multiple System Atrophy: Recent Developments and Future Perspectives. *Mov Disord* 2019;34(11):1629-1642.
2. Rossi M, Candelise N, Baiardi S, et al. Ultrasensitive RT-QuIC assay with high sensitivity and specificity for Lewy body-associated synucleinopathies. *Acta Neuropathol* 2020.
3. Shah Nawaz M, Mukherjee A, Pritzkow S, et al. Discriminating alpha-synuclein strains in Parkinson's disease and multiple system atrophy. *Nature* 2020;578(7794):273-277.

Multiple System Atrophy: Recent Developments and Future Perspectives, *continued from p. 19*

Therapy	Patients	Presumed mechanism of action	Phase	Design	Primary Endpoint (Secondary Endpoint)	Outcome
Growth hormone	43	Pro-survival effects	II	RCT	Total UPDRS score and autonomic tests at 6 and 12 months (total UMSARS score at 6 and 12 months)	Ineffective, high dropout rate
Minocycline	63	Inhibition of microglial activation	III	RCT	Change in UMSARS II score at 48 weeks (change in UMSARS I, III, UPDRS III, SF-12 and EQ-5D at 48 weeks; [11C]-PK11195-PET was assessed in small ancillary study, n=8)	Ineffective (reduced microglial activation on PET in ancillary study)
Riluzole	404	Anti-excitotoxic activity, free-radical scavenging	III	RCT	Survival (rate of decline in motor function)	Ineffective
MSC delivery (intra-arterial and intravenous)	33	Neurotrophic effects, neural cell differentiation	II	RCT	Change in total UMSARS score at 12 months (change in UMSARS II score and imaging outcomes at 12 months)	Smaller increase in total UMSARS score (smaller increase in UMSARS II score and positive effects on imaging outcomes), safety concerns (ischemic MRI brain lesions in one third)
Rifampicin	100	Inhibition of formation of α -synuclein fibrils	III	RCT	Change in UMSARS I score (slope) at 12 months (change in UMSARS I, II and total, COMPASS-select at 12 months)	Study prematurely terminated, ineffective
Rasagiline	174	MAO-B inhibitor	II	RCT	Change in total UMSARS score at 48 weeks (change in GCI-I, COMPASS-select and MSA-QoL at 48 weeks, change in total UMSARS II at 24 weeks; Putaminal diffusivity was assessed in ancillary imaging study)	Ineffective
Epigallocatechin gallate (EGCG)	92	Inhibition of α -synuclein aggregation	III	RCT	Change in UMSARS II score (exploratory assessment of MRI parameters)	Ineffective
BHV-3241 (formerly AZD3241)	58	Myeloperoxidase inhibition	II	RCT	Safety and tolerability, striatal change in [11C]-PBR28 binding as indicator of microglial activation	Safe and well tolerated, no change in [11C]PBR28 binding
Fluoxetine	81	Serotonin reuptake inhibition, increased neurotropic support	II	RCT	Change in total UMSARS at 3 months (change in SCOPA-Aut, BDI, MSA-QoL, SF-36, change in total UMSARS at 6 months)	Ineffective (preliminary results only reported for primary outcome)
Intrathecal MSC delivery	24	Neurotrophic mediation, neural cell differentiation	I/II	OL	Frequency and type of adverse events (change in total UMSARS (slope) and indices of autonomic failure at 12 months)	Safe and well tolerated, except for low back/leg pain, associated with thickening of lumbar nerve roots in highest-dose group, slower rate of UMSARS progression compared to historical control group
α -synuclein targeted active immunization	30	Induction of immune response against toxic α -synuclein forms	I	Patient + examiner blind	Safety and tolerability, immunogenicity against α -synuclein	Safe and well tolerated, PD01 induced immune response

Table. Completed clinical trials in MSA. BDI, Beck Depression Inventory; COMPASS, Composite Autonomic Symptom Score; MRI, Magnetic Resonance Imaging; MSA-QoL, Multiple System Atrophy Health-related Quality of Life; MSC, Mesenchymal Stem Cells; OL, Open label; PET, Positron Emission Tomography; PD, Parkinson Disease; RCT, Randomized Placebo-Controlled Trial; SCOPA-Aut, Scales for Outcomes in Parkinson's disease-Autonomic; SF-12/36, Short-Form Survey 12/36; UPDRS, Unified Parkinson's Disease Rating Scale; UMSARS, Unified Multiple System Atrophy Rating Scale.

Discriminating Alpha-Synuclein Strains in Parkinson's Disease in Multiple System Atrophy

— Mohammad Shahnawaz, MB, BCh, Mitchell Center for Alzheimer's Disease and Related Brain Disorders, Department of Neurology, University of Texas McGovern Medical School at Houston, Houston, TX, USA

— Wolfgang Singer, MD, Department of Neurology, Mayo Clinic, Rochester, MN, USA



Mohammad Shahnawaz



Wolfgang Singer

Anhar Hassan, a member of the *Moving Along* Editorial Board, compiled the following questions for Mohammad Shahnawaz, and Wolfgang Singer regarding their recent publication in *Nature*, titled "Discriminating alpha-synuclein strains in Parkinson's disease in multiple system atrophy."

Both Parkinson's disease (PD) and multiple system atrophy (MSA) are synucleinopathies, associated with misfolding and aggregation of alpha-synuclein. It can be clinically challenging to differentiate these two disorders, particularly in the early disease stages. In this study, you used a special alpha-synuclein assay (termed "protein misfolding cyclic amplification", PMCA) to differentiate patients with clinically diagnosed PD and MSA, with high sensitivity. Could you briefly review the background of previously used techniques to detect alpha-synuclein in the CSF, and their limitations to discriminate between synucleinopathies?

The central event in both diseases, Parkinson's disease (PD) and Multiple System Atrophy (MSA), is misfolding of normal alpha-synuclein, formation of alpha-synuclein aggregates, and resulting perpetuation of misfolding that results in alpha-synuclein buildup in the brain cells in the form of Lewy bodies and glial cytoplasmic inclusions. These buildups interfere with the normal function of brain cells and eventually culminate in cell death. Because of this, a number of studies have focused on detecting alpha-synuclein, phosphorylated alpha-synuclein, and alpha-synuclein oligomers/aggregates in cerebrospinal fluids (CSF) as a surrogate marker for the diagnosis of PD, and for differentiating PD from other synucleinopathies.

Using immunoassays such as ELISA, lower total alpha-synuclein in CSF of PD patients as compared to healthy controls have been reported. However, the diagnostic accuracy of total alpha-synuclein in differentiating PD from controls was unsatisfactory, and even more so in distinguishing PD from other synucleinopathies such as MSA and dementia with Lewy bodies (DLB). Until recently, there were no data available for the detection of alpha-synuclein aggregates in CSF for discriminating the different synucleinopathies.

Could you explain the PMCA assay?

PMCA is conceptually similar to "DNA amplification" by polymerase chain reaction, which has been used previously for the detection of misfolded protein aggregates associated with prion disease and Alzheimer's disease. Recently, we have adapted this PMCA assay for the detection of misfolded alpha-synuclein in the CSF of patients with PD and related synucleinopathies. In the PMCA assay, a sample believed to contain misfolded protein is allowed to interact with an excess of normal protein at a defined experimental condition, which results in misfolding of normal protein to misfolded protein, which cyclically amplifies the amount of misfolded protein.

In your study, you examined 94 samples of CSF from patients with PD, 75 from patients with MSA, and 56 from patients with other neurological diseases. You found that the assay could discriminate between PD and MSA patients with a sensitivity of 95.4%. Can you expand on your key findings?

In this study, we show that the detection of alpha-synuclein aggregates in CSF by PMCA assay can clearly distinguish PD from MSA with an overall sensitivity of 95.4% and specificity of 94.5%. To gain insight into the characteristics of amplified alpha-synuclein aggregates by PMCA, we used a combination of biochemical, biophysical, and biological methods. We found that characteristics of amplified alpha-synuclein aggregates from CSF samples of PD and MSA patients were markedly different. Interestingly, the properties of amplified aggregates from CSF were similar to those amplified from brain samples, suggesting alpha-synuclein aggregates circulating in CSF are representative of those deposited in the brain. Overall, we show that alpha-synuclein aggregates associated with PD and MSA are conformationally distinct.

Specific key findings are:

- (1) The aggregation kinetics of alpha-synuclein in the presence of samples from PD and MSA patients are distinct.
- (2) There is differential affinity of conformational dye towards amplified alpha-synuclein aggregates from samples of PD and MSA patients.
- (3) Alpha-synuclein aggregates amplified from MSA patients have a higher proportion of β -sheet structure as compared to aggregates from PD.
- (4) Alpha-synuclein fibrils from patients with MSA had shorter twists as compared to those from patients with PD.
- (5) Alpha-synuclein aggregates from patients with MSA were more toxic to cells as compared to aggregates from PD.

Discriminating Alpha-Synuclein Strains in Parkinson's Disease in Multiple System Atrophy, *continued from p. 20*

- (6) The characteristics of amplified aggregates from CSF were similar to those amplified from brain samples.

The mean disease duration in this study for MSA patients was 3.8 ±2.6 years, and for PD patients was 8.13 ±4.7 years. However, in the clinic often there is difficulty discriminating between these diagnoses early on, particularly in the first year or two of symptoms, when MSA patients may not yet have developed prominent autonomic symptoms. Did the assay show a difference between MSA and PD patients with very early disease duration?

We have been able to distinguish both PD and MSA as early as in the first year of the disease. In fact, we could previously show that the PMCA assay was capable of detecting alpha-synuclein aggregates in CSF of individuals at the presymptomatic stage, 5 years before they developed clinically manifest PD.

What were the strengths and limitations of the study?

The main strength of this study is that the PMCA assay can not only detect alpha-synuclein aggregates in CSF for the diagnosis PD and MSA with high sensitivity and specificity, but it is capable of distinguishing conformationally distinct alpha-synuclein aggregates associated with PD and MSA. The main limitation of our assay is that it is currently optimized for CSF; given the invasive nature of spinal fluid collection, detecting alpha-synuclein aggregates in easier accessible biological fluids would be

desirable. We are currently optimizing the assay to detect aggregates in more accessible biological fluids such as blood, urine, and saliva, so that a non-invasive, low cost, and routine diagnostic test could be developed.

Going forward, do you think this technique would also be useful to help discriminate patients with dementia with Lewy bodies, another synucleinopathy that may be difficult to differentiate from Parkinson's disease in both early and late clinical stages?

It is possible that alpha-synuclein aggregates associated with DLB might also be conformationally distinct. Using a small number of CSF samples, DLB samples showed similar aggregation kinetics as PD samples, but larger numbers are needed to further explore potential differences.

How else do you envisage these results could be used to further improve understanding of MSA and PD in the future?

It can be challenging to distinguish between PD and MSA because they share similar clinical signs and symptoms, particularly at an early disease stage. Enhancing diagnostic certainty at an early or even prodromal stage should not only improve future clinical studies into these disorders, but also allow for enrollment into clinical trials at earlier disease stages when disease-modifying therapies would be expected to be most efficacious and impactful.

Changing the Model for How Parkinson's Disease is Treated: The Patient is the Sun

An Interview with Michael Okun, MD



Daniel Martinez-Ramirez, a member of the *Moving Along* Editorial Board and former University of Florida fellow and assistant professor, interviewed Michael S. Okun, Chair of Neurology at University of Florida Health, Medical Director of Parkinson's Foundation and Executive Director of the Norman Fixel Institute for Neurological Diseases. Dr. Okun and his team are changing the way Parkinson's disease (PD) is treated. In this interview, we discussed the current and future perspectives of PD treatment and how we can shift to better models of care.

Daniel: How was the idea of an interdisciplinary service for PD born?

Michael: Kelly Foote, my neurosurgery partner, and I moved to the University of Florida in 2002 from Emory University in Atlanta, GA, where we enjoyed the fabulous mentorship of Mahlon DeLong, Jerry Vitek and Ray Watts. At the time, Kelly had recently completed a fellowship with Alim Benabid in Grenoble, France. Honestly, we were two young and somewhat naïve doctors who dreamed of creating an interdisciplinary model of care for Parkinson's disease and movement disorders patients and we dreamed of a model that would reach beyond surgical care and research. University of Florida offered us an opportunity of a lifetime. We started with two docs, one physician assistant and one nurse and together we built a small program. In 2011, we opened the first interdisciplinary all under one roof center (a single floor of a building) and Janet Reno was our first patient to experience all the services in one place. In 2019, we opened the Norman Fixel Institute (a free-standing building), which is comprised of over 120 members spread over 30 departments across the University of Florida Campus.

Daniel: Why build a science hub for Parkinson's Disease?

Michael: The US healthcare system is founded on a primary care gatekeeper model, in which patients are encouraged to select a primary care physician for routine healthcare delivery. When a medical problem exceeds the expertise or scope of practice of the primary care physician, optimal management requires consultation with an appropriate specialist. However, the delivery of specialized care for complex disorders in the United States tends to be expensive, inefficient, and less effective than it should be because of important weaknesses in prevalent specialty care practices. One in 15 of us will be affected by a Parkinson's diagnosis over a lifetime. It is time for us to create better models of care to address these needs before we bankrupt Medicare.

Daniel: What were the challenges found back in 2011 when the UF Movement Disorders Center was initiated?

Michael: The early challenges involved recruiting faculty and researchers to the effort. Our start-up package in retrospect was too small, but at the time we thought we had hit the "jackpot." We received \$150,000 which we quickly spent on operating room equipment. Our strategy was focused on the development of our people and in building on strengths rather than filling boxes or trying to be something that we were not. We identified great people all over the UF campus and we invited them to collaborate and be part of a new clinical-research-education model for Parkinson's disease and movement disorders. We discovered a treasure trove of untapped talent across the entire campus which is one of the largest land-based campuses in the country. There were less than 10 neurologists at UF when we joined and there are now over 50. We were fortunate to recruit Hubert Fernandez from Brown who stayed with us for 7 years and was a critical early piece of our foundation. He is now the Center Director at Cleveland Clinic and remains a close friend and collaborator. We have trained 58 fellows and many of them like Ramon Rodriguez, Irene Malaty, Leo Almeida and Addie Patterson have helped us cement a strong foundation of excellence. The magic of UF was and will always be the people. Early challenges for us also focused on the economics and removing the financial disincentive to collaborate (e.g. rent, overhead costs).

Daniel: What are the challenges now almost ten years later?

Michael: We believe success is anchored on adaptability. We believe that the UF team has been adaptable to the changing climate of healthcare and to the increasing challenges facing research funding and fellowship funding. The challenges include retention of excellent faculty, research funding, fellowship funding and moving into the telemedicine-remote monitoring era.

Changing the Model for How Parkinson's Disease is Treated: The Patient is the Sun, *continued from p. 23*

Daniel: What are the benefits/advantages of a neuromedicine hub for PD patients and for doctors?

Michael: The delivery of specialized healthcare in the United States is commonly hindered by poor communication, wide variations in methods of care delivery with a paucity of outcomes data to develop reliable best practice recommendations, minimal focus on preventive care, insufficient clinical research to improve global care, suboptimal education of future care practitioners, and a general failure to exploit the collective expertise of a true interdisciplinary team. There is a paucity of published data on multidisciplinary care models, and there is a need for careful examination of outcomes and cost while accounting for differences in care delivery. The model is based on 4 core principles. First, all interdisciplinary specialists who might possibly be needed to provide optimal care for a given complex disorder are co-located at 1 center. In the case of Parkinson's disease and movement disorders, for example, neurologists, neurosurgeons, neuropsychologists, psychiatrists, physical therapists, occupational therapists, speech and swallow therapists, and social workers see patients at a common facility tailored to its interdisciplinary mission. Second, each specialist develops and communicates a patient-specific care plan within their area of expertise so that follow-up can be accomplished in the local community. Third, every patient is a potential research participant, and outcomes of all therapeutic interventions are carefully documented and tracked over time. Each patient signs an institutional review board–approved database consent, so that every contact with a patient in the center becomes part of the clinical record and the research database. Fourth, the relationship between the patient and each of the care or research practitioners is bidirectional. Interactions are not unidirectional and solely for the patient's benefit. More information on the service and science hub is available in *JAMA Neurology* at: <https://jamanetwork.com/journals/jamaneurology/fullarticle/2666956>

Daniel: What is this science hub model of care based on?

Michael: The model is based on our many years of experience caring for Parkinson's disease patients and also on our collective experience from our mentors and colleagues all over the world. The experience of our center as a Parkinson's Foundation Center of Excellence and also our experience in developing true multidisciplinary screening for DBS therapy has helped to drive our model. We envision something practical and deployable over large geographical regions. We have enormously benefited from my role as the Medical Director of the Parkinson's Foundation as I have been able to learn from the best centers in the world and adapt best practices for UF.

Daniel: Any comments on future perspectives in the treatment of PD?

Michael: PD is associated with a range of pathophysiological processes, including α -synuclein aggregation, neuroinflammation, mitochondrial dysfunction, neuronal vulnerability, iron deposition and neural network alterations. The complexity of these intertwined pathways and the heterogeneity in clinical phenotypes require a targeted approach for therapy. Although current treatment options provide symptomatic relief, advances in high-throughput screening methods for small molecules, improved disease modelling and progress in analytical technologies are likely to facilitate novel discovery. Deep Brain Stimulation is an established therapy for Parkinson disease, but there is growing interest in non-invasive electrical stimulation modalities and optogenetic stimulation modalities. Non-invasive electrical stimulation might be achieved with interference of two electric fields with slightly different frequencies (temporal interference), leading to localized stimulation. In optogenetic stimulation, an opsin is delivered to specific neurons that then express a light-sensitive channel on their membrane, permitting their stimulation with direct light source. Alternatively, certain nanoparticles, if delivered inside the brain, are able to convert infrared light from an extracranial source to visible light in the brain and hence permit the non-invasive stimulation of optogenetically modified neurons. Electrical stimulation approaches are generally non-specific, whereas optogenetic approaches have the potential for targeting specific neurons. Immunotherapies could provide a novel mechanism for the body to boost its response to α -synuclein. Research in the field of cell-based therapies has provided an improved comprehension of the disease, and some iPSC therapies could be used in personalized therapy. Adaptive DBS and optogenetically inspired DBS might aid the definition of more specific targets. Taken together, these advancements suggest that the future of PD therapies is promising. These have been recently reviewed by our group in: <https://www.nature.com/articles/s41582-019-0155-7.pdf>

Daniel: Any recommendations for those who are interested in building an interdisciplinary model of care for PD?

Michael: Our best recommendation is to focus on development of a vision for your program or center and to focus and to build your strengths. The real secret is to develop your people and don't try to do everything. These types of centers and models cannot be built overnight, but with perseverance, new models of care for Parkinson's disease and movement disorders can be successful. Think "we" and not "me." Our founding philosophy that the patient is the sun and we should orbit around the patient drives everything we do at UF. Find your strength, develop your philosophy and invest in a healthy culture where everyone can succeed.

MDS-AOS Rare Movement Disorders – Bengaluru, India, March 6-7, 2020

The MDS-AOS Rare Movement Disorders course took place at the National Institute of Mental Health and Neurosciences (NIMHANS) Convention Center in Bengaluru, India on March 6-7, 2020. The course was led by local Course Directors, Prof. Pramod Kumar Pal and Dr. Ravi Yadav, both of NIMHANS, and 12 additional faculty from India, Australia, Malaysia, South Korea, the United Kingdom, and the United States. The course was attended by 86 participants. Three quarters of attendees came from India and others from Bahrain, Malaysia, Nepal, New Zealand, and Sri Lanka.

Prashanth Kukkle and Bettina Balint, members of the *Moving Along* Editorial Board, sat down with Prof. Pramod Pal at the MDS-AOS Rare Movement Disorders Course in Bengaluru, India.

Prashanth: What is the scope and requirement for Rare Movement Disorders in India? What is your personal perspective and experience with Rare Movement Disorders?

Pramod: India has a Rare Disorders Society, but not a Rare Movement Disorders group. With the increased interest in Movement Disorders, neurometabolic disorders and genetics, the focus on rare movement disorders is emerging. Since I am in a tertiary care teaching and research institute which has the facilities, I get a large number of referrals since these are difficult to diagnose and treat.

Bettina: What is the level of awareness and setup available for Rare Movement Disorders in India?

Pramod: As in rest of the world, awareness of RMD as a special group is limited in India. There is no special setup available for diagnosis and management of these disorders. However, at an individual level, many neurologists and paediatricians are doing a commendable job in diagnosis and treatment of several of these disorders.



Prashanth: What were the primary goals for the Rare Movement disorders session in India? Can you also highlight resources which are required to address the Rare Movement Disorders in India?

Pramod: The primary goal was to introduce the concept of RMD to neurologists, pediatricians, geneticists and practicing physicians. More specifically, the scope was to

- (i) Understand the epidemiology and clinical profile of RMDs
- (ii) Decipher the clinical clues for a differential diagnosis of RMDs
- (iii) Comprehend the diagnostic approach to RMDs
- (iv) Recognize the general and specific treatment of RMDs

Laboratories with facilities for neurometabolic workup and genetic testing at minimal cost to the patients are the most important facilities which are needed going forward.

Bettina: I was very impressed by the knowledge and experience in rare movement disorders of the faculty and the audience. How rare is RMD in India? It appears that you see “many rare” cases there, and with the advance of genetics can also reach a final diagnosis. India is often considered a resource-limited country, but I got the impression that there are also many chances - can you put this in perspective? Where do you see the chances, where are the gaps?

Pramod: India has a population of ~1.3 billion and the absolute number of currently recognized RMDs (~185-200) is high. Most patients with RMDs will consult or be referred to Neurologists. Since there are around 2000 neurologists in the country and approximately 15% with special interest in Movement Disorders (~300 current members of Movement Disorders Society of India), each neurologist/ movement disorders specialist gets to see a large number of patients with RMDs in their clinical practice. So, for us, rare movement disorders may not be that rare. Moreover, in the past few years, genetic and neurometabolic testings are easily done and at affordable rates so diagnosis has improved.

We have a higher prevalence of many RMDs, especially autosomal recessive disorders (e.g. Wilson’s disease) in comparison to other countries. In our Neurology residency program, emphasis is given on the recognition of atypical/rare movement disorders. Most neurologists in India are abreast of current developments by attending CMEs and conferences (National and International) on a regular basis.

So, though India may have resource limitations, the standard of neurology training and expertise is quite high, which helps us to in imparting one of the best Neurology/ Movement Disorders services in the world.

MDS-AOS Rare Movement Disorders, *continued from p. 25*

Prashanth: In there a resource constraint to increase the awareness of Rare and treatable Movement Disorders in a large country like India?

Pramod: We need to involve the neurologists, paediatricians and geneticists for diagnosis and treatment of rare movement disorders. A dedicated Rare Movement Disorders organization needs to be created and frequent CMEs, live courses and international collaborations will definitely help in increasing the awareness of RMDs in India.

Bettina: Are other organizations or societies working for Rare Movement Disorders in India? Can MDS-AOS collaborate to create an optimal impact?

Pramod: There is an organization for Rare Diseases in India, but not a dedicated one for Rare Movement Disorders. We will be happy to collaborate with MDS-AOS in this area.



MDS-AOS Rare Movement Disorders Course – Coffee Break Conversations

“What have you learned?”



Shweta Prasad

PhD Scholar, Dept. of Neurology and Clinical Neurosciences, National Institute of Mental Health and Neuro-Sciences, Bangalore

“I learned that diagnosing a rare movement disorder is highly dependent on thorough history taking, clinical assessment, and most importantly attention to detail. Common movement

disorders may often have uncommon presentations and vice-versa, and appropriate diagnostic modalities should be utilized to avoid missing the diagnosis of a treatable disorder.”

“How did you like the meeting?”



Vikram V Holla

Assistant Professor of Neurology, National Institute of Mental Health and Neuro-Sciences, Bangalore

“I thought the meeting was highly enjoyable and informative, as within a short period of time such a complicated and diverse topic was delivered in a systematic and simplistic manner by top-notch faculty. The ability for any delegate to interact

with faculty to clarify even the simplest of doubts further enhanced my experience at the meeting.”

“From your vast experience as clinician - what is the most important skill when dealing with rare movement disorders in India?”



Meenakshisundaram Umaiorubahan

Professor of Neurology, Senior Consultant and Head of Neurology, Apollo Hospitals, Chennai

“The important aspect is to get the basics right - proper history including a detailed family history, and a systematic examination leading to a clinical syndromic diagnosis to begin with - and to keep the possibility(ies) at the back of your mind.”

“You spoke about movement disorders related to rare infections - which are the most relevant insights from the Indian experience?”



Sanjay Pandey

Professor of Neurology at Govind Ballabh Pant Institute of Postgraduate medical education and research, New Delhi

“The encephalitis most commonly observed in India are Japanese encephalitis (JE), herpes simplex, and dengue. Movement disorders are common and severe in JE mainly due to their typical (thalamus and basal ganglia) anatomical involvement. The movement disorders observed in encephalitis patients are mostly parkinsonism, dystonia or both; rarely chorea, myoclonus, and athetosis can also be one of the presenting symptoms.”

MDS-AOS Rare Movement Disorders Course – Coffee Break Conversations, *continued on p. 27*

“India is the country with probably the most experience in Wilson's, and you are the Wilson's expert - where do you see knowledge gaps or unmet needs?”



Mohit Bhatt
Consultant Neurologist & Movement Disorders Specialist, Kokilaben Hospital, Mumbai

“Patients with Wilson's disease often default on treatment (over 30%), in part, because it has to be continued lifelong even after the disease-related symptoms are resolved, medications have to be taken in multiple daily doses separated from meal times, and some patients experience treatment-related adverse effects. Therefore, it would be valuable to find treatment regimens that are easier to adhere to detect when treatment is discontinued without the doctor's awareness, and develop practices that encourage treatment compliance.”

“What is the relation of zebras and rare juvenile parkinsonism?”



Victor Fung
Professor of Neurology, University of Sydney
Director of the Movement Disorders Unit and Co-Director of the Parkinson's Disease and Movement Disorders Research Centre, Westmead Hospital

“In medical school, we are taught that when we hear hooves outside the window, we should think of horses, not zebras. That remains true even for movement disorder specialists, but our job also requires us to know about zebras, and even rarer creatures such as albino zebras, as we are often the last hope for those seeking the reassurance of a diagnosis, and hope of a cure.”

“Which is rarer - zebra fishes or OMAS?”



Shen-Yang LIM, MD, FRACP

Professor in the Division of Neurology at the University of Malaya, Kuala Lumpur, Malaysia

“Two fantastic speakers (Victor Fung and Bettina Balint) highlighted in their talks that “zebras” may not be quite as rare in specialized clinical settings, and these conditions should therefore always be considered. I took this opportunity to mention my hobby of keeping and breeding *Hypancistrus zebra* fish (picture shows 10-day old “babies”), which are threatened with extinction in the Brazilian Amazon due to dam construction. Although these fish are quite rare (and expensive!), OMAS (opsoclonus-myoclonus ataxia syndrome) may be even more so if one expects to see the full triad of clinical features. In my adult movement disorder practice at a large tertiary centre in Kuala Lumpur, I have encountered only a small handful of cases over the past decade. Admittedly, there could be childhood cases (mainly associated with neuroblastoma) managed wholly by the paediatricians.”

“You gave a great lecture about the topic, what is your take on neurometabolic disorders?”



Prashanth L. Kukkle

Consultant Neurologist & Movement Disorders Specialist

Center for Parkinson's Disease and Movement Disorders, Vikram Hospital, Bengaluru

“Neurometabolic disorders are under recognized in regular practices in Indian setup. However, I can see that there are quite a few well established centers across India, which cater to the Neurometabolic disorders including extensive metabolic workup and the genetic workups. The only thing which has to be addressed is to increase the awareness about the potential treatable neurometabolic disorders to the general practicing levels (Physicians, Paediatricians and Neurologists) and referring them to the apt centers.”

MDSICON 2020 – 5th Annual Conference of Movement Disorders Society of India – Kovalam, Thiruvananthauram, January 31 - February 2, 2020

The 5th Annual Conference of Movement Disorders Society of India (MDSICON) was held between January 31 to February 2, 2020 at Thiruvananthapuram, Kerala, India. The conference was attended by more than 550+ delegates including from the SAARC countries. There were 24 academic sessions, conducted by about 80 faculty (including 9 International faculty) and included plenary sessions, parallel sessions, hands on workshop for botulinum toxin and DBS planning, Grand Rounds and Video Akhada. The International faculties included Prof. Anthony Lang, Prof. Mark Hallett, Prof. Kailash Bhatia, Prof. K Ray Chaudhuri, Prof. Andres Lozano, Prof. Emmanuel Roze, Dr. Sabine Meunier, Dr. Neil Mahant and Dr. Vinod Metta. A total of 108 scientific abstracts were presented in the conference in platform sessions, and Award paper sessions.



Valedictory session of MDSICON 2020, with office-bearers of the Society and the Organizing Committee



Sri. Arif Mohammed Khan, Hon'ble Governor of Kerala State, inaugurating MDSICON 2020, the 5th Annual Conference of Movement Disorders Society of India



The Ambassadors, along with other overseas and national faculty participating in the Video Challenge session and Clinical Grand Rounds.

WORLD BRAIN DAY

July 22, 2020



move together to end
parkinson's
disease

World Brain Day 2020 is dedicated to raising awareness for Parkinson's Disease, a neurodegenerative brain disease that affects more than 7 million people of all ages worldwide. Parkinson's can impact movement and almost all aspects of brain function, and COVID-19 is a dramatic reminder that healthcare is a global issue.



Learn more at
wfneurology.org/world-brain-day-2020

