# "Takamatsu" International Symposium for PD & MD in Tokyo

Let's learn the Hot Topics In "Movement Disorders" from international experts !

Date 2018. 2. 23 (Fri) ~ 2. 25 (Sun)

Venue

Tokyo International Exchange Center Tokyo Academic Park, 2-2-1 Aomi, Koto-ku, Tokyo, Japan

Secretariat Department of Neurology, Juntendo University School of Medicine

# Welcome to Takamatsu International Symposium for PD and MD in Tokyo 2018

#### Dear colleagues,

It is our great honor and pleasure to invite all of you to "The 17th Takamatsu international symposium for Parkinson's disease and Movement disorders in Tokyo 2018" which will be held in Odaiba, Tokyo, February 23-25, 2018. This symposium was initiated by Dr. Yamamoto, and this symposium has been operated by Dr. Yamamoto for 16 years and this year, Department of Neurology, Juntendo University will host the symposium. As planned for the time being, we plan to hold it every other year in Tokyo and Takamatsu. We invited many experts from the world, Asian and Oceania, EU, South and North America. It is a very exciting chance to exchange knowledge and expertise, and further a good chance of education for young neurologists. It is a very important step for globalization of movement disorders area for Asian colleagues and us. We do hope that many colleagues, especially young to participate to this symposium. Odaiba is a large artificial island in Tokyo Bay, Japan. It was initially built for defensive purposes in the 1850s, dramatically expanded during the late 20th century as a seaport district, and has developed since the 1990s as a major commercial, residential and leisure area. Odaiba, along with Yokohama Minato Mirai 21, is the only place in the metropolitan area that is accessible to the coast and is not blocked by industry and port areas. Odaiba is well accessible from Haneda Airport and it is in a convenient place. In contrast, although there is a little distance from the city center, it is an opportunity for everyone to participate in acquiring various knowledge. Finally, through this symposium, we hope to warm up old friends and make new friends. This would be really fantastic time for all participants.

#### Sincerely,



Nobutaka Hattori, MD, PhD Chair



Atsushi Takeda, MD, PhD Co-Chair

The Organizing Committee

#### Venue :

Tokyo International Exchange Center Tokyo Academic Park, 2-2-1 Aomi, Koto-ku, Tokyo 135-8630 Japan **会場:** 東京国際交流館内 国際交流会議場・会議室 〒135-8630 東京都江東区青海2-2-1

#### Secretariat:

Department of Neurology, Juntendo University School of Medicine 2-1-1 Hongo, Bunko-ku, Tokyo, 113-8421, Japan TEL:+81-3-3813-3111(ext. 3328)/FAX:+81-3-5800-0547 E-mail:ipdstjimu@gmail.com

#### 事務局:

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MAattai

Atanshi Takeda

#### The Organizing Committee

#### Chair

Nobutaka Hattori, MD, PhD Department of Neurology, Juntendo University School of Medicine, Tokyo

#### Co-Chair

Atsushi Takeda, MD, PhD National Hospital Organization, Sendai Nishitaga Hospital, Sendai

#### Advisor

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Genjiro Hirose, MD, PhD Epilepsy Center, Asanogawa General Hospital, Kanazawa

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Yoshikazu Ugawa, MD, PhD Department of Neurology, Fukushima Medical University, Fukushima

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Yih-Ru Wu, MD Chang-Gung Memorial Hospital, Taipei, Taiwan

#### Program

#### 1st Day: 23 Feb 2018 (Friday)

#### 08:30-08:50

#### **Opening remarks & Welcome speech**

Nobutaka Hattori / Werner Poewe / Eduardo Tolosa

#### 08:50-10:20

#### Symposium I

Evidence-based medicine (EBM) applied to Parkinson's disease treatment Chair: Atsushi Takeda / Yasushi Shimo

- 1. Recent updates in the diagnosis and diagnostic criteria for PD Speaker: Werner Poewe
- 2. Evidence Based Treatment for Non-Motor Symptoms in PD Speaker: Kazushi Takahashi
- 3. Device Aided Therapy, When?, How?, Which? Speaker: Shinsuke Fujioka

#### 10:20-10:35 Break

#### 10:35-12:05

#### Symposium II

How to diagnose Parkinsonism and related Movement disorders Chair: Yoshikazu Ugawa / Hideki Mochizuki

- 1. Eye movements in Parkinsonism and related movement disorders. Speaker: Genjiro Hirose
- 2. Clinical Features and Pathophysiology of Motor Complications in Parkinson's disease

Speaker: Louis Tan

3. Immune- Mediated Movement Disorders Speaker: Yih Ru Wu

#### 12:05-12:25 Break

#### 12:25-13:25

Luncheon Seminar (Sponsored Seminar: Kyowa Hakko Kirin Co., Ltd.) Does PD start in the gut? Chair: Hirohisa Watanabe Speaker: Werner Poewe

13:25-13:45 Break

#### 13:45-14:45

#### Symposium III

- Indispensable issues in Movement Disorders Chair: Hirohisa Watanabe / Tetsuya Maeda
- 1. Emergencies in parkinsonism Speaker: Eduardo Tolosa
- disorders in Parkinson's disease? Speaker: Roongroj Bhidayasiri

#### 14:45-15:00 Break

#### 15:00-16:45

#### VTR session (open)

Chair: Mitsutoshi Yamamoto / Nobutaka Hattori Speaker: Mai Hamaguchi / Jongsam Baik / Akimitsu Suda / Katsuo Kimura / Junya Ebina / Shogo Furuya / Hitomi Onomura

#### 16:45-17:00 Break

#### 17:00-18:00

#### Evening Seminar (Sponsored Seminar: Novartis Pharma K.K.) Medical treatment in advanced Parkinson's Disease Chair: Kenjiro Ono

Speaker: Olivier Rascol

#### 2nd Day: 24 Feb 2018 (Saturday)

#### 08:30-10:00

#### Symposium IV

Biomarkers in Parkinson's Disease and Related Disorders (1): How to diagnosis early Parkinson's Disease Chair: Norihiro Suzuki / Hidefumi Ito 1. Genetic and Environmental factors in Parkinson's Disease

- Speaker: Eng-King Tan
- for diagnosis of parkinsonism. Speaker: Shinji Saiki
- 3. Peripheral tissue markers in PD Speaker: Beomseok Jeon

2. Getting a good night's sleep? The importance of recognising and treating sleep

2. Metabolomics and Parkinson's Disease and Related Disorders; New Technology

#### 10:15-11:45

#### Symposium V

Biomarkers in Parkinson's Disease and Related Disorders (II): Neuroimaging and Neuropathology in Parkinson's Disease and related Disorders

Chair: Seiji Kikuchi / Hidemoto Saiki

- 1. Functional Nueroimaging in Parkinsonism and Dementia Speaker: Makoto Higuchi
- 2. What's New; Cranial MRI in Movement Disorders Speaker: Joaquim Ferreira
- 3. The key pathological and clinical features of Parkinsonism Speaker: Renpei Sengoku

#### 11:45-12:00 Break

#### 12:00-13:00

#### Luncheon Seminar (Sponsored Seminar: AbbVie Inc.)

Medical Management of Fluctuations in Parkinson's Disease Chair: Satoshi Orimo Speaker: Francisco Cardoso

#### 13:15-14:00

#### Education Seminar (Sponsored Seminar: Takeda Pharmaceutical Co., Ltd.)

Non-Motor Symptoms in Parkinson's disease: ethnic difference and the impact on the QOL Chair: Ryosuke Takahashi Speaker: Yoshio Tsuboi

#### 14:00-14:15 Break

#### 14:15-15:45

#### (Parallel session) Small Conference for Young Neurologist

#### Room A International Conference Hall (1F)

Update on Treatment for Motor and Non-Motor Symptoms of Parkinson's Disease

Lecturer: Roongroj Bhidayasiri / Werner Poewe / Eduard Tolosa Case Presenter and Facilitator: Taku Hatano / Keisuke Suzuki

#### Room B (4F)

Update on Treatments for Neuropsychiatric Symptoms of Parkinson's Disease

Lecturer: Olivier Rascol /Heinz Reichmann

Case Presenter and Facilitator: Hidetomo Murakami / Katsuo Kimura

#### Room C (4F)

Update on NeuroImaging in Neurodegenerative Disorders Lecturer: Joaquim Ferreira / Beomseok Jeon Case Presenter and Facilitator: Shigeki Hirano / Hitoshi Shimada

#### Room D (4F)

How to diagnose and treat atypical parkinsonism. Lecturer: Eng King Tan / Louis CS Tan / Yi-Ru Wu Case Presenter and Facilitator: Jun Tashiro / Osamu Kano

#### Room E (4F)

How to diagnose and treat dystonia and hyperkinetic movement disorders.

Lecturer: Christine Klein / Francisco Cardoso Case Presenter and Facilitator: Masashi Hamada / Takashi Osada

#### 15:45-16:00 Break

#### 16:00-17:00

#### Hot Topics (Sponsored Seminar: Sumitomo Dainippon Pharma Co., Ltd.) Monogenic Movement Disorders Chair: Tatsushi Toda Speaker: Christine Klein

#### 17:00-17:20 Break

#### 17:20-18:20

#### Symposium VI

Social cares for Parkinson's Disease Chair: Tadashi Ichikawa / Miho Murata 1. Neurorehabilitation for Parkinson's Disease and related movement disorders

- Speaker: Toshiyuki Fujiwara
- 2. Not-so-big data analysis: What Korean Health Insurance Data tells us. Speaker: Woong-Woo Lee

#### 19:00

#### Reception & Gala dinner (Buffet)

Room: Pegasus B2C at the Hilton Hotel Odaiba Tokyo

#### 3rd Day: 25 Feb 2017 (Sunday)

08:30-9:00	
Japanese Symposium 1 レボドパ併用療法におけるドパミンアゴニストの Chair: 長谷川一子 Kazuko Hasegawa	本ベーリンガーインゲルハイム株式会社 D役割
Speaker: 前田 習也 Tetsuya Maeda	
09:00-9:30 Japanese Symposium 2	エフピー株式会社
運動障害疾患における情報通信技術(ICT)の応 Chair: 永山 寛 Hiroshi Nagayama Speaker: 大山 彦光 Genko Oyama	用
09:30-10:00	
Japanese Symposium 3 パーキンソン病における歩行障害 Chair: 服部 信孝 Nobutaka Hattori Speaker: 大熊 泰之 Yasuyuki Okuma	大塚製薬株式会社
10:00-10:30	
Japanese Symposium 4 Neuroradiological diagnosis for Parkinson's disorders by nuclear medicine Chair: 下畑 享良 Takayoshi Shimohata Speaker: 高橋 牧郎 Makio Takahashi	日本メジフィジックス株式会社 disease and the related
10:30-11:00	
Japanese Symposium 5 エビデンスに基づいたパーキンソン病治療 Chair: 宇川 義一 Yoshikazu Ugawa Speaker: 武田 篤 Atsushi Takeda	グラクソ・スミスクライン株式会社
11:00-11:30	
Closing remarks Nobutaka Hattori	

#### Information for Participants

#### **Tokyo International Exchange Center Meeting Facilities**

Tokyo International Exchange Center (TIEC), Plaza Heisei, have International Conference Hall, Media Hall, and 5 conference rooms of varying sizes. As a rule, use of the entrance hall, foyers, and other common areas is limited to guest reception and related usage only. The user wishing to use common areas for coffee breaks or other nonstandard purposes need to consult with TIEC.

- electrical system under the floor of the International Conference Hall.
- Smoking is permitted only in the designated smoking areas.

#### Reception & Gala Dinner (Buffet)

Date and Time : Feb. 24, 2018 19:00-21:00 Place : Room Pegasus, B2 C, Hilton Tokyo Odaiba (refer to Access Map on page 12) Participation fee : JPY 15,000 -

- Please avoid spilling a drink. There is a possibility that damage to the

#### Access, Floor Map







#### 1F 国際交流会議場(Room A) International Conference Hall





1st Day 23 Feb 2018(Friday)

#### Symposium I Evidence-based medicine (EBM) applied to Parkinson's disease treatment

#### Chair:

Atsushi Takeda, MD, PhD National Hospital Organization, Sendai Nishitaga Hospital Yasushi Shimo, MD, PhD Department of Neurology, Juntendo University

#### 1. Recent updates in the diagnosis and diagnostic criteria for PD

#### Speaker:

Werner Poewe, MD, PhD Department of Neurology Medical University Innsbruck Anichstraße 35, A-6020 Innsbruck, Austria



#### Abstract:

The clinical diagnosis of Parkinson's Disease can be straight forward in subjects with full expression of the classical clinical features. Nevertheless, there is considerable overlap of clinical signs with other conditions, like MSA, PSP or secondary forms of parkinsonism and 20 % or more of patients are initially misclassified. Recently, an MDS Task Force has proposed revised clinical diagnostic criteria for PD and preliminary results of a validation study suggest superior specificity and predictive value for a gold standard expert diagnosis of PD over previous sets of criteria. Nevertheless, it remains unlikely that clinical criteria in themselves will be able to provide optimum diagnostic accuracy and current efforts focus on the performance of diagnostic biomarkers. These include a variety of imaging modalities, molecular and genetic markers, as well as tissue biopsies. The latter focus on detection of pathological alpha synuclein aggregates in components of the peripheral autonomic nervous system. Some of these markers might also be useful to detect the early stages of disease in at-risk populations - a crucial need when it comes to the development of disease-modifying therapies. Preliminary studies support that the recently proposed MDS criteria for prodromal PD might be useful in predicting future PD at the population level.

#### **Curriculum Vitae:**

Professor Werner Poewe is Professor of Neurology and Director of the Department of Neurology at Medical University Innsbruck, Austria since 1995.

Professor Poewe's main research interests in the field of movement disorders are focussed on differential and early diagnosis of Parkinson's disease, its natural history and pharmacological treatment. He has been involved in the steering committees of numerous drug trials in different stages of Parkinson's disease for the past 20 years and has authored and co-authored more than 650 original articles and reviews in the field of movement disorders.

Professor Poewe served as President of the Austrian Society of Neurology from 2002-2004 as well as as President of the Austrian Parkinson's Disease Society from 1996-2009. He has been awarded Honorary Membership of the German Society of Neurology as well as the Japanese Society of Neurology and the International Parkinson & Movement Disorder Society. His awards include the Walther-Birkmayer-Prize of the Austrian PD Society, the Dingebauer-Prize of the German Neurological Society as well as the Research Excellence Award of Innsbruck Medical University.

Professor Poewe served as President of the International Movement Disorder Society from 2000-2002. Professor Poewe took over as chair of the MDS European Section from 2011-2013 and is currently active as member of the Managing Board of the Movement Disorder Scientific Panel of the European Academy of Neurology.

He has served on the Editorial Board of international neurology journals, including Movement Disorders, Journal of Neurology and European Journal of Neurology and is a regular reviewer for major journals, like Lancet Neurology, Brain, Movement Disorders, Neurology and Annals of Neurology.

Symposium I

#### Evidence-based medicine (EBM) applied to Parkinson's disease treatment 2. Evidence Based Treatment for Non-Motor Symptoms in PD

#### Speaker:

Kazushi Takahashi, MD, PhD Department of Neurology, Saitama Medical University

#### Abstract:

Although Parkinson's disease (PD) is generally considered a movement disorder, a majority of PD patients also suffer from non-motor symptoms (NMS). NMS in PD are numerous and include sleep disturbance (insomnia, excessive daytime sleepiness, sudden onset of sleep, REM sleep behavior disorders (RBD), restless legs syndrome), mood disorders (depression, anxiety, apathy) and fatigue, neuro-psychiatric disturbance (hallucination, delirium, delusion, impulse control disorders, dopamine dysregulation syndrome, cognitive dysfunction, dementia), autonomic dysfunction (orthostatic hypotension, constipation, urinary dysfunction, sexual dysfunction, hyperhydrosis) and sensory disturbance (pain, olfactory disturbance). Despite the importance of NMS is now widely acknowledged, we are still hampered by a lack of well-conducted research into effective treatments. Many symptoms are managed by strategies that are timehonored, but have never been scientifically assessed. The new Japanese "Practical Guideline for PD 2018 (in press)" updates the previous Japanese "Therapeutic Guideline for PD 2011" and incorporates new data (published from Jan 2009 to Feb 2016) on efficacy, safety, and implications for clinical practice of treatments for NMS of PD. The present available therapeutic approach of major NMS (RBD, dementia, psychosis, depression and autonomic dysfunction) will be outlined, based on "Q & A" in the new Japanese "Guideline 2018" and "NICE Guideline 2017". Latest major evidence, such as systematic review and meta-analysis will be introduced.

#### Curriculum Vitae:

Kazushi Takahashi obtained his MD degree from Keio University School of Medicine in 1987 and received his neurological training at Keio University Hospital in Tokyo. He spent seven years as assistant professor at Department of Neurology, Keio University School of Medicine from 2005 to 2012. He is Professor of Neurology, Saitama Medical University since 2014. He is a present committee member of the Movement Disorder Society of Japan and a member of International Parkinson and Movement Disorder Society.



#### Symposium I Evidence-based medicine(EBM) applied to Parkinson's disease treatment 3. Device Aided Therapy, When?, How?, Which?

#### Speaker:

Shinsuke Fujioka, MD\*, Yoshio Tsuboi, MD, PhD Department of Neurology, Fukuoka University



#### Abstract:

Motor symptoms of patients with Parkinson's disease (PD) can adequately be managed with conventional oral medications during the early stage of the illness. The management with the oral medications becomes challenging in advanced stage of the illness because of severe motor complications including wearing off, dyskinesia, and sudden on-off. The advanced PD patients can also present with other problems such as cognitive impairment, drug induced psychiatric symptoms, and swallowing problems during the disease course which make it more difficult to treat the patients with only oral medications. So far, three device-aided therapies have been available as additional therapeutic options for advanced PD patients with severe motor complications: deep brain stimulation; continuous jejunal infusion of levodopa-carbidopa intestinal gel; bolus or continuous subcutaneous infusion of apomorphine. The decision-making process regarding the selection of the therapies is complex and is influenced by multiple factors including patient ages, patients' preference and lifestyle, cognitive and psychiatric status, domestic environment, and availability of the therapies. It is also noted that patients need to be assessed by multidisciplinary treatment team including neurologists, neurosurgeons, nurses, psychiatrist, physical therapists, occupational therapists, speech therapists, neuropsychologists, and social workers before making a decision. Increasing number of papers have reported the advantage and disadvantage of each therapy; however, no definite guidelines for which therapy should be chosen for individual patients have been available. Thus, head-to-head randomized clinical trials are definitely warranted to overcome the problem.

#### Curriculum Vitae:

Dr. Fujioka was born and raised in Hiroshima, Japan. He obtained his medical degree (2003) and completed his residency (2003-2005) at Fukuoka University in Fukuoka, Japan. He then pursued a fellowship in clinical and pathological research on movement disorders and frontotemporal dementia at the Mayo Clinic in Florida (2010-2014). Since 2014, he has worked as an Assistant Professor of Neurology at Fukuoka University. Dr. Fujioka is currently a clinical neurologist in the Movement Disorders Unit of the Neurology Division at Fukuoka University. He has published many peer-reviewed articles in international journals and is also the author of several book chapters. His research interests are in Parkinson's disease (particularly non-motor symptoms such as dysphagia and osteoporosis as well as device aided therapy), atypical parkinsonism, including progressive supranuclear palsy, multiple system atrophy, and corticobasal degeneration.

#### Symposium II How to diagnose Parkinsonism and related Movement disorders

#### Chair:

Yoshikazu Ugawa, MD, PhD Department of Neurology, Fukushima Medical University Hideki Mochizuki, MD, PhD Department of Neurology, Osaka University Graduate School of Medicine

#### 1. Eye movements in Parkinsonism and related movement disorders.

#### Speaker:

Genjiro Hirose, MD, PhD, FANA Neurological Center, Asanogawa General Hospital, Kanazawa City, Japan

#### Abstract:

The careful clinical examination of eye movements in patients with Parkinsonism and related movement disorders can be a valuable tool to the neurological assessment and in some cases serves to make a diagnosis (e.g. PSP). For diagnostic purposes, the laboratory oculomotor assessment adds little to the well performed clinical eye movement examination. As a general rule, slow saccades and excessive small amplitude square wave jerks (SWJ) are indicative of brainstem involvement, nystagmus is evidence of brainstem and cerebellar dysfunction, increased latency of saccade is consistent with cortical and associative cognitive disorders, and errors on antisaccade are consistent with frontal dementia.

Will review the eye movement abnormalities in patients with the Parkinsonian disorders and show some cases with their slides and video.

#### Curriculum Vitae:

#### CURRENT STATUS:

- Full-time Consultant, Director of Neurological Center Director of Epilepsy Center, Asanogawa General Hospital, Kanazawa City, Japan
- MEDICAL SCHOOL:

Kyoto Prefectural University of Medicine (1959-1966)

- INTERNSHIP:
- US Air Force Hospital, Tachikawa, Japan (1966-1967)

#### **RESIDENCY:**

Medical resident at the US Air Force Hospital (1967-1968) Neurology resident at the University of Virginia (1968-1971)

#### FELLOWSHIP:

Clinical Fellow, Department of Neurology Harvard Medical School Neurophysiology Section, Children's Hospital Medical Center, Boston (1971-1973)

#### ACADEMIC POSITION:

Assistant professor, Department of Medicine Kanazawa Medical University (1973-1974) Associate Professor, Department of Medicine Chief Neurologist of Division of Neurology Kanazawa Medical University (1974-1985) Professor & Chairman, Department of Neurology Kanazawa Medical University (1985-2005) Emeritus Professor, Kanazawa Medical University (2005) Full-time Consultant, Neurological Center, Asanogawa General Hospital (2005-2018)



#### Symposium II How to diagnose Parkinsonism and related Movement disorders

#### 2. Clinical Features and Pathophysiology of Motor Complications in Parkinson's disease

#### Speaker:

Louis Tan, MBBS, MRCP, FAMS, FRCP National Neuroscience Institute, Singapore



#### Abstract:

Levodopa is the most potent medication available to treat the Parkinson's disease. There are however, both short term and long term complications associated with its use. The long term complications of levodopa include motor fluctuations and dyskinesias (abnormal involuntary movements). Motor fluctuations most commonly manifest as predictable wearing-offs; unpredictable sudden offs; or no-on, delayed or partial-ons. Levodopa-induced dyskinesias may manifest as peak-dose dyskinesias in the form of chorea, dystonia, myoclonus, or respiratory dyskinesia. End of dose or lowdose dyskinesia often manifest as off-period dystonia or diphasic dyskinesia. Nonmotor fluctuations in the form of neuropsychiatric, autonomic, or sensory symptoms may also occur.

The pathophysiology of motor fluctuations and levodopa-induced dyskinesias are complex. The underlying pathophysiological mechanism is related to a combination of severe nigro-striatal deficit; higher doses of levodopa used; and the effect of discontinuous, pulsatile levodopa administration. Various pharmacokinetic and pharmacodynamics factors underlying motor complications will be discussed.

#### **Curriculum Vitae:**

Dr Louis Tan Chew Seng MBBS, MRCP(UK), FAMS(Neurology), FRCP(Edin) Senior Consultant, Department of Neurology; Deputy Director, Research National Neuroscience Institute

Co-Director Parkinson's Disease and Movement Disorders Centre USA National Parkinson Foundation International Centre of Excellence

Dr Louis Tan is a Senior Consultant Neurologist and Deputy Director, Research at the National Neuroscience Institute, Singapore. He is also Co-Director of its Parkinson's Disease and Movement Disorders Centre (TTSH campus) and an Adjunct Associate Professor of Duke-NUS Graduate Medical School, Singapore.

He is Treasurer-elect of the International Parkinson and Movement Disorder Society and previously served as Chair of the Education committee and Asian-Oceanian Section of the Society.

Upon graduating from the National University of Singapore and completing his neurology training at Tan Tock Seng Hospital, he underwent a movement disorders fellowship at the Parkinson's Institute in Sunnyvale, California.

His areas of specialty and research interests are Parkinson's disease and movement disorders. He is also interested in the interested in the epidemiology, clinical studies and clinical trials in Parkinson's disease and other movement disorders.

#### Symposium II How to diagnose Parkinsonism and related Movement disorders 3. Immune- Mediated Movement Disorders

#### Speaker:

Yih Ru Wu, MD Chang Gung Memorial Hospital and Chang Gung University, Taipei, Taiwan

#### Abstract:

There are growing list of movement disorders previously considered idiopathic or degenerative, which are now recognized as immune-mediated. Some are paraneoplastic, such as anti-CRMP5-associated chorea, anti-Ma2 hypokinesia/ rigidity, and anti-Yo cerebellar ataxia/tremor. Another category of disorders, either paraneoplastic or nonparaneoplastic, are associated with antibodies against cell-surface or synaptic proteins. These disorders include anti-N-methyl-D-aspartate receptor (anti-NMDAR) encephalitis, the spectrum of stiff-person syndrome (glutamic acid decarboxylase, amphiphysin, GABA (A) -receptor-associated protein, or glycine receptor antibodies), neuromyotonia (Caspr2 antibodies), and opsoclonus--myoclonus-ataxia (unknown antigens). Futhermore, the field of anitibody-associated movement disorders keeps expanding with the discovery of antibodies against leucine rich glioma inactivated protein 1 (LGI1), dipeptidyl-peptidase-like protein-6, ARHGAP26- or Na/K ATPase, and alpha 3 subunit (ATP1A3). Other nonparaneoplastic movement disorders including Sydenham's chorea, or chorea related to systemic lupus erythematosus and antiphospholipid syndrome are known to be triggered by molecular mimicry or unknown mechanisms.

In this talk, I will discuss the most relevant advances in immune-mediated movement disorders, with emphasis on the clinical--immunological associations and treatment.

#### Curriculum Vitae:

Dr Wu was trained in the department of Neurology at the Chang Gung Memorial Hospital, LinKou Medical Center from 1990-1994 and became an attending physician since 1994. She then undertook one-year research fellowship training in Movement Disorders Center at Toronto Western Hospital from 1998-1999. Her research interests include genetics of Parkinson's diseases and other movement disorders as well as non-motor symptoms and clinical researches of Parkinson's disease. She has published more than 150 related peer-reviewed, Science Citation Index papers and has been a reviewer of more than 30 SCI Journals. Currently she is the Section Editor of Movement Disorder in BMC Neurology and is on the editorial board of Parkinsonism and Related Disorders.

Dr. Wu was the present of Taiwan Movement Disorder Society from 2015 to 2017 and she has served on AOS-MDS education committee from 2011 to 2015. She is also an executive committee member of AOS-MDS and a web editor committee member of MDS since 2015. Currently, she is the professor of the Chang Gung Memorial Hospital and Chang Gung University.



#### Luncheon Seminar

(Kyowa Hakko Kirin Co., Ltd.)

#### Chair:

Hirohisa Watanabe, MD, PhD Brain and Mind Research Center, Nagoya University Graduate School of Medicine

#### Does Parkinson's Disease start in the gut?

#### Speaker:

Heinz Reichmann, MD, PhD Department of Neurology, Technische Universitaet Dresden, Germany



#### Abstract:

Parkinson's disease (PD) follows a rather uniform pattern of progression. There are roughly 10% of all patients in Europe suffering from a genetically defined PD while the others have a so-called idiopathic Parkinson syndrome. These patients present with preclinical signs such as hyposmia, which is present in about 80-90%, REM sleep behavior disorder, constipation and depression. If there are more than one of these preclinical signs present in a person his risk to develop PD increases steadily. Only after years with just a preclinical sign patients develop a typical Parkinson syndrome, i.e. a movement disorder consisting of bradykinesia, rigidity, tremor and postural instability.

There is good evidence that Lewy bodies with  $\alpha$ -synuclein pathology are present in the enteric nervous system before they can be found in the basal ganglia. A possible hypothesis for these findings of Braak and others is that an exogenous toxin or virus may be inhaled and swallowed and then start to cause abnormal  $\alpha$ -synuclein accumulation in the enteric nervous system of the stomach and gut. In line with these neuroanatomical findings is the work by Shannon and others who demonstrated that patients with PD present with Lewy bodies in the colon which was shown by colon biopsies. In addition, this group could gain colon biopsies who presented with PD and had coloscopy years before they developed motor symptoms. In these biopsies again Lewy bodies with abnormal  $\alpha$ -synuclein could be found. In addition, our group could demonstrate that the application of rotenone via a tubing system to the gut could create in mice Lewy bodies and typical PD pathology via the vagal nerve to the brain. In summary there is ample evidence from post-mortem studies, from animal models and from clinical observations that PD begins in the gut.

#### Curriculum Vitae:

Heinz Reichmann MD PhD graduated from the University of Freiburg, Germany in 1979. He spent the following four years as a research fellow at the Institute for Biochemistry, University of Konstanz, Germany and the Institute of Neurology, Columbia University, USA. This was paid for by honorary grants for excellency to Dr. Reichmann. He returned to Germany where he held a number of positions at the University of Würzburg, becoming Professor of Neurology in 1990. In 1996, he was appointed Chairmann of the Department of Neurology at the University of Dresden, where he is now also Dean of the Medical Faculty.

Heinz Reichmann is a member of numerous scientific societies including the German Neurological Society, the European Neurological Society, the American Academy of Neurology, the Royal Society of Medicine and the Movement Disorder Society. In addition, Dr Reichmann serves on the editorial boards for a number of prestigious neurology journals. His major research interests are energy metabolism, neuroprotection, premotor symptoms in Parkinson's disease, etiopathogenesis and treatment in PD. Prof. Reichmann is a Fellow of the Royal College of Physicians and of the American Academy of Neurology. He serves on many Neurological Boards and was President of the German Parkinson Society and the German Muscle Society. In 2009 Professor Reichmann started his 2-year term as President of the German Neurological Society. He is Past-President of the European Neurological Society and has helped to initiate the new European Academy of Neurology, starting from 2014.

#### Symposium III Indispensable issues in Movement Disorders

#### Chair:

Hirohisa Watanabe, MD, PhD Brain and Mind Research Center, Nagoya University Graduate School of Medicine Tetsuya Maeda, MD, PhD Department of Neurology, Iwate Medical University

#### 1. Emergencies in parkinsonism

#### Speaker:

Eduardo Tolosa, MD, PhD Neurology Service, Hospital Clinic de Barcelona, IDIBAPS, CIBERNED, Barcelona, Spain

#### Abstract:

Although Parkinson's disease is characterized by slow progression of disability over years, a growing number of patients can experience life-threating complications. Identifying and managing this situations is challenging, even for the specialist. Some complication, e.g. "sleep attacks" or prominent dysphagia, even though not "emergencies" in the sense of life threatening, are also critical and if not addressed properly can lead to serious problems. My presentation will summarize the precipitant factors, clinical presentation and optimal treatment of the major emergencies in Parkinson's disease, which include : severe OFF's and dyskinesias, Parkinsonism–hyperpyrexia and dyskinesia–hyperpyrexia syndrome, acute psychosis and pseudo intestinal obstruction. Emergencies related to advanced therapies such as levodopa-carbidopa intestinal gel infusion, subcutaneous apomorphine infusions and deep brain stimulation will also be reviewed.

#### Curriculum Vitae:

Eduardo Tolosa obtained his MD degree from the University of Barcelona and received his neurological training at the University of Minnesota in Minneapolis.. He is a founding member and past President of the Movement Disorder Society. He is also past President of the Spanish and of the European Neurological Society. He is the recipient of the American Academy of Neurology 2014 Movement Disorders Research Award. Prof. Tolosa is currently Vice Director of Research of the Centro de Investigacion en Red de Enfermedades Neurodegenerativas at the Instituto de Salud Carlos III in Spain and Emeritus Professor at the University of Barcelona Professor Tolosa's research interests are in movement disorders. He was involved in pioneering studies defining the mechanisms underlying levodopa-related motor fluctuations and the role of DAT SPECT in the diagnosis of Parkinson disease and his team has been among the first in Europe to evaluate the

efficacy of novel therapeutic strategies for Parkinson's disease, such as subthalamic nucleus stimulation, subcutaneous dopamine agonist infusions and intraduodenal infusions of levodopa. Areas of current research include assessment of non-motor symptoms in asymptomatic carriers of Parkinson-associated genetic mutations and the study of diagnostic biomarkers in premotor Parkinson disease.



#### Symposium III Indispensable issues in Movement Disorders

# 2. Getting a good night's sleep? The importance of recognising and treating sleep disorders in Parkinson's disease?

#### Speaker:

Roongroj Bhidayasiri, MD, FRCP, FRCPI Neurology, Chulalongkorn Comprehensive Movement Disorders Center, Chulalongkorn University Hospital, Bangkok, Thailand



#### Abstract:

Despite a high prevalence of sleep disturbances amongst Parkinson's disease (PD) patients, these problems are frequently overlooked and many physicians still consider night-time symptoms as secondary problems. One the main reasons is the difficulty for patients and carers to recall their night-time symptoms during consultations. Some PD patients may not even aware that their night-time symptoms occur as a continuum of day-time manifestations. Although specific scales (e.g. Modified Parkinson's Sleep Scale; PDSS-2) have been evaluated and recommended by the Movement Disorder Society Task Force for rating overall sleep problems, they are not designed to capture specific night-time symptoms and do not have the capability for monitoring. With the advances of circuit technology, wearable sensors have been developed to monitor movement patterns during the night in PD patients. The advantages of these sensors include their capability to capture real-time data; thus, providing the opportunities for monitoring various night-time symptoms in real-life situations. It is likely that continuous nocturnal monitoring will open many new applications for physicians and researchers to understand the spectrum and the fluctuations of night-time symptoms, delineate the subtle differences, and identify new objective outcomes that can be applied for therapeutic armamentarium of sleep disorders amongst PD patients.

How can we apply the above information in the treatment of night-time symptoms in PD patients? In order to deliver successful treatment, we need to first involve patient's carers to help identify the most troublesome night-time symptom for treatment. Analyse individual symptom but involve multidisciplinary team early is the key for optimal night-time management. If the main problem is related to dopamine responsive night-time symptoms, good strategy to replace nocturnal dopamine is warranted with the aim to balance motor benefits and the risk of adverse events, such as psychosis. For dopamine non-responsive symptoms, individualised approach is recommended to target disabling symptom if pharmacologic interventions are available, but not to forget that a practice of good sleep hygiene is equally important. For example, bedroom modifications can provide sleep-friendly environment; thus, potentially improving sleep-related breathing disorders and lessen the risk of night-time injuries. In this lecture, examples of pertinent PD-related sleep disorders will be highlighted with proposed assessment methods, evidence-based therapeutic approach and roles for adaptation.

#### Curriculum Vitae:

Graduated in medicine at Chulalongkorn University, Thailand in 1994. Received the membership of the Royal College of Physicians of London and Ireland in 1998 and certified by the American Board of Psychiatry and Neurology in 2005. Awarded the fellowship of the Royal College of Physicians of London in 2008 and the Royal College of Physicians of Ireland in 2010. In addition to his role as a clinician and fellowship program director, Dr. Bhidayasiri's research interest is in objective monitoring and assisted devices in Parkinson's disease. He co-develops devices for tremor and nocturnal monitoring as well as tremor's glove for tremor suppression. His development on adjustable laser-guided walking stick has been adopted nationwide by the Ministry of Social Development and Human Security of Thailand for patients with freezing of gait. Dr. Bhidayasiri has published over 140 articles in peer-reviewed journals in the field of movement disorders and 5 international textbooks in neurology. He serves in the editorial board of Parkinsonism and Related Disorders journal and Journal of the Neurological Sciences as well as a writing committee panel member of the American Academy of Neurology on the practice parameters of tardive syndromes. Dr. Bhidayasiri is currently a chair-elect of the Asian Oceanic section of the International Movement Disorder Society.

#### VTR session (open)

#### Chair:

Mitsutoshi Yamamoto, MD, PhD Takamatsu Neurology Clinic, Takamatsu Nobutaka Hattori, MD, PhD Department of Neurology, Juntendo University School of Medicine, Tokyo

#### Speaker:

Mai Hamaguchi, MD Dokkyo Medical University, Tochigi, Japan

#### Title : A 77-year-old man presenting with involuntary movement of the left leg.

Jongsam Baik, MD, PhD Department of Neurology, Sanggye Paik Hospital, College of Medicine, Inje University, Seoul, Korea

Title : 58-year man with an unsteady posture.

Akimitsu Suda, MD Juntando University, Tokyo, Japan

Title : A 77-year-old female with gait disturbance.

Katsuo Kimura, MD, PhD Yokohama City University Medical Center, Kanagawa, Japan Title : A 67-year-old man presenting with choreic involuntary movement.

Junya Ebina, MD Toho University, Tokyo, Japan

Title: 48-year-old female presenting with involuntary movement in lower extremities

Shogo Furuya Juntendo Shizuoka Hospital, Shizuoka, Japan

Title: 73-year-old man with involuntary movements of the left arm and leg.

Hitomi Onomura, MD TOYOTA Memorial Hospital, Aichi, Japan Title : A 78-year-old male with gait disturbance.

#### **Evening Seminar** Medical treatment in advanced Parkinson's Disease

#### Chair:

Kenjiro Ono, MD, PhD Department of Neurology, Showa University School of Medicine

#### Speaker:

Olivier Rascol, MD, PhD Department of Neurology and Clinical Pharmacology Toulouse University Hospital, Toulouse, France

#### Abstract:

Later stage Parkinson's disease (PD), often referred to as "advanced" disease, is characterized by motor complications (L-DOPA-induced fluctuations and dyskinesia), as well as by the emergence of L-DOPA-resistant motor (falls) and non-motor (mood, cognitive and behavioral disorders, cognitive and autonomic dysfunction, and sleep disorders...) symptoms. Significant improvement have been achieved during the last 3 decades to treat such problems, but an optimal management of PD patients at this stage of the disease often remains complex, challenging and sometimes disappointing Briefly, following the end of the L-DOPA "honeymoon", OFF problems can be initially successfully managed by L-DOPA optimization regimen (dose and timing adjustments), combined with dopaminergic (oral or transdermal dopamine agonists, catechol-Omethyltransferase (COMT) inhibitors and monoamine oxidase B (MAO-B) inhibitors) and non-dopaminergic (A2A and glutamate antagonists) agents. This strategy generally reduces the duration of time spent OFF by few hours per day, which is usually sufficient for few years. However, as PD continues to worsen, the severity and duration of OFF episodes increases. The efficacy of such conventional approaches then wanes and can be limited by the emergence of dyskinesia. At this stage, more invasive and expensive devise-based therapies (deep-brain stimulation, subcutaneous apomorphine or intrajejunal L-DOPA) are considered as second-line strategies to manage such drugrefractory OFF problems. Unfortunately comparative studies that could help choosing between these invasive approaches are still lacking. Treatment strategies to overcome dyskinesia include adjustment of timing, type and amount of dopaminergic medications, treatment with NMDA antagonists like amantadine and, in resistant cases, second-line devise-based approaches. In many patients in the late stage of PD, non-motor symptoms, especially dementia, affect quality of life more than motor PD symptoms. Their management is still in its infancy, mostly based on empirical and unsuccessful treatments. This remains one of the main unmet needs of the current management of PD. Similarly, there is no efficacious medication to treat L-DOPA-resistant balance problems and falls, while the benefit of physical- and/or physio-therapy remains limited and poorly known. Many advanced Parkinson's disease patients will likely benefit from multi and interdisciplinary PD teams with multiple professionals collaborating to develop a collective and tailored strategy for an individual patient. Ongoing clinical and preclinical research has led to the discovery of promising new therapeutic targets that offer new hopes for a better management of advanced PD. Newer approaches modulating non-dopaminergic systems including for example adenosine A2A antagonists, glutamatergic antagonists, adrenergic receptor antagonists and serotonergic agents have been developed, with variable results. We also home that recent developments in L-DOPA or dopamine agonist delivery formulations (including for example subcutaneous infusion or inhaled formulations of a L-DOPA/carbidopa, new extended-release L-DOPA and oral pro-L-DOPA form, sublingual apomorphine) will improve in the future our therapeutic armamentarium to better manage advanced PD.



#### **Curriculum Vitae:**

Doctor Olivier Rascol is Professor of Clinical Pharmacology at the Toulouse University Hospital since 1993. He obtained his MD in Neurology (Toulouse, 1985) and his PhD in Neurosciences (Paris, 1992). Dr Rascol is running the Toulouse Clinical Investigation Centre since 1994 and the Toulouse European Space Clinic since 1998. He is also running a Research Group on Motricity in the Research Unit INSERM U1436 and is the coordinator of the French Reference Center for Multiple System Atrophy (Atypical Parkinsonism). Dr Rascol is the chair of the national network of the 56 French Clinical Investigation Centers since 2008 and the chair of the NS-Park Neurosciences Network of the French CIC since 2010. From 2011, Dr Rascol is now coordinating the National French Clinical Research Infrastructure Network F-CRIN.

As a neuropharmacologist, Dr Rascol's main fields of interest are Parkinson's disease and movement disorders, drug development for Parkinson's disease and functional neuroimaging. Dr Rascol has been actively involved in the development of several marketed antiparkinsonian medications (ropinirole, rasagiline). He is currently running several research programs for disease progression and symptomatic management of PD (motor signs, dyskinesias and on-off problems, non-motor signs such as pain and sleep problems) with new dopaminergic (dopamine agonists, dopamine reuptake inhibitors, MAO-B inhibitors...) and non-dopaminergic (serotonergic, glutamatergic, adenosine, alpha-adrenergic...) drugs in collaboration with several academic and industry research centres in the US and in Europe. He is acting in this field as an external advisor for French and European scientific organisations, patients' associations, drug agencies and international pharmaceutical companies. He is at the board of the Evidence-Based Medicine MDS Task Force in charge of the continuous assessment of all antiparkinsonian treatments. He is involved in the process of editing French (HAS) and European (EFNS / MDS-ES) guidelines for the treatment of Parkinson's disease. As the chair of the French CIC Network and of the National F-CRIN Clinical Research infrastructure, Dr Rascol has been deeply involved within the last few years in the management and organisation of clinical research in France.

Dr Rascol is member of several French and American neurological and pharmacological societies. He was the Secretary of the international Movement Disorders Society (2006-2009) and is a member of the WFN Research Committee on Parkinsonism and Related Disorders. Dr Rascol is chair of the European Section of the Movement Disorders Society (2013-15). Dr Rascol is working or has worked as associate-editor for the Journal Fundamental and Clinical Pharmacology and is or has been a member of the editorial board of Lancet Neurology, Neurology, the European Journal of Neurology, the Evidence Medicine.

Dr Rascol has published more than 400 articles in International Scientific journals (New England Journal of Medicine, Lancet, Lancet neurology, Annals of Neurology, Neurology, Archives of Neurology, Brain, Movement Disorders...). His H factor is 50. He has also been invited to give more than 250 lectures in various European, North and South American and Asian universities or national and international meetings.

## Abstracts

2nd Day 24 Feb 2018(Saturday)

#### Symposium IV Biomarkers in Parkinson's Disease and Related Disorders(I): How to diagnosis early Parkinson's Disease

#### Chair:

Norihiro Suzuki, MD, PhD Department of Neurology, Keio University Hospital Hidefumi Ito, MD, PhD Department of Neuroloty, Wakayama Medical University

#### 1. Genetic and Environmental factors in Parkinson's Disease

#### Speaker:

Eng-King Tan, MD, MRCP, FRCP Singapore General Hospital, National Neuroscience Institute, Singapore



#### Abstract:

The relative role of genes and environmental factors in Parkinson's disease (PD) has been debated. To date, more than 20 gene loci and numerous disease-causing genes have been linked with PD or parkinsonism. Studies of proteins encoded by disease causing genes have uncovered pathogenic pathways and provided new insights into mechanisms of neurodegeneration in familial and sporadic PD. Potential screening for genetic PD-related risk factors, risk stratification and the role of genetic testing are becoming important issues to address in a clinical setting. This is especially so with the widespread availability of high throughput genomic screening to the public. There is also increasing evidence that environmental and lifestyle factors can modulate risk of PD. Some of these include chronic pesticide exposure, caffeine intake and cigarette smoking. The role of gene and environmental interactions has received limited attention. Studies in prospective large population cohorts can yield important information that could provide the basis for future biological validation that may ultimately lead to an integrated behavioural and genetic program that can lead to better informed patient care.

#### Symposium IV Biomarkers in Parkinson's Disease and Related Disorders (1): How to diagnosis early Parkinson's Disease

#### 2. Metabolomics and Parkinson's Disease and Related Disorders; New Technology for diagnosis of parkinsonism.

#### Speaker:

Shinji Saiki, MD, PhD Department of Neurology, Juntendo University Graduate School of Medicine

#### Abstract:

Several lines of evidences illuminate on the critical signature in body fluids that reflect the pathophysiology of Parkinson's disease (PD), but dominant therapeutic strategies for PD, which is dopaminergic medications, result in temporal reduction of the disease severity with no cure. Thus, it is highly prioritized to establish the novel disease-modifying therapy to attenuate or halt the underling pathologic processes because 30-50 % neurons of the substantia nigra pars compact have been already lost when apparent motor symptoms are detected. First of all, what we need is to establish easily obtained, disease-specific, surrogating biomarkers reflecting PD pathogenesis. Thus, we have been performing metabolome analysis in serum/plasma of PD patients in association with validations of the related genes, especially highlighting presymptomatic or early diagnostic profile. According to this concept, 5 independent cohorts studies are ongoing in our lab including patients with PD, progressive supranuclear palsy, multiple system atrophy and Alzheimer's disease.

In this presentation, I would like to summarize the latest achievements of PDassociated metabolic biomarkers discovered in bio specimen. Next, I would like to show two novel metabolic findings, skeletal muscle beta-oxidation changes and caffeine metabolic changes detected in early stage of PD (Scientific Reports 72:7328, 2017; Neurology 2018). Adding on that, we will mention some preliminary results.

#### **Curriculum Vitae:**

Dr EK Tan is a senior consultant neurologist and clinician scientist at the National Neuroscience Institute (NNI), a Professor at Duke-NUS medical school and an honorary Professor at Lee Kong Chian school of medicine (a joint initiative with Imperial College London). Dr Tan is the director of research at NNI.

Dr Tan is an editor of European Journal of Neurology, Parkinsonism Related Disorders, and Parkinson's disease Journal, among others. Dr Tan has served in various committees in the International Movement Disorders Society (MDS) and a founding member of the MDS Asian Oceanic Section. He is also member of American Neurological Association. He has been involved in numerous educational activities in the Asian Oceanic region and has received various national and international research awards.

Dr Tan's primary research interests are in clinical and functional genomics and experimental therapeutics in Movement Disorders.

#### Curriculum Vitae:

Current Position :

Associate Professor (Department of Neurology, Juntendo University Graduate School of Medicine) Education and Degrees :

Luucati		Jeglees
2011	PhD	Juntendo University Graduate Scho
1999	MD	Faculty of Medicine, Kyoto Prefect
		Research and Professional experier
2011.4		Associate Professor, Department of
2008.4		Instructor, Department of Neurolo
2006.8-	2008.3	Research Associate, Department
		Research, University of Cambridge
2001-20	05.6	Instructor, Department of Neurolo
1999-20	001	Resident in Internal Medicine, Kan

Honours and Awards : Eli Lilly Pergolide Fellowship (2005-2006), Fellowship from British Council Japan Association (2005)



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f Neurology, Juntendo University School of Medicine gy, Juntendo University School of Medicine of Medical Genetics, Cambridge Institute for Medical

gy, Kanazawa Medical University, Ishikawa, Japan azawa Medical University Hospital

#### Symposium IV Biomarkers in Parkinson's Disease and Related Disorders(I): How to diagnosis early Parkinson's Disease

#### 3. Peripheral tissue markers in PD

#### Speaker:

Beomseok Jeon, MD, PhD Seoul National University Hospital, Seoul, South Korea



#### Abstract:

There has been a growing interest in detecting alpha-synuclein (AS) accumulation in peripheral tissues using immunohistochemistry (IHC) as a possible in vivo pathological and prodromal biomarker of Parkinson's disease (PD). Among such peripheral tissues, Gastrointestinal (GI) tract including submandibular gland and skin biopsies have shown considerable promise as potential biomarkers. According to Braak's hypothesis, AS aggregation is first observed in the enteric nervous system (ENS), following which aggregates travel to the dorsal motor nucleus of the vagus nerve- one of the earliest sites in the central nervous system affected by Lewy pathology in patients with PD. Autopsy studies have revealed that AS accumulation in the GI tract is more frequent in patients with PD than in healthy controls. Furthermore, AS pathology has also been identified in tissue biopsied from the stomach or colon of patients with PD, even at the prodromal stage. However, a substantial number of studies argue that positive AS IHC staining in GI tissues does not constitute a biomarker of PD because AS accumulation in the GI tract has been observed in neurologically healthy individuals. In this presentation, detecting AS accumulation in peripheral tissues using IHC as a possible in vivo pathological and prodromal biomarker of PD will be critically reviewed.

#### Symposium V Biomarkers in Parkinson's Disease and Related Disorders(II): Neuroimaging and Neuropathology in Parkinson's Disease and related Disorders

#### Chair:

Seiji Kikuchi, MD, PhD National Hospital Organization Hokkaido Medical Center Hidemoto Saiki, MD, PhD Department of Neurology, Kitano Hospital, The Tazuke Kofukai Medical Research Institute

#### 1. Functional Nueroimaging in Parkinsonism and Dementia

#### Speaker:

Makoto Higuchi, MD, PhD National Institute of Radiological Sciences, National Institutes for Quantum and Radiological Science and Technology, Chiba, Japan

#### Abstract:

Numerous research evidences have supported mechanistic links between depositions of alpha-synuclein and tau and deteriorations of neuronal functions in movement disorders. We have demonstrated that positron emission tomography (PET) ligands dubbed PBB3 and PM-PBB3 are capable of capturing tau lesions in diverse tauopathies with progressive supranuclear palsy and amyotrophic lateral sclerosis phenotypes. Derivatives of PBB3 were also proven to illuminate alpha-synuclein deposits in autopsy brain samples. As these compounds are also self-fluorescent, bimodal optical and PET imaging assays of alpha-synuclein-inoculated mice and marmosets are underway to track spreading of alpha-synuclein aggregations. Dysregulated neurotransmissions triggered by misfolded proteins can be assessed at an incipient stage by monitoring altered binding of PET ligainds to dopamine and glutamate receptors during stimulation of brain activities. Finally, our latest nonclinical findings indicate that the use of machine learning classifiers for analyzing optical imaging and functional MRI data allows detection of disrupted functional networks in proteinopathies.

#### **Curriculum Vitae:**

Professor Beomseok Jeon is Medical Director of the Movement Disorder Center at Seoul National University Hospital. He is the past President of the Korean Movement Disorder Society, and served as the International Delegate of the Korean Neurological Association. He also served as the Director of Office of the Medical Policy and Communication, Seoul National University. Currently, he is President of the Asia-Oceanian Association of Neurology, and Chair of MDS-AOS.

#### Curriculum Vitae:

Makoto Higuchi a geriatrician/neuroscientist by training. He performed nuclear medicine research including clinical PET imaging in 1993-1997, and was awarded the PhD in medicine at Tohoku University. He worked as a postdoctoral research fellow at University of Pennsylvania in 1999-2003, being committed to the development of rodent models of neurodegenerative disorders. Higuchi became Staff Scientist at RIKEN Brain Science Institute in 2003, and was appointed Team Leader at National Institute of Radiological Sciences in 2005. His primary focus is translational molecular imaging research on Alzheimer's, Parkinson's and diverse other neuropsychiatric diseases bidirectionally connecting animal models and humans.



#### Symposium V Biomarkers in Parkinson's Disease and Related Disorders (II): Neuroimaging and Neuropathology in Parkinson's Disease and related Disorders

#### 2. What's New; Cranial MRI in Movement Disorders

#### Speaker:

Joaquim Ferreira, MD, PhD Department of Neurology and Clinical Pharmacology, Faculty of Medicine, University of Lisbon and Head of CNS - Campus Neurológico, Portugal



#### Abstract:

Advances in magnetic resonance imaging (MRI) support the move of neuroimaging from the single exclusion of secondary causes to the emergence of imaging biomarkers with impact in early diagnosis and disease progression monitoring and the true investigation of disease mechanisms. This results from the development of new MRI sequences like the neuromelanin-sensitive MRI, iron studies and the use of high- and ultra-high-field MRI.

Diffusion Tensor Imaging colour maps and tractigraphy also complement the conventional structural MRI, identifying reduction of specific neuronal fibres.

The capacity to represent structural connectivity in vivo also makes diffusion MRI an attractive tool for the evaluation and treatment of movement disorders.

In this review, we will also discuss the role of multi-modal MRI analysis algorithms and specific movement disorders MRI protocols.

#### Symposium V

Biomarkers in Parkinson's Disease and Related Disorders (II): Neuroimaging and Neuropathology in Parkinson's Disease and related Disorders

#### 3. The key pathological and clinical features of Parkinsonism

#### Speaker:

Renpei Sengoku, MD, PhD Departments of Neurology and Neuropathology, Tokyo Metropolitan Geriatric Hospital and Institute of Gerontology

#### Abstract:

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by bradykinesia, rigidity, postural instability and tremor. In addition to previously mentioned symptoms, non-motor symptoms such as sleep disorder, orthostatic hypotension and olfactory dysfunction are known. PD is a syndrome that is impaired in the peripheral autonomic nervous system as well as in the central nervous system. The disease process is multifocal and involves select central nervous system neurons and peripheral autonomic nervous system neurons. Therefore, the pathological study of patients with PD requires not only the central nervous system including the spinal cord, but also the peripheral autonomic nervous system such as the skin and the sympathetic ganglion as systemic pathological findings. It seems to be related to the fact that PD is a heterogeneous disease and where the Lewy body pathology arises from the whole body. Based on the systematic pathology findings of our center, we outline the pathological findings of Parkinson 's disease including recent findings.

#### Curriculum Vitae:

Education and Training : 1999-2001 Resident Internal Medicine Tokyo Saiseikai Central Hospital 2001-2002 Resident Neurology Department of Neurology, The Jikei University Hospital 2002-2003 Resident Neurology Department of Neurology, Yokohama Rosai Hospital 2003-2005 Clinical Assistant Neurology Department of Neurology, The Jikei University Hospital 2005-2008 Research Fellow Neuropathology Tokyo Metropolitan Institute of Gerontology 2008-2009 Research Fellow Neuropathology Department of Neuropathology, New York Brain Bank, Columbia University

2012-2013 Assistant Professor Neurology Department of Neurology, The Jikei University Hospital 2013- Chief Physician Neurology and Neuropathology Departments of Neurology and Neuropathology, Tokyo Metropolitan Geriatric Hospital and Institute of Gerontology

Honors:

- Association of Neuropathologists 2008 Annual Meeting. (2008 San Diego, USA)
- Best Award for Young Research of the Japan Foundation For Aging and Health. (2009 Tokyo, Japan)
- Award for Research of Jikei Medical Association. (2009 Tokyo, Japan)

#### Curriculum Vitae:

Joaquim Ferreira completed his medical degree and PhD in Neurology at the University of Lisbon. He is Professor of Neurology and Clinical Pharmacology at the Faculty of Medicine, University of Lisbon and Head of the Laboratory of Clinical Pharmacology and Therapeutics. He is also the head of CNS- Campus Neurológico Sénior in Portugal.

He became interested in movement disorders during his medical degree and later undertook a Clinical Pharmacology fellowship with Prof. Olivier Rascol in Toulouse, France.

He is currently the past-chair of the European Section of the International Parkinson and Movement Disorder Society. His major research interests are neuropharmacology, Parkinson's disease, dystonia and Huntigton's disease.



· Moore Award for the Best Paper on Clinico-Pathological Correlation Presented at the American

#### Luncheon Seminar (AbbVie Inc.) Medical Management of Fluctuations in Parkinson's Disease

#### Chair:

Satoshi Orimo, MD, PhD Kanto Central Hospital

#### Speaker:

Francisco Cardoso, MD, PhD, FAAN Medical School of the Federal University of Minas Gerais, Belo Horizonte, Brazil, Belo Horizonte, Brazil



#### Abstract:

Levodopa remains the gold standard of the management of Parkinson's disease (PD). Although the underlying mechanism remains to be determined, PD patients develop irregularities of the response to levo-dopa, fluctuations and dyskinesias, at a rate of 10% a year. Fluctuations are classified in motor and non-motor; as well as related to the cycle of levo-dopa in delayed on, wearing off, on-off phenomenon, nocturnal akinesia and early morning akinesia. As fluctuations are characterized by a hypodopaminergic state, their management is primarily based on increase of the dopamine content in the synapsis. The medical options currently available to achieve this goal are dopamine agonists (pramipexole, ropinirole, rotigotine, piribedil, apomorphine, and cabergoline), COMT inhibitors (tolcapone, entacapone, and opicapone), MAOB inhibitors (selegeline, rasagiline, and safinamide), and management of levo-dopa. The latter involves fractioning of the dosage, increase of individual dosages and use of different formulations (dispersible levo-dopa, long release levo-dopa and dual release levo-dopa). There are also non-dopaminergic options such as anti-adenosine agents (istradefylline) and drugs with unknown mechanism such as zonisamide. Dyskinesias are also classified according to their relationship to the levo-dopa cycle: peak dose, biphasic, square wave dyskinesias, and off dyskinesias. The main issue related to the treatment of dyskinesias is that they almost invariably co-exist with fluctuations and get worse with the treatment of the latter. The only proven agent to improve dyskinesias is amantadine. There are several issues relevant to clinical practice that are not addressed by available studies: proportion of patients who respond to each of the agents previously mentioned, effect of association of agents with different mechanisms of action, and number of individuals who fail to all available medical treatments and become candidates to invasive therapies.

#### Curriculum Vitae:

Dr. Cardoso, a Brazilian Neurologist, is Professor of Internal Medicine – Neurology at the Medical School of the Federal University of Minas Gerais (UFMG) in Belo Horizonte, MG, Brazil. He obtained his MD at the Alagoas School of Medical Sciences in 1986, did his Neurology Residency at UFMG and his movement disorders training at Baylor College of Medicine in Houston, TX, USA under the supervision of Joseph Jankovic MD. He is a clinician with particular interest in the investigation of infectious-induced autoimmune choreas, epidemiology of parkinsonism and genetics of movement disorders. He is one of the discoverers of the DYT16 gene. He has authored more than 200 peer reviewed papers and 110 book chapters. He is Honorary Member of the Japanese Neurological Society, Fellow of the American Academy of Neurology and has had a long career in the International Parkinson and Movement Disorders Society (MDS). He has been Secretary of MDS, Chair of the MDS Pan-American Section and is currently the Chair of the MDS Publications Oversight Committee.

#### **Education Seminar** (Takeda Pharmaceutical Co., Ltd.) Non-Motor Symptoms in Parkinson's disease: ethnic difference and the impact on the QOL

#### Chair:

Ryosuke Takahashi, MD, PhD Department of Neurology, Kyoto Univ. Graduate School of Medicine

#### Speaker:

Yoshio Tsuboi, MD, PhD Department of Neurology, School of Medicine, Fukuoka University

#### Abstract:

Non-motor symptoms (NMS) in PD patients are common and can occur across all stages of the disease. NMS have a great impact on quality of life (QOL) of PD patients and the care givers. NMS are frequently unrecognized by general neurologists. We evaluated frequency and severity of NMS in Japanese PD patients to demonstrate the prevalence and the impact on QOL in PD patients. Data of 1054 PD patients from 7 facilities in Japan were collected. Movement disorder experts examined all patients and administered the structured NMSS interview. Disease severity was graded according to Hoehn and Yahr stage and UPDRS was used to evaluate motor disability. There were 465 men (44.1%) and mean age was 69.8 years with mean age at disease onset of 62.9 years. Mean duration of PD was 6.9 years. Sleep/fatigue domain was the most frequent complaint (86.9%), followed by Urinary disturbance (85.8%), and Gastrointestinal symptoms (79.4%) Men more frequently related urinary and sexual dysfunctions than women. Most items on NMS scale correlated positively with HY stage. We found a high prevalence of NMS in Japanese PD patients and the prevalence was mostly identical to that in European studies, however, the severity of NMS was less than those of European studies. The impact on QOL is undoubted and supports their important role in clinical manifestations of PD and the need to improve diagnostic accuracy and treatment.

#### Curriculum Vitae:

Yoshio Tsuboi, MD, PhD. is a Professor and Chairman in Department of Neurology, School of Medicine, Fukuoka University, Fukuoka, Japan since 2011. Dr. Tsuboi graduated from the School of Medicine, Chiba University in 1986 and received his medical training in clinical Neurology at the Chiba University Hospital. In 2000, he became a clinical research fellow at the Department of Movement Disorder, Mayo Clinic Jacksonville until 2003. Dr. Tsuboi's research interest includes clinical, pathological and molecular genetic researches in Parkinson's disease and other Movement Disorders. Dr. Tsuboi is member of several Japanese and international neurological societies. He is the member of Japanese Society of Neurology, Movement Disorders Society Japan, Movement Disorders Society, and American Academy of Neurology.

Dr. Tsuboi has published more than 200 peer-reviewed articles in Japanese and International Scientific journals.



#### (Parallel session) Small Conference for Young Neurologist

#### Room A : Update on Treatment for Motor and Non-Motor Symptoms of Parkinson's Disease

#### Lecturer:

Roongroj Bhidavasiri, MD, FRCP, FRCPI Neurology, Chulalongkorn Comprehensive Movement Disorders Center, Chulalongkorn University Hospital, Bangkok, Thailand

Werner Poewe, MD, PhD Department of Neurology, Medical University of Innsbruck, Austria

Eduardo Tolosa, MD, PhD Neurology Service, Hospital Clinic de Barcelona, IDIBAPS, CIBERNED, Barcelona, Spain

#### **Case Presenter and Facilitator:**

Taku Hatano, MD, PhD Department of Neurology, Juntendo University School of Medicine

Keisuke Suzuki, MD, PhD Department of Neurology, Dokkyo University School of Medicine

# Room B : Update on Treatments for Neuropsychiatric Symptoms of Parkinson's Disease

#### Lecturer:

Olivier Rascol, MD, PhD Clinical Pharmacology at Toulouse University Hospital, Toulouse, France

Heinz Reichmann, MD, PhD Department of Neurology, University Hospital Carl Gustav Carus, Dresden University of Technology, Dresden, Germany

#### **Case Presenter and Facilitator:**

Hidetomo Murakami, MD, PhD Department of Neurology, Showa University

Katsuo Kimura, MD, PhD Department of Neurology, Yokohama City University

#### Room C : Update on NeuroImaging in Neurodegenerative Disorders

#### Lecturer:

Joaquim Ferreira, MD, PhD University of Lisbon and Head of CNS -Campus Neurológico, Portugal

Beomseok Jeon, MD, PhD Seoul National University Hospital, Seoul, South Korea

#### **Case Presenter and Facilitator:**

Shigeki Hirano, MD, PhD Department of Neurology, Chiba University

Hitoshi Shimada, MD, PhD Department of Functional BrainImaging Research, NIRS Chiba

#### Room D: How to diagnose and treat atypical parkinsonism

#### Lecturer:

Eng King Tan, MD, PhD Singapore General Hospital, National Neuroscience Institute, Singapore

Louis Tan, MBBS, MRCP, FAMS, FRCP National Neuroscience Institute, Singapore

Yi-Ru Wu. MD Chang-Gung Memorial Hospital, Taipei, Taiwan

#### **Case Presenter and Facilitator:**

Iun Tashiro, MD, PhD Sapporo Parkinson MS Neurological Clinic

Osamu Kano, MD, PhD Department of Neurology, Toho University School of Medicine

#### Room E : How to diagnose and treat dystonia and hyperkinetic movement disorders.

#### Lecturer:

Christine Klein, MD, FEAN Institute of Neurogenetics, University of Lübeck, Lübeck, Germany TBA

#### **Case Presenter and Facilitator:**

Masashi Hamada, MD, PhD Department of Neurology, The University of Tokyo

Takashi Osada, MD, PhD Department of Neurology, Keio University Hospital

#### (Sumitomo Dainippon Pharma Co., Ltd.)

#### Hot Topics Monogenic Movement Disorders

#### Chair:

Tatsushi Toda, MD, PhD Department of Neurology, The University of Tokyo

#### Speaker:

Christine Klein, MD, FEAN Institute of Neurogenetics, University of Lübeck, 23538 Lübeck, Germany



#### Abstract:

Monogenic movement disorders comprise a broad spectrum of inherited conditions sharing common features of impaired or uncontrolled movement that can be hyperkinetic, hypokinetic or mixed. According to the recommendations of the International Parkinson and Movement Disorder Society Task Force for Nomenclature Genetic Movement Disorders, the following subgroups can be distinguished: genetically determined parkinsonism, dystonia, cerebellar ataxia, chorea, myoclonus, paroxysmal movement disorders, hereditary spastic paraplegia, primary familial brain calcification, and neurodegeneration with brain iron accumulation. The present lecture will focus on monogenic forms of parkinsonism. Although genetic forms cause only a minority of Parkinson disease (PD), the disease mechanisms they elucidate advance the understanding of idiopathic cases. Moreover, recently identified susceptibility variants contribute to complex-etiology PD and broaden the contribution of genetics beyond familial and early-onset cases. Dominantly inherited monogenic forms mimic idiopathic PD and are caused by mutations of SNCA, LRRK2, and VPS35. On the other hand, early-onset forms are associated with PARKIN, PINK1 and DJ1 mutations, nominating mitochondrial dysfunction and oxidative stress as another important molecular pathway in the causation of the disease, in addition to alpha-synuclein accumulation. Common variants in GBA are a major risk gene for PD and select variants may even be viewed to act in a dominant fashion with highly reduced penetrance. Current guidelines recommend testing for LRRK2 variants in familial PD or in specific populations (ancestry), and for the recessive genes in early-onset PD. However, gene panels have made testing for multiple forms of genetic PD a viable approach. First gene-specific clinical trials targeting GBA mutations are currently underway.

#### **Curriculum Vitae:**

Dr. Christine Klein is a Professor of Neurology and Neurogenetics. She studied medicine in Hamburg, Heidelberg, Luebeck, London, and Oxford. She moved to Boston from 1997-1999 for a fellowship in Molecular Neurogenetics with Dr. X.O. Breakefield and completed her neurology training at Luebeck University in 2004, followed by a series of summer sabbaticals in movement disorders with Dr. A.E. Lang in Toronto, Canada in 2004-2015. She was appointed Lichtenberg Professor at the Department of Neurology of Luebeck University in 2005, where her research has focused on the clinical and molecular genetics of movement disorders and its functional consequences. In 2009, Dr. Klein been appointed Schilling Professor of Clinical and Molecular Neurogenetics at the University of Luebeck and became Director of the newly founded Institute of Neurogenetics in 2013.

Dr. Klein has published over 400 scientific papers. She is an Associate Editor of 'Annals of Neurology' and of 'Movement Disorders', served as chair of the Congress Scientific Program Committee of the 2016/2017 Annual Congresses of the International Parkinson and Movement Disorder Society, and is President-Elect of the German Neurological Society.

Symposium VI Social cares for Parkinson's Disease

#### Chair:

Tadashi Ichikawa, MD, PhD Saitama Rehabilitation Center Miho Murata, MD, PhD National Center Hospital of Neurology & Psychiatry

## 1. Neurorehabilitation for Parkinson's Disease and related movement disorders

#### Speaker:

Toshiyuki Fujiwara, MD, PhD Department of Rehabilitation Medicine, Juntendo University Graduate School of Medicine.

#### Abstract:

Parkinson's disease is a neurodegenerative disorder characterized by progressive bradykinesia, rigidity, tremor, and gait disturbances. In most patients, gait disturbance start in early stages of the disease. As the disease progresses, gait becomes slower and the typical Parkinson gait. Freezing and postural instability develop later and are less dopamine responsive. In this lecture, I will discuss about the effect of neurorehabilitation on gait disturbance and postural instability.

#### Curriculum Vitae:

Toshiyuki Fujiwara, MD, PhD Professor and Chairman Department of Rehabilitation Medicine, Juntendo University Graduate School of Medicine. 1993-1996 Resident, Department of Rehabilitation Medicine, Keio University School of Medicine, Tokyo, Japan 1996-1997 Department of Rehabilitation Medicine, National Murayama Hospital, Tokyo, Japan 1997-1999 Department of Rehabilitation Medicine, Keio University Tsukigase Rehabilitation Center, Shizuoka, Japan 2000-2002 Department of Rehabilitation Medicine, Saitama General Rehabilitation Center, Saitama, Japan 2002-2003 Research Fellow Sobell Department of Motor Neuroscience and Movement Disorders, Institute of Neurology (Prof. John Rothwell), UK 2003-2004 Department of Rehabilitation Medicine, Keio University School of Medicine Assistant Professor, Department of Rehabilitation Medicine, Keio University School of 2005-2014 Medicine 2014-2016 Associate Professor, Department of Rehabilitation Medicine, Tokai University School of Medicine, Isehara, Japan 2017-Present Professor and Chairman, Department of Rehabilitation Medicine, Juntendo University Graduate School of Medicine, Tokyo, Japan

#### CERTIFICATION :

Board Certification of Japanese Society of Rehabilitation Medicine Board Certification of Clinical Neurophysiology (EMG & Nerve conduction study)

#### <sup>liatry</sup> (inson's Disease and related



Symposium VI Social cares for Parkinson's Disease

#### 2. Not-so-big data analysis: What Korean Health Insurance Data tells us.

#### Speaker:

Woong-Woo Lee, MD

Department of Neurology, Nowon Eulii Medical Center, Eulii University, Seoul, South Korea



#### Abstract:

We are living in the digital era. Most of the information can be digitized, and the converted information can simply be stored in the huge storage. We can easily access and analyze these big data. Korea has been in the era of national health insurance since 1989. In 2000, all medical insurance services were integrated into one system. Especially since 2007, 99% of the whole claim data were registered through the computer-based program. Therefore, the Korean Health Insurance Data (KHID) can show us something about almost the whole population, not about the part of them. In this session, I want to introduce the various analysis data for the Korean patients with Parkinson's disease (PD) based on KHID. I analyzed the epidemiologic data of the Korean PD patients and discussed the differences from the previous studies. And I also analyzed how the PD patients in the early stage choose hospitals. To know the patterns of selecting hospitals would be helpful in understanding the results of single-center studies as well as in setting up the health care policies. Lastly, I studied the prognosis of the Korean PD patients according to whether the neurologists treat them or not. The current medical big-data have several limitations including the problem of diagnostic accuracy, the absence of laboratory and imaging data, and the difficulty in

assessing the outcomes of medical interventions. At the same time, however, those data can help us guess the overall outline and get the insight of a picture of PD. Further efforts are necessary to improve the accuracy of medical big-data and to apply the analyzed results to the healthcare system.

#### **Curriculum Vitae:**

Present Position : 2015/03 – present	Assistant professor, Department of Neurology, Nowon Eulji Medical Center, Eulji University, Seoul, Korea
Educational Backgro 1999/03 - 2005/02 2008/03 - 2013/02 Neuroscience)	ound : College of Medicine, Seoul National University, Seoul, Korea The Graduate School of Medicine, Seoul National University, Seoul, Korea (Master in
2013/09 - present	The Graduate School of Medicine, Seoul National University, Seoul, Korea (Ph.D. course in Neuroscience)
Post-graduate Profe 2006/03 - 2010/02 2013/05 - 2015/02	ssional Training : Residency, Seoul National University Hospital, Seoul, Korea Fellowship, Department of Neurology, Seoul National University Hospital, Seoul, Korea
Achievements and A 2010/01 Scientific 2010/11 Best Pape 2014/04 Fellow Av	Awards : paper award, Seoul National University Hospital er Award, 29th Annual Meeting of the Korean Neurological Association vard, The Korean Movement Disorders Society

2017/06 Travel grant award, 21th International Congress of Parkinson's disease and Movement disorders

## **Abstracts**

3rd Day 25 Feb 2018(Sunday)

#### Japanese Symposium 1 (日本ベーリンガーインゲルハイム株式会社) レボドパ併用療法におけるドパミンアゴニストの役割

#### Chair:

長谷川 一子 Kazuko Hasegawa, MD, PhD 独立行政法人国立病院機構相模原病院 神経内科

#### Speaker:

前田 哲也 Tetsuya Maeda, MD, PhD 岩手医科大学医学部内科学講座 神経内科·老年科分野



#### Abstract:

ドパミンアゴニストはその運動症状改善作用とジスキネジア抑止効果から、永く早期パーキンソン病の 第一選択薬の地位にあった。レボドパに比して血中半減期が長いため、持続的ドパミン受容体刺激の概 念に合致し、さらに徐放製剤や貼付剤の開発によりパーキンソン病治療には欠かせない薬剤となった。 一方、近年、ドパミンアゴニストには負の側面もまた明らかとなり、症例の背景を考慮して使用する必 要がある。まず麦角系アゴニストには負の側面もまた明らかとなり、症例の背景を考慮して使用する必 要がある。まず麦角系アゴニストは心臓弁膜症や胸腹膜線維症などが問題となるため、特に高齢者では 第一選択薬としては使用されなくなった。そのため非麦角系アゴニストが普及したが、突発的睡眠や衝 動制御障害に代表される特殊な精神症状などを生じうることが明らかとなった。レボドパはその運動症 状改善作用でドパミンアゴニストに勝り、運動合併症の問題はあるものの忍容性は極めて高いことから 標準的治療薬とされる。パーキンソン病の長い臨床経過には欠かすことができないことは自明であるが、 レボドパとその関連薬剤のみでは治療を乗り切ることはできない。ドパミンアゴニストとレボドパの併 用療法に関して実臨床に則して考えてみたい。

#### Japanese Symposium 2 運動障害疾患における情報通信技術(ICT)の応用

#### Chair:

永山 寛 Hiroshi Nagayama, MD, PhD 日本医科大学 神経内科

#### Speaker:

大山 彦光 Genko Oyama, MD, PhD 順天堂大学医学部 脳神経内科

#### Abstract:

情報通信技術 (Information communication technology; ICT) の進歩は目覚ましく、医療において も徐々に利用が加速されてきている。医療におけるICTの利用は大きく3つの軸があると考えられる。1 つ目の軸として、「医療情報・電子カルテ/レセプトシステム」があげられる。電子カルテ/レセプトシ ステムによるデータベース化が進むと、ビッグデータとして活用、さらには人工知能 (AI)を用いた解 析に応用することができ、新しい知見に結び付くことが期待される。2つ目の軸としては、「遠隔医療 (Telemedicine)」があげる。これは遠隔地にいる患者や、離れた場所にいる診療所と専門家が、テレビ 会議システム、タブレット端末、スマートフォンなどを用いて、医療を行うという概念であり、診断、治療、 教育、医療連携、治験などへの応用が期待されている。3つ目の軸としては、情報入力システムとしての「モ ニタリングデバイス」があげられる。検査機器データのデジタル化のみならず、モーションキャプチャー や、ウェアラブルデバイスなどによるモニタリングがある。これらの軸は相互に補完しあい発展しており、 様々な新しい試みが行われている。本シンポジウムでは、運動障害疾患におけるICTの応用について概略 を紹介する。

# 略歴: 1993年、弘前大学医学部卒業、弘前大学医学部第三内科入局 1997年、弘前大学医学部附属脳神経疾患研究施設臨床神経部門、松永宗雄教授の指導のもと弘前大学大学院医学研究科にて博士(医学)修得(パーキンソン病モデルラット線条体のシナプス前D2受容体によるドーパミン放出調節機構-マイクロダイアリーシス法による検討-) 2001年、滋賀医科大学解剖学第一講座、新井良八教授のもとでドパミンニューロンおよびセロトニンニューロンの形態学的基礎研究 2002年、弘前大学医学部附属病院第三内科助手 2003年から秋田県立脳血管研究センター神経内科、研究員、2009年神経内科診療部部長、2014年難治性脳疾患研究部部長に就任

2016年より現職の岩手医科大学医学部内科学講座神経内科・老年科分野、特任准教授に就任。

#### 略歴:

2002年(平成14年)3月 均玉医科大学医学部医学科卒業 2002年(平成14年)5月 順天堂大学 脳神経内科 レジデント/チーフレジデント 2006年(平成18年)4月 順天堂大学 大学院医学研究科 神経学講座 大学院生 2009年(平成20年)7月 2011年(平成23年)7月 順天堂大学 脳神経内科 助教 2014年(平成26年)4月~ 順天堂大学 脳神経内科 准教授 2015年(平成27年)3月~ フロリダ大学 神経内科 客員准教授 現在に至る



#### Japanese Symposium 3

#### パーキンソン病における歩行障害

Role of dopamine agonists in combination therapy with levodopa

#### Chair:

服部 信孝 Nobutaka Hattori, MD, PhD 順天堂大学 神経学講座

#### Speaker:

大熊 泰之 Yasuyuki Okuma, MD, PhD 順天堂静岡病院 脳神経内科



#### **Abstract:**

パーキンソン病の歩行障害は患者のADLを著しく低下させる。歩行障害の結果生じる転倒は骨折など外 傷の原因となり、寝たきりや施設入所のきっかけになることでQOLの低下をもたらす。歩行障害のなか でも治療に難渋するのはすくみ足である。すくみ足の機序には諸説あるが、大事なのは大脳基底核から (SMAを中心とした)前頭葉のmalfunctionによる内的ドライブの低下、automaticityの障害といわれて いる。我が国の中村(隆一)らが世界に先駆けて注目したリズム形成障害hasteningも重要である。近年 hasteningを加速度計で捉えて定量化する試みが世界中で行なわれている。治療としては、すくみ足は オフ時に見られることが多いので、wearing off対策が大事である。ただしドパミン過剰状態でもすくみ 足が悪化するので注意が必要である。非ドパミン系治療薬では確固たるエビデンスを有するものは報告 されていない。今後の研究成果が期待される。非薬物的interventionも研究されており、その一端を紹 介する。

# 略歴: 1982年 順天堂大学医学部卒業、神経学教室(脳神経内科)入局 1992年10月から1994年12月まで、Department of Clinical Neurosciences, University of Calgary, Canada 留学、 臨床神経生理学の研究に従事 1995年1月 順天堂大学脳神経内科助手 2000年6月 順天堂大学伊豆長岡病院(現・静岡病院)脳神経内科講師 2001年8月 同助教授 2009年4月 順天堂大学静岡病院 脳神経内科教授 2017年4月 順天堂大学理事、保健看護学部長併任 現在に至る。

#### Japanese Symposium 4 (日本メジフィジックス株式会社) Neuroradiological diagnosis for Parkinson's disease and the related disorders by nuclear medicine

#### Chair:

下畑 享良 Takayoshi Shimohata, MD, PhD 岐阜大学 神経内科

#### Speaker:

高橋 牧郎 Makio Takahashi, MD, PhD 大阪赤十字病院 神経内科

#### Abstract:

Dopamine transporter scintigraphy (DAT-SPECT) and I<sup>123</sup>-meta-iodobenzylguanidine (MIBG) scintigraphy play a major role in the diagnosis of Parkinson 's disease (PD) and the assessment of the pathological condition. Furthermore, with the combination of cerebral blood flow scintigraphy, the accuracy of differentiation in PD from parkinson related disorders including DLB, PSP, and CBD accompanying cognitive dysfunction could be increased. Reduction of MIBG uptake is thought to indirectly reflect peripheral postganglionic fiber density of the cardiac sympathetic nerve and has also been standardized as a diagnostic biomarker of  $\alpha$ -synucleinopathy. In particular, the specificity in PD and DLB is high, and the H / M ratio decreases according to Hoehn-Yahr severity. On the other hand, diagnostic sensitivity by DAT-SPECT is high, since it indirectly reflects dopamine nerve terminal density in the striatum, and it is excellent in distinguishing PD, DLB, PSP, CBD, etc. that cause Parkinsonism from other diseases. However, its interpretation must be considered with the problem of Scans Without Evidence of Dopamine Deficits (SWEDDs) and with the fact that the signal binding ratio (SBR) decreases with age in normal cases. In our study of 433 patients under DAT-SPECT assessed with left and right average values of SBR, the decline of SBR in healthy volunteers including non-parkinson's disease was -0.055 / year, whereas PD was affected by - 0.094 / year, MSA and PSP by - 0.18 / Year, which implies that the speed of dopaminergic neurodegeneration accelerates in pathological conditions. Therefore, the chronological assessment with SBR of DAT-SPECT may be useful to evaluate the effect of drugs to inhibit neurodegeneration of dopaminergic neurons. Furthermore, asymmetry index (AI) of SBR is also important in the diagnosis of PD (versus MSA) with AI of 32% or more (sensitivity 44%, specificity 64%) and in the diagnosis CBS (versus PSP) with AI> 230% (sensitivity 32%, specificity 80%). In addition, the signal reduction of DAT - SPECT in its form is also important. The uptake is generally lower in the dorsolateral putamen in PD, while the decrease in the caudate nucleus is seen from the early stage in DLB. In cerebral blood flow scintigraphy, it is characterized that CIS (cingulate island sign) in which the blood flow in the posterior cingulate gyrus is kept in the island shape is seen as a feature of DLB distinct from AD, and CIS is included as a supportive biomarker for DLB diagnostic criteria in 2017. However, the CIS evaluation has not been recapitulated in our small study of DLB cases. In a recent report, CIS disappears in the advanced stage of DLB (lizuka T et al., Scientific reports, 2017), and its interpretation requires careful attention.



#### 略歴:

1993年3月 京都大学医学部医学科 卒業 1994年4月 (財)天理よろず相談所病院神経内科 医員 1996年5月 (財)住友病院神経内科 医員 1999年4月 京都大学大学院医学研究科 臨床脳生理学講座 入学 1996年6月 米国ニューヨーク州Albert Einstein医科大学/Montefiore Medical Center神経病理部門 visiting research fellow 2001年8月 東京大学大学院薬学研究科 臨床薬学教室 委託研究院生 2003年3月 京都大学大学院医学研究科 臨床脳生理学講座 修了、医学博士 2004年4月 米国ニューヨーク州 Mount Sinai医科大学 research fellow 2005年1月 米国フロリダ州 Mavo Clinic 医科大学 senior research fellow 2007年9月 (財)田附興風会医学研究所北野病院神経内科 副部長 2010年4月 京都大学大学院医学研究科神経内科学講座 助教 2011年4月 大阪府済生会中津病院神経内科 部長 2013年4月 日本赤十字社 大阪赤十字病院神経内科 部長 2015年4月 京都大学医学部臨床教授、関西医科大学臨床教授 資格等 京都大学医学博士 日本神経学会専門医・指導医・代議員・近畿地方会評議員 日本内科学会認定医・総合内科専門医・指導医 日本老年学会専門医・指導医 日本認知症学会専門医・指導医 日本脳卒中学会専門医 日本頭痛学会指導医 日本神経学会 認知症ガイドライン作成委員

#### Japanese Symposium 5 エビデンスに基づいたパーキンソン病治療

Chair:

宇川 義一 Yoshikazu Ugawa, MD, PhD 福島県立医科大学 神経内科

#### Speaker:

武田 篤 Atsushi Takeda, MD, PhD 独立行政法人国立病院機構 仙台西多賀病院

#### Abstract:

今年出版が予定されている新ガイドラインはこれまでの治療に限定したものから、検査や診断基準など を含む「診療ガイドライン」となった。また治療に関する記載は、豊富な文献データがある早期治療と進 行期治療に関する部分については、Minds2014に沿ってGRADEシステムによる厳密な文献検証を行っ た上で記載された。その他の部分については、これまで通りの文献検索とレビューを行った上で記載さ れた。早期治療については、ドパミン補充療法が不十分なままだとその後の運動機能障害が不可逆的に 固定化してしまう可能性が示唆されていることから、前ガイドラインに引き続き、早期からレボドパを 含めたドパミン補充療法を十分に行うことの重要性がさらに強調されている。進行期治療については、 ウェアリングオフやジスキネジアと言った運動合併症への対応について、前回のガイドライン作成後に 承認された薬剤を含むドパミン系・非ドパミン系薬剤の使用方法を示すとともに、通常の薬物療法で十 分な効果が得られない場合には、適応を検討の上で、脳深部刺激や経小腸レボドパ・カルビドバゲル持 続注入療法などのDevice-aided therapy (DAT)の導入を検討すべきであることが記載された。多様な非 運動症状への対処法については前ガイドラインに引き続いて重点が置かれ、さらに医療経済の観点から パーキンソン病治療を論じる項や終末期治療を論じる項も新たに付け加えられた。治療ガイドライン作 成の目標は治療の標準化である。しかしながら標準的な治療は必ずしも個々の症例に於いてベストチョ イスではないことに常に注意する必要がある。新ガイドラインでも幾つかの治療アルゴリズムが提案さ れているが、これはあくまで個々の治療法の位置付けを示す概念図の様なものである。その実践にあたっ ては症例毎の多様な情報を、総合的に考慮した上でなされる主治医の判断が最優先されることを前ガイ ドラインに引き続き強調したい。

#### 略歴:

 1985年
 東北大学医学部卒業・同附属病院研修医(神経内科)

 1985年
 東北大学院医学研究科卒業

 1994年
 東北大学医学部助手(神経内科)

 1998年
 米国Case Western Reserve大学病理研究所・神経病理部門留学

 2006年
 東北大学大学院 神経内科講師

 2007年
 東北大学大学院 神経・感覚器病態学講座 神経内科学分野准教授

 2013年
 国立病院機構 西多賀病院・副院長

 2014年
 国立病院機構 仙台西多賀病院・院長

 2016年
 東北大学連携大学院高齢者認知・運動機能障害学講座 客員教授(併任)

(グラクソ・スミスクライン株式会社)



#### Acknowledgments

We would appreciate greatly to their generous support.

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よりトレ	飲み さら	やす。	<.	
より	飲みて	に取		
トレ	さら	に取	161276	
トレ			·/]/X	11
<b>r</b> <i>V</i>				-
	<b>7</b>	R	レ動	5
〔1:1日50mgの〕 〔2:錠剤の両面〔	服用が1錠となり に製品名を印刷し	ます。 しています。		
:3:錠剤の両面( -レリーフ錠25mg比	に割線を入れまし と較)	た。		
禁忌(次の患	者には投与し	ないこと)		
<ol> <li>(1) 妊婦又は 婦・授乳如</li> </ol>	:妊娠している 帰等への投与」	可能性のある の項参照〕	>婦人 し添付乂	書の頃
(2) 本剤の成	分に対して過	<u> 敢症の既往歴</u>	のある患者	
が、効果	ゴレパムナ制く	としていたか	キンットの声素を	
いーキンワン病に	ンホトハ 2月 表見 ゆった場合)	判に他の抗ハー	■キノリノ病楽を	11日し
」法・田里 に剤は、レボドパ含	有製剤と併用す	3.	ルトートマ	
1日、成人にノーブ 、お、パーキンソン	病における症状	』25mgを程口指 の日内変動(w	zチ9る。 earing-off現象)(	の改善に
0mgを栓口投子。  <用法・用量に関	する。  連する使用トの	)注意>		
1. ゾニサミドをて は、てんかんの效	んかん(本剤の) 加能・効果を有す	承認外効能・效 る製剤(エクセク	」果)の治療目的で ブラン等)を用法・	ご投与す 用量どま
すること。 2.本剤の1日50r	mg投与において	、1日25mg投与	時を上回るon時	の運動
善効果は確認さ 3.本剤は口腔内	れていない。〔添く 」で崩壊するが、」	付文書の「臨床 口腔粘膜からの	成績」の項参照〕 の吸収により効果	発現を
製剤ではないた の項参照]	め、唾液又は水	で飲み込むこ	と。〔添付文書の	「適用」
使用上の注意(抜	粋)			
<b>慎重投与(次の</b> をのある患者(血中	患者には慎重に  濃度が上昇する	- 投与すること) おそれがある。	重篤な肝機能	障害又
・ 重要な基本的 があるので注意	注意 (1)本剤技 すること。〔「重大な	と与中乂は投与 な副作用」の項	中止後に <b>悪性症(</b> 参照〕(2)連用中に	<b>医群</b> がる ま定期的
い血液検査を行 「起こることがある	うことが望ましい。 るので、本剤投与・	。(3)眠気、注意 中の患者には <b>自</b>	力・集中力・反射 動車の運転等危	連動能 険を伴
Fに従事させない 本温の上昇するこ	いよう注意すること とがあるので、本	1。(4)発汁減少 剤投与中は体	があらわれること 温上昇に留意し、	があり、 このよう
「温環境下をでき 小児等への投与	るだけ避け、適切 」の項参照〕 (5) オ	辺な処置を行う 本剤投与中又は	こと。[] 重大な副 :投与中止後に、自	作用」、 1殺企区
ことがあるので、。 )他の副作用」、「そ	患者の状態及び の他の注意」の項	病態の変化を注 〔参照〕	意深く観察するこ	と。〔添1
相互作用本語	剤は、王として楽物	7代謝酵素CYF	'3Aで代謝される。	【添付】
Ħ注意(併用に) にてんかん剤:フェ	注意すること) ェニトイン、カルバマ	マゼピン、フェノノ	ベルビタール、バル	プロ酸
、三堤糸抗うつ剤 事体:レセルピン等	判:アミトリブチリン 奈、フェノチアジン	/等、四境糸抗、系薬剤:クロル	うつ剤:マブロチリ プロマジン等、ブラ	ン等、L Fロフェ
いロペリドール等、	スルビリド、メトクロ	1プラミド		
バーキンソン病	<b>jの場合&gt;</b> 用量追 を含む副作用が。	加承認までのみられた。主なも	臨床試験842例 のは眠気(8.4%)	₽3936 、食欲
バスキネジア(5.7% その用量追加承認	5)、悪心(4.8%)、約 2時)	J覚(4.4%)、気	り低下(4.2%)等で	ごあった
r定使用成績調査 こなものはめまい	1542例中62例(1 ・ふらつき(2.4%)	1.4%)に臨床検 、幻覚(1.7%)、3	: 金値異常を含む ジスキネジア(1.5%	副作用 6)等で
ーフ錠の再審査 てんかん(承認)	終 「時) 外 効能・効果、用	法・用量) <b>の場</b> (	合>承認までの臨	床試馴
、使用成績調査・ っれた。主なものは	特別調査5,368 は眠気(11.7%)、食	例の合計6,376 【欲不振(4.9%)	i例中1,575例(24 、γ- GTP・ALP・	.7%)に ALT((
GOT)の上昇等(	(0.10/) Int Int 1	白愁州瓜下/0	and we do at the state	



#### (1)**重大な副作用**

(1)悪人な副FFH 1)悪性症候群(1%未満)本剤投与中又は投与中止後に悪性症候群があらわれることが ある。観察を十分に行い、発熱、意識障害、無動無言、高度の筋硬直、不随意運動、嚥下 困難、頻脈、血圧の変動、発汗、血清CK(CPK)の上昇等があらわれた場合には、体冷 却、水分補給等の全身管理、及び再投与後に漸減するなど適切な処置を行うこと。 なお、本症発症時には、ミオグロビン尿を伴う腎機能の低下がみられることがある。 「重要な基本的注意」の項参照〕2)中毒性表皮壊死融解症(Toxic Epidermal Necrolysis: TEN)(頻度不明)、皮膚粘膜眼症候群(Stevens-Johnson 症候 料(0.1%未満<sup>41</sup>)、紅皮症(剥脱性皮膚炎)(頻度不明)観察を十分に行い、発熱、紅 斑、水疱・びらん、瘙痒感、咽頭痛、眼充血、口内炎等の異常が認められた場合には、投 与を中止し、副腎皮質ホルモン剤の投与等の適切な処置を行うこと。3)過敏症症候群 (頻度不明)初期症状として発疹、発熱がみられ、さらにリンパ節腫脹、肝機能障害等の 臓器障害、白血球増加、好酸球増多、異型リンパ球出現等を伴う遅発性の重篤な過敏 症状があらわれることがあるので、観察を十分に行い、このような症状があらわれた場合 には、投与を中止し、適切な処置を行うこと。なお、ヒトヘルペスウイルス6(HHV-6)等のウ イルスの再活性化を伴うことが多く、発疹、発熱、肝機能障害等の症状が再燃あるいは 遷延化することがあるので注意すること。4)再生不良性貧血、無顆粒球症、赤芽球癆 (頻度不明)、血小板減少(1%未満)観察を十分に行い、異常が認められた場合には、投 与を中止し、適切な処置を行うこと。5)急性腎障害(頻度不明)観察を十分に行い、異 常が認められた場合には、投与を中止し、適切な処置を行うこと。6)間質性肺炎(頻度 不明)発熱、咳嗽、呼吸困難、胸部X線異常、好酸球増多等を伴う間質性肺炎があらわ れることがあるので、このような症状があらわれた場合には、投与を申止し、副腎皮質ホル モン剤の投与等の適切な処置を行うこと。7)肝機能障害(0.1%未満注1)、黄疸(頻度不 (U) AST(GOT)、ALT(GPT)、y-GTPの上昇等を伴う重篤な肝機能障害、黄疸があら われることがあるので、観察を十分に行い、異常が認められた場合には、投与を中止し、 適切な処置を行うこと。8)横紋筋融解症(0.1%未満) 観察を十分に行い、筋肉痛、脱力 感、CK(CPK)上昇、血中及び尿中ミオグロビン上昇等があらわれた場合には、投与を中止 し、適切な処置を行うこと。また、横紋筋融解症による急性腎障害の発症に注意するこ と。9)腎・尿路結石(0.1%未満)観察を十分に行い、腎疝痛、排尿痛、血尿、結晶尿、頻 尿、残尿感、乏尿等があらわれた場合には、投与を中止するなど適切な処置を行うこと。 10)発汗減少に伴う熱中症(頻度不明)発汗減少があらわれ、体温が上昇し、熱中症を 10)元イ協クに住て統一進(須度/や初)元イ(減)かかのうれない体価が上すたごが不定 きたすことがある。発汗減少、体温上昇、顔面潮紅、意識障害等がみられた場合には、投 与を中止し、体冷却等の適切な処置を行うこと。[「重要な基本的注意」、添付文書の「小 児等への投与」の項参照〕11)幻覚(1%以上)、妄想(1%未満)、錯乱(1%未満)、せん妄 (0.1%未満)等の精神症状観察を十分に行い、このような症状があらわれた場合には、 投与を中止するなど適切な処置を行うこと

注1)てんかん(承認外効能・効果、用法・用量)に使用した場合の頻度

その他の使用上の注意等につきましては、製品添付文書をご参照ください。



2017.12作成

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Ð 2015年1月作成

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2017年1月作成



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〈'16.11作成〉



作成:2012.05





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(Printed in December 2016) OZCAEb02-K





