The 23rd “Takamatsu” International Symposium for PD & MD in TOKYO

Date

2024. 3. 16（Sat） ・ 3. 17（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

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
〒135-8630 東京都江東区青海2-2-1

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Welcome to The 23rd “Takamatsu” International Symposium for PD and MD in TOKYO

Welcome message from Chairpersons.

Dear Colleagues,

We are excited to announce the 23rd "Takamatsu" PD & MD International Symposium in TOKYO, taking place on March 16th and 17th, 2024. The symposium, themed "Toward a Bright Future for Parkinson's Disease", will be held at the Tokyo International Exchange Center in Koto Ward, Tokyo.

We are in the process of inviting five international speakers to join us at the Tokyo International Exchange Center for this event, and we look forward to their participation and presentations.

As with our previous event, in order to prevent the spread of COVID-19, this will be a hybrid event with pre-registration and real-time web broadcasting. We apologize for any inconvenience this may cause, but we will be conducting the symposium with the utmost attention to infection control measures during the event. Please note that changes may occur, and we appreciate your understanding in advance.

We look forward to your participation.

Nobutaka Hattori, MD, PhD, FANA
Chair

Atsushi Takeda, MD, PhD
Co-Chair

The Organizing Committee

Chair

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

Co-Chair

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

Advisor

Mitsutoshi Yamamoto, MD, PhD
Takamatsu Neurology Clinic, Kagawa, Japan

Genjiro Hirose, MD, PhD
Neurological Center, Asanogawa General Hospital, Ishikawa, Japan

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Department of Neurology, Juntendo University School of Medicine, Tokyo, Japan

International Advisory Board

Werner Poewe
Innsbruck

Eduardo Tolosa
Barcelona

Francisco Cardoso
Belo Horizonte

Eng-King Tan
Singapore

Louis Tan
Singapore

Program

Theme: Medical care of Movement Disorders for sustainable development

1st Day：16 Mar 2024 (Saturday)

10：00-10：10
Opening Remarks
Nobutaka Hattori, Mitsutoshi Yamamoto

10：10-11：40
Symposium 1　Frontiers in Diagnosis and Treatment of Movement Disorders
Chair：Ryosuke Takahashi, Hirohisa Watanabe
1. New evidence of treatment for PD
   Speaker：Eduardo Tolosa
2. Biological Subtypes of PD
   Speaker：Francisco Cardoso
3. The Role of Neuro-Imaging in Diagnosing Parkinsonian Disorders
   Speaker：Werner Poewe

11：40-11：50　**Short Break**

11：50-12：50
Symposium 2　Is the Brain-First and Body-First Progression Hypothesis correct in Parkinson's Disease?　Kyowa Kirin Co., Ltd.
Chair：Tatsushi Toda, Kazushi Takahashi
1. Pathological Progression in PD from the viewpoint of pathology
   Speaker：Renpei Sengoku
2. Pathological progression in PD from the viewpoint of neuroimaging
   Speaker：Tomoko Totsune

12：50-13：50　**Lunch Break**

13：50-14：50
Premium Seminar　Novel findings in Parkinson's disease
Chair：Genjiro Hirose, Mitsutoshi Yamamoto
1. Biomarkers for PD
   Speaker：Louis Tan
2. GWAS studies in Parkinson’s disease: recent advances and implications
   Speaker：Eng-King Tan

14：50-15：50
Symposium 3　Development of new treatment for Parkinson's disease
ONO PHARMACEUTICAL CO., LTD.
Chair：Atsushi Takeda, Yoshio Tsuboi
1. The use of patient iPSCs for translational research of neurodegenerative diseases
   Speaker：Haruhisa Inoue
2. Gene-based PD drug development
   Speaker：Hiroyuki Ishiura

15：50-16：00　**Coffee Break**

16：00-17：00
Symposium 4　Parkinson's disease treatment using patients data
Takeda Pharmaceutical Co., Ltd.
Chair：Kazunori Ito, Masahiko Tomiyama
1. Biomarker analysis in prodromal cohort of Lewy body disease
   Speaker：Masahisa Katsuno
2. Movement disorder's treatment from the perspective of community
   Speaker：Tetsuya Maeda

17：00-18：00
Evening Seminar　ACP in Movement Disorders　Eisai Co., Ltd.
Chair：Tadashi Ichikawa, Shinji Saiki
1. Parkinson's disease treatment from the viewpoint of levodopa blood levels
   Speaker：Noriko Nishikawa
2. ACP in Movement Disorders
   Speaker：Genko Oyama

18：00-18：10
Closing Remark
Nobutaka Hattori

18：30-
Social Gathering

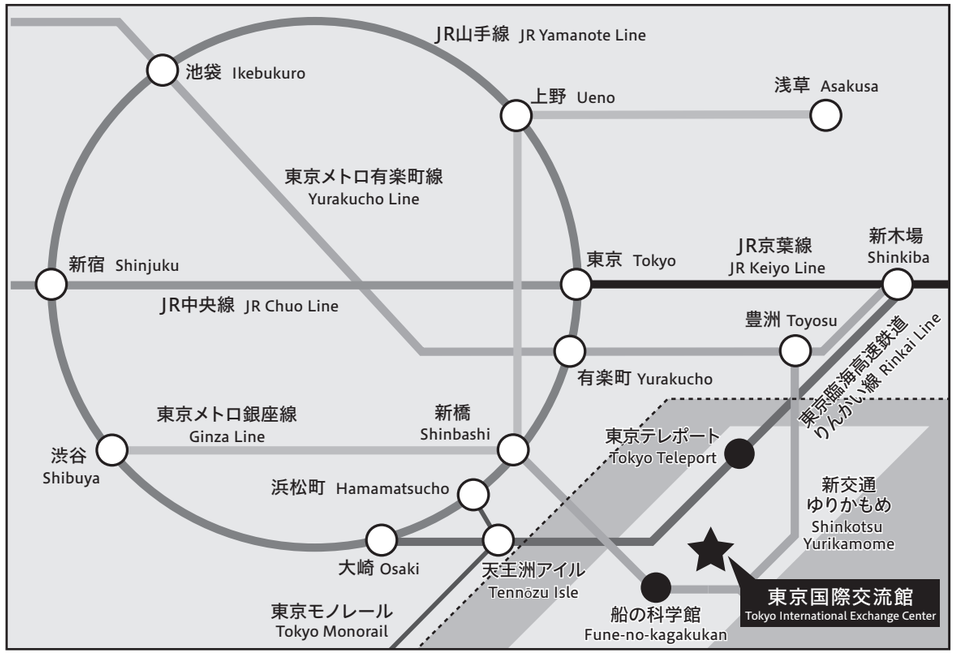
2nd Day：17 Mar 2024 (Sunday)　Japanese Session

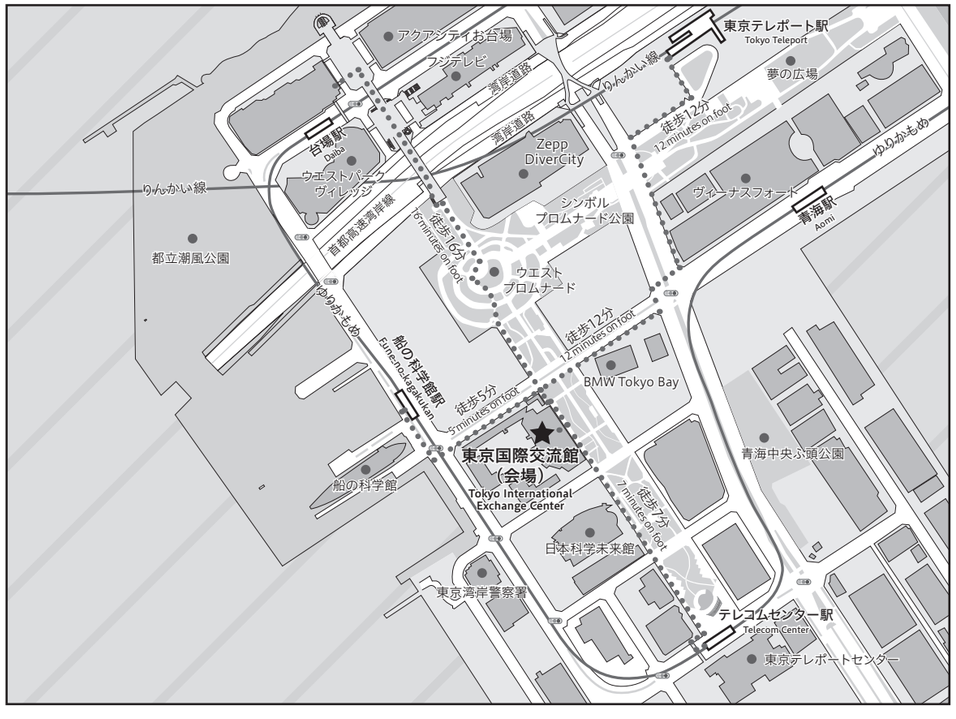
10：00-10：50
パーキンソン病の在宅医療　大塚製薬株式会社
Chair：宇川 義一　Speaker：織茂 智之

10：50-11：40
パーキンソン病の脳ネットワーク　住友ファーマ株式会社
Chair：花島 律子　Speaker：坪井 崇

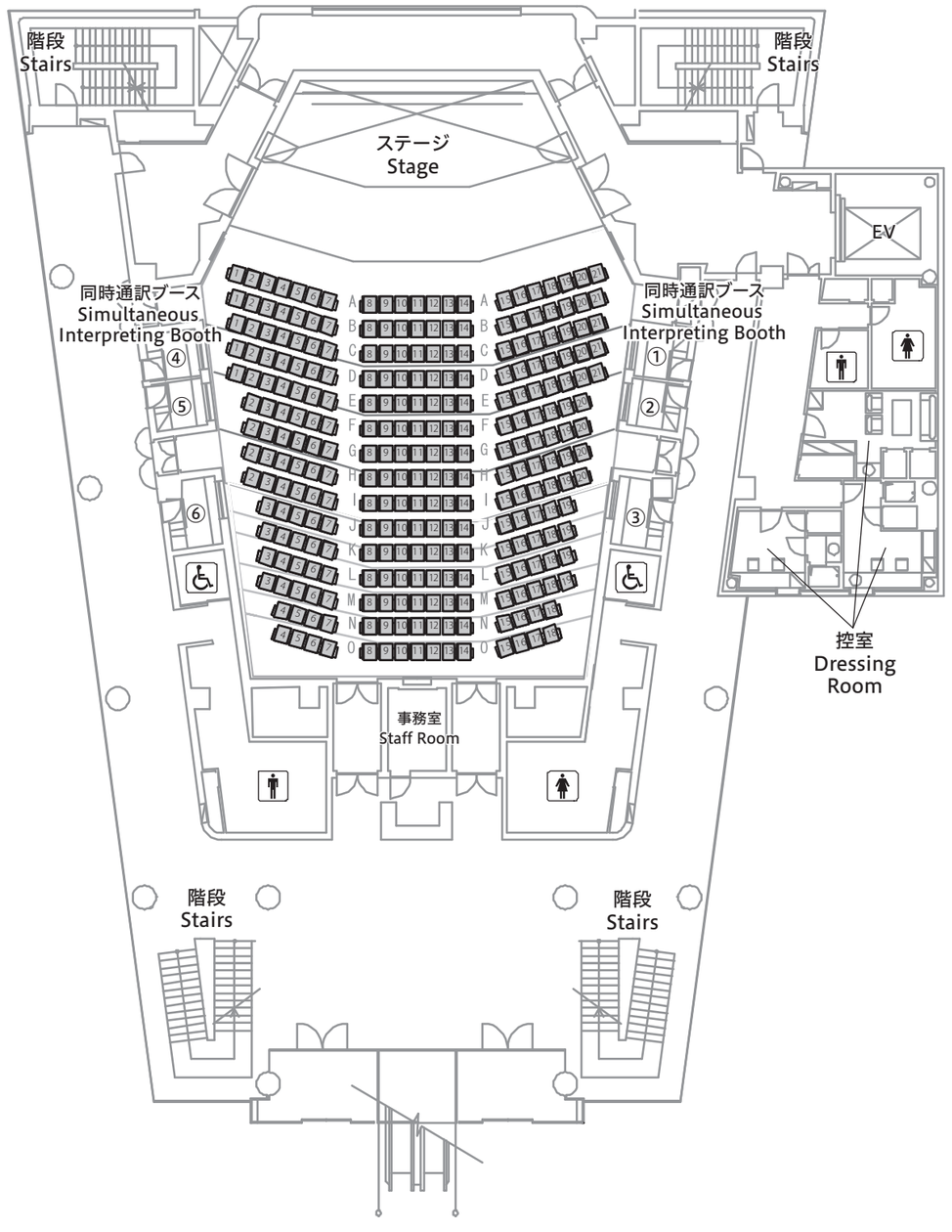
11：40-12：30
デバイス補助療法の未来　アッヴィ合同会社
Chair：大熊 泰之　Speaker：下 泰司

Access, Floor Map





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



Abstracts

1st Day
16 Mar 2024 (Saturday)

Chair:
Ryosuke Takahashi
Department of Neurology, Kyoto University

Hirohisa Watanabe
Department of Neurology & Neuroscience, Fujita Health University

1. New evidence of treatment for PD

Speaker:
Eduardo Tolosa
University of Barcelona

Abstracts:

The cause of Parkinson disease remains largely unknown except for about 5% of cases that have a known genetic cause. Still, in recent years and based on solid scientific advances, novel targets and promising candidates for a disease-modifying intervention have been identified. Targets of high interest include α-synuclein, GBA, LRRK2, Parkin, the lysosome/autophagy system, c-abl and inflammation. Interventions directed at these targets are actively being studied in the laboratory, and many have demonstrated striking neuroprotective benefits in relevant animal models. In patients, disease modification trials have also been initiated to correct relevant physiopathological abnormalities. In my presentation I shall review "**New evidence of treatment for PD**" with emphasis to advances in therapy for monogenic- autosomal dominant- Parkinson disease, including challenges in implementing disease modification trial in people who carry pathogenic mutations.

Biosketch:

Prof. Eduardo Tolosa obtained his MD degree from the University of Barcelona and received his neurological training at the University of Minnesota in the US. He is a founding member and past President of the Movement Disorder Society. He is the recipient of the American Academy of Neurology 2014 Movement Disorders Research Award. Prof. Tolosa is the past Chairman of the Department of Neurology at the University of Barcelona Hospital and past President of the Spanish Neurological Society and the European Neurological Society. He 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. Professor Tolosa was involved in pioneering studies on motor fluctuations and the role of DAT SPECT in Parkinson disease and his team has been among the first in Europe to evaluate the efficacy of novel therapeutic strategies for Parkinson's disease. His research is currently focused on the search of biomarkers in the prodromal phase of Parkinson disease, both idiopathic and genetic forms.

Key articles (Up to 5):

1. Tolosa E, Garrido A, Scholz SW, Poewe W. Challenges in the diagnosis of Parkinson's disease. Lancet Neurol. 2021 May; 20(5): 385-397. doi: 10.1016/S1474-4422(21)00030-2.
2. Tolosa E, Vila M, Klein C, Rascol O. LRRK2 in Parkinson disease: challenges of clinical trials. Nat Rev Neurol. 2020 Feb; 16(2): 97-107. doi: 10.1038/s41582-019-0301-2. Epub 2020 Jan 24.PMID: 31980808
3. San Luciano M, Tanner CM, Meng C, Marras C, Goldman SM, Lang AE, Tolosa E, Schüle B, Langston JW, Brice A, Corvol JC, Goldwurm S, Klein C, Brockman S, Berg D, Brockmann K, Ferreira JJ, Tazir M, Mellick GD, Sue CM, Hasegawa K, Tan EK, Bressman S, Saunders-Pullman R; Michael J. Fox Foundation LRRK2 Cohort Consortium. Nonsteroidal Anti-inflammatory Use and LRRK2 Parkinson's Disease Penetrance. Mov Disord. 2020 Oct; 35(10): 1755-1764. doi: 10.1002/mds.28189. Epub 2020 Jul 14.
4. Garrido A, Fairfoul G, Tolosa E, Marti MJ, Ezquerra M, Green AJE. Brain and Cerebrospinal Fluid α-Synuclein Real-Time Quaking-Induced Conversion Identifies Lewy Body Pathology in LRRK2-PD. Mov Disord. 2023 Feb; 38(2): 333-338. doi: 10.1002/mds.29284. Epub 2022 Dec 5.PMID: 36471633
5. Garrido A, Fairfoul G, Tolosa ES, Martí MJ, Green A; Barcelona LRRK2 Study Group. α-synuclein RT-QuIC in cerebrospinal fluid of LRRK2-linked Parkinson's disease. Ann Clin Transl Neurol. 2019 May 9; 6(6): 1024-1032. doi: 10.1002/acn3.772. eCollection 2019 Jun.

2. Biological Subtypes of PD

Speaker:
Francisco Cardoso, MD, PhD
Professor of Neurology, the Federal University of Minas Gerais,
Belo Horizonte, Brazil

Abstracts:

The first well-recognized effort to define subtypes of Parkinson's Disease (PD) was made by Jankovic and colleagues (Neurology 1990; 40: 1529). They proposed the existence of a tremor-dominant and a postural instability and gait difficulty (PIGD) subtypes of PD. The former has a better levodopa response, diminished risk of falls and cognitive impairment, with a better overall prognosis. Patients with PIGD PD respond less to levodopa, fall more often, and develop more dementia, resulting in worse prognosis. Since then, several clinical studies replicate this dichotomic classification. There are proposals of subtyping PD based on non-motor symptoms. Marras and Chaudhuri (Mov Disord 2016; 31: 1095) show that the burden of non-motor findings is greater in PIGD. They suggest there are the following subtypes of non-motor PD: Cognitive, Neuropsychiatric, Sleep, Olfactory, Autonomic. A brainstem route of spread of pathology results in marked sleep dysfunction and dysautonomia. Depression, fatigue, central pain, and weight loss are a result of olfactory to limb progression. Finally, a neocortical subtype is associated with amnestic MCI, apathy, anxiety, and falls with cognitive impairment. Based on clinic-pathological assessment of 111 individuals, De Pablo-Fernández et al (JAMA Neurol 2019; 76: 470) proposed that there are three subtypes of PD: mild motor-predominant, intermediate and diffuse malignant. There are initial pathological differences among them that disappear as the disease progress towards an advanced stage with falls and cognitive decline. More recently, a task force of the International Parkinson Disease and Movement Disorder Society concluded that there are significant shortcomings in the current subtyping of PD. They proposed that the purposes of PD subtyping should be: 1) to predict disease progression; 2) to predict response to treatments; and 3) to identify therapeutic targets for disease modification (Marras et al. Mov Disord 2024; doi: 10.1002/mds.29708).

Biosketch:

Francisco Cardoso MD PhD FAAN is a Professor at the Internal Medicine Department (Neurology Service) of the Federal University of Minas Gerais (UFMG) in Belo Horizonte, Brazil. He is the founder and current Director of the UFMG Movement Disorders Clinic. He did a Neurology Residency at his current institution and a Movement Disorders Fellowship at the Baylor College of Medicine under the supervision of Joseph Jankovic MD. He is the immediate Past-President of the International Parkinson's Disease and Movement Disorders Society (MDS). His main areas of research are choreas, particularly those of auto-immune origin; epidemiology of parkinsonism (he and his associates performed the first population-based study of prevalence of parkinsonism in Brazil); genetics of dystonia (one of the studies of his group led to the discovery of the DYT16 gene). He has authored more than 267 peer-reviewed papers and 120 chapters of books. He is a proud honorary member of the Japanese Neurological Society. During the 5th Pan American Parkinson's Disease and Movement Disorders Congress held in Cartagena, Colombia (February 9-11, 2024), he received the MDS-PAS Leadership Award.

Key articles (Up to 5):

1. Cardoso F, Goetz CG, Mestre TA, Sampaio C, Adler CH, Berg D, Bloem BR, Burn DJ, Fitts MS, Gasser T, Klein C, de Tijssen MAJ, Lang AE, Lim SY, Litvan I, Meissner WG, Mollenhauer B, Okubadejo N, Okun MS, Postuma RB, Svenningsson P, Tan LCS, Tsunemi T, Wahlstrom-Helgren S, Gershanik OS, Fung VSC, Trenkwalder C. A Statement of the MDS on Biological Definition, Staging, and Classification of Parkinson's Disease. Mov Disord. 2023 Dec 13. doi: 10.1002/mds.29683.

2. Camargos S, Scholz S, Simón-Sánchez J, Paisán-Ruiz C, Lewis P, Hernandez D, Ding J, Gibbs JR, Cookson MR, Bras J, Guerreiro R, Oliveira CR, Lees A, Hardy J, Cardoso F, Singleton AB. DYT16, a novel young-onset dystonia-parkinsonism disorder: identification of a segregating mutation in the stress-response protein PRKRA. Lancet Neurol. 2008; 7(3): 207-15.
3. Barbosa MT, Caramelli P, Maia DP, Cunningham MC, Guerra HL, Lima-Costa MF, Cardoso F. Parkinsonism and Parkinson's disease in the elderly: a community-based survey in Brazil (the Bambuí study). Mov Disord. 2006 Jun; 21(6): 800-8.
4. Cardoso F, Seppi K, Mair KJ, Wenning GK, Poewe W. Seminar on choreas. Lancet Neurol. 2006; 5(7): 589-602.
5. Church AJ, Cardoso F, Dale RC, Lees AJ, Thompson EJ, Giovannoni G. Anti-basal ganglia antibodies in acute and persistent Sydenham's chorea. Neurology. 2002; 59(2): 227-31.

3. The Role of Neuro-Imaging in Diagnosing Parkinsonian Disorders

Speaker:
Werner Poewe, MD
Emeritus Professor & Past Chair, Dept of Neurology, Medical University Innsbruck, Innsbruck Austria

Abstracts:

Sensitivity and specificity of current clinical diagnostic criteria parkinsonian disorders are suboptimal, particularly in early disease stages, and clinico-pthological series have reported error rates of up to 20% in distinguishing PD from MSA or PSP. In addition, clinical diagnostic criteria are insensitive to the earliest stages of neuro-degeneration in these disorders which may begin many years before clinical symptoms emerge. Neuroimaging is able to provide additional diagnostic information in both areas of clinical uncertainty. Structural MRI as well as advanced MRI techniques are powerful tools to distinguish between PD, MSA and PSP as consistently shown by many studies and AI algorithms may further enhance the diagnostic yield of MRI datasets. Molecular imaging using SPECT or PET tracers targeting the dopaminergic system has limited specificity for different types of degenerative parkinsonism. However, a striatal dopaminergic deficit on DAT-SPECT is required for a diagnosis of PD and is a valid marker of neurodegeneration in prodromal disease. Very recently , research proposals for a biological defintion of PD have indeed included imaging evidence of striatal dopaminergic denervation as an anchor for both clinical and pre-clinical stages of PD. Ongoing research into PET tracers of α-synuclein will further enhance the role of imaging in detecting the earliest phases of synucleinopathies, as is the case for tau-tracers in tauopathies like PSP. While the sensitivity of MRI contrasts to preclinical neuro-degeneration is still uncertain there is evidence for abnormalities of neuromelanin, iron-sensitive or free water imaging in prodromal stages of PD.

In addition to diagnostic utility neuroimaging also has the potential to measure disease progression and dopaminergic imaging has become a standard outcome in many trials of disease-modification trials in PD. MR volumetry, DTI and neuromelanin imaging have also been studied for their performance in quantifyig disease progression and are starting to be used in trials of disease modifying therapies.

Biosketch:

Professor Werner Poewe is emeritus Professor of Neurology in the Department of Neurology at the Medical University of Innsbruck in Austria. He completed a residency in clinical neurology and psychiatry at the University of Innsbruck and then a British Council research fellowship at University College and Middlesex Hospital Medical School in London. He previously served as a senior lecturer in the Department of Neurology at the University of Innsbruck and as a professor of neurology and acting director of the Department of Neurology at the Virchow Hospital of the Free University of Berlin in Germany before becoming director of the Department of Neurology at the Medical University of Innsbruck in 1995 – a position he held until 2019.

Professor Poewe has served as president of the International Parkinson and Movement Disorder Society (MDS), chair of the MDS European Section, president of the Austrian Society of Neurology, and president of the Austrian Parkinson's Disease Society. He is a corresponding member of the American Neurological Association and French Neurological Society and an honorary member of the German Neurological Society, Japanese Neurological Society, and MDS. He has received the Walther Birkmayer Prize from the Austrian Parkinson's Disease Society, the Dingebauer Prize from the German Neurological Society, and the Research Excellence Award from the Medical University and Leopold-Franzens University of Innsbruck.

Professor Poewe's main research interests are in the field of Parkinson's disease and movement disorders, with particular emphasis on the diagnosis, natural history and clinical trials in the fields of Parkinson's

disease and atypical parkinsonism. He has authored or co-authored more than 800 original articles and reviews in the field of movement disorders with a total of more than 120,000 citations and an h-index of 165 (Google Scholar).
Professor Poewe is listed among top 1% of, highly cited researchers' in neuroscience (Clarivate Web of Science 2023).

Key articles (Up to 5):

1. Höglinger GU, Adler CH, Berg D, Klein C, Outeiro TF, **Poewe W**, Postuma R, Stoessl AJ, Lang AE. A biological classification of Parkinson's disease: th SynNeurGe research diagnostic criteria. Lancet Neurol 2024; 23: 191-204
2. **Poewe W**, Stankovic I, Halliday G, Meissner WG, Wenning GK, Pellecchia MT, Seppi K, Palma JA, Kaufmann H. Multiple system atrophy. Nat Rev Dis Primers. 2022 Aug 25;8(1):56. doi: 10.1038/s41572-022-00382-6. PMID: 36008429
3. Tolosa E, Garrido A, Scholz SW, **Poewe W**. Challenges in the diagnosis of Parkinson's disease. Lancet Neurol. 2021 May;20(5):385-397. doi: 10.1016/S1474-4422(21)00030-2. PMID: 33894193; PMCID: PMC8185633.
4. Mangesius S, Mariotto S, Ferrari S, Pereverzyev S Jr, Lerchner H, Haider L, Gizewski ER, Wenning G, Seppi K, Reindl M, **Poewe W**. Novel decision algorithm to discriminate parkinsonism with combined blood and imaging biomarkers. Parkinsonism Relat Disord. 2020 Aug;77:57-63. doi: 10.1016/j.parkreldis.2020.05.033. Epub 2020 Jun 22. PMID: 32622301.
5. **Poewe W**, Seppi K, Tanner CM, Halliday GM, Brundin P, Volkmann J, Schrag AE, Lang AE. Parkinson disease. Nat Rev Dis Primers. 2017 Mar 23;3:17013. doi: 10.1038/nrdp.2017.13. PMID: 28332488.

Symposium 2 Is the Brain-First and Body-First Progression Hypothesis correct in Parkinson's Disease?

(Kyowa Kirin Co., Ltd.)

Chair:
Tatsushi Toda
Department of Neurology, University of Tokyo

Kazushi Takahashi
Tokyo Metropolitan Neurological Hospital

1. Pathological Progression in PD from the viewpoint of pathology

Speaker:
Renpei Sengoku, MD, PhD
Department of Neurology, The Jikei Univ. Daisan Hospital

Abstracts:

The ongoing discourse surrounding the progression patterns of Parkinson's Disease (PD) has centered on two prominent paradigms: "Brain First" and "Body First." This abstract conducts a pathological evaluation of these progression models, with a specific focus on their associated challenges. The concepts of Brain First and Body First emerged from plotting the results of REM sleep behavior disorder (RBD) presence alongside Metaiodobenzylguanidine (MIBG) and Dopamine transporter imaging. This conceptual framework, considering clinical symptoms, including non-motor manifestations of PD, is highly compelling and reasonable.

However, it's essential to acknowledge that these two patterns alone may not comprehensively explain all reported cases, suggesting that they might not encompass the full spectrum of PD progression. In the context of Body First progression, the potential early detection of changes in peripheral tissues and bodily fluids holds promise for contributing to early diagnosis and biomarker discovery. Moreover, the emphasis on systemic factors and environmental influences underscores the potential for initiating a comprehensive approach to treatment strategies. In conclusion, the determination of which progression pattern is pathologically accurate remains inconclusive. Both the pathological advantages and challenges associated with Brain First and Body First paradigms have the potential to significantly contribute to the evolution of future research and therapeutic approaches in PD.

Biosketch:

1999 School of Medicine, The Jikei University
2008 Graduate School of Medicine, The Jikei University
2008 Department of Neuropathology, New York Brain Bank, Columnia University, NY, NY, USA
2009 Department of Neurology, The Jikei University Hospital
2013 Department of Neurology, Tokyo Metropolitan Geriatric Hospital and Institute of Gerontology
2020 Associate Professor, Depratment of Neurology, The Jikei University
2020 Director, Department of Neurology, The Jikei University Daisan Hospital

Key articles (Up to 5):

1. Sengoku R, Saito Y, Ikemura M, et al. Incidence and extent of Lewy body-related alpha-synucleinopathy in aging human olfactory bulb. J Neuropathol Exp Neurol. 2008; 67: 1072-83.
2. Sengoku R, Matsushima S, Bono K, et al. Olfactory function combined with morphology distinguishes Parkinson's disease. Parkinsonism Relat Disord. 2015; 21: 771-7.
3. Sengoku R. Aging and Alzheimer's disease pathology. Neuropathol. 2020; 40: 22-29.
4. Sengoku R. Neuropathological features of cognitive decline in Lewy body dementia. Neurol Clin Neurosci. 2020; 8: 356-61.
5. Sengoku R, Nakahara A, Umehara T, et al. Frontal lobe dysfunction is associated with reduced DAT-SPECT accumulation in Lewy body disease. J Neurol Sci. 2021; Nov 15; 430: 119998.

2. Pathological progression in PD from the viewpoint of neuroimaging

Speaker:
Tomoko Totsune, MD, PhD
Department of Neurology, NHO Sendai Nishitaga Hospital
Department of Aging Research and Geriatric Medicine, IDAC, Tohoku University

Abstracts:

Parkinson's disease (PD) encompasses multiple subtypes, and the Body-first and Brain-first hypothesis attempts to divide PD into two subtypes based on the onset and progression pattern of alpha-synuclein pathology. The theory has received a lot of attention in recent years, but it is a hypothetical pathophysiological model that is still controversial.

Recently we have demonstrated an unbiased imaging biomarker-based classification of PD based on the degree of impairment in the cardiac sympathetic nerve and nigro-striatal system assessed by nuclear imaging. We demonstrated that PD can be classified into two major subtypes, namely 'cardio-cortical impairment (CC)' and 'dopaminergic-dominant dysfunction (DD)' subtype. Patients with the CC subtype showed diffuse imaging abnormalities in both the peripheral and central nervous systems in the early stage suggesting poor prognosis. In contrast, the DD subtype showed relatively confined nigro-striatal damage and developed cortical asymmetry during the disease progression suggesting a benign clinical course with preserved treatment response.

Imaging biomarker heterogeneity in PD has been also argued in the Brain-first and Body-first hypothesis. However, some of our observations show inconsistencies with their hypothesis and require further discussion. The current session provides insights into heterogeneity of PD from the perspective of nuclear imaging.

Biosketch:

2013.03	Graduated from Tohoku University School of Medicine
2013-2015	Iwate Prefectural Central Hospital: Resident
2015-2016	Dept. Geriatrics and Gerontology, IDAC, Tohoku University: Clinical Fellow
2016-2020	Dept. Nuclear Medicine and Radiology (Dept. Aging Research and Geriatric Medicine), IDAC, Tohoku University: Doctoral course
2020-	Dept. Neurology, NHO Sendai Nishitaga Hospital: Clinical Fellow

Key articles (Up to 5):

1. **Totsune T**, Baba T, Sugimura Y, et al. Nuclear Imaging Data-Driven Classification of Parkinson's Disease. Mov Disord. 2023; 38(11): 2053-2063. doi: 10.1002/mds.29582

Chair:
Genjiro Hirose
Neurological Center, Asanogawa General Hospital
Mitsutoshi Yamamoto
Takamatsu Neurology Clinic

1. Biomarkers for PD

Speaker:
Louis Tan Chew Seng, MBBS, MRCP (UK), FAMS (Neurology), FRCP (Edin)
Senior Consultant, Department of Neurology
Research Director, National Neuroscience Institute
Co-Director
Parkinson's Disease and Movement Disorders Centre
USA Parkinson Foundation
International Centre of Excellence

Abstracts:

Biomarkers are defined characteristics that are measured as an indicator of normal biological processes, pathogenic processes or responses to an exposure or intervention. Biomarkers may be divided into various categories: 1. Diagnostic Biomarkers, 2. Monitoring Biomarkers, 3. Pharmacodynamic / Response Biomarkers, 4. Predictive Biomarkers, 5. Prognostic Biomarkers, 6. Safety Biomarkers, 7. Susceptibility / Risk Biomarker, 8. Digital Biomarkers. All these categories have applications and implications in PD. However, some of these categories are considered more important and being more actively researched in PD.

Biomarkers in PD may range from clinical, genetic, body fluid (blood, CSF, etc), and imaging biomarkers. In PD much work is being focused on validating such biomarkers for prodromal PD, diagnosis of PD, PD subtypes, and prognostic biomarkers. Prognostic biomarkers are also being studied to understand the progression of motor, cognitive, and non-motor features of PD. Key findings from these studies will be presented during the talk.

Several advances in fluid and tissue-based biomarkers have been made in the recent few years. Much work has been performed on alpha-synuclein and other proteins which can be measured from CSF and plasma samples, immunohistochemistry and immunofluorescence from peripheral tissue biopsies, and alpha-synuclein seedling amplification assays (alpha-synuclein SAA). Alpha-synuclein SAA have been found to classify PD patients with high sensitivity and specificity. This finding has set the stage for the development of a biological definition of PD at an early or prodromal stage based on the presence of an abnormal alpha-synuclein SAA and abnormal dopaminergic imaging.

Biosketch:

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

He is the Chair of the Publications Oversight Committee of the International Parkinson and Movement Disorder Society and previously served as its Treasurer, Chair of the Education committee, Chair of the Asian-Oceanian Section of the Society, and a member of the International Executive Committee.

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.

2. GWAS studies in Parkinson's disease: recent advances and implications

Speaker:
Eng-King Tan, MD, MRCP, FRCP
National Neuroscience Institute of Singapore

Abstracts:

Genome-wide association studies (GWAS) is a hypothesis free approach to investigate the genomes from patients and healthy controls to identify genetic variants that are associated with risk of disease or specific clinical features. GWAS studies in Parkinsons disease (PD) have identified > 90 common independent variants, which together accounted for 16–36% of the observed PD heritability. Specific GWAS-linked variants correlated with the age of the disease onset or specific PD subtypes, and also rate of cognitive and motor progression, risk of developing dyskinesia, motor fluctuations, RBD, and daytime sleepiness.

The lecture will summarize key PD GWAS variants, genotype-pheotype correlations and also highlight the potential clinical applications and future research directions.

Biosketch:

Professor Tan Eng King is the Deputy Chief Executive Officer (Academic Affairs), and Senior Consultant with the Department of Neurology, National Neuroscience Institute (NNI). He is also a Professor at the Duke-NUS Medical School and Lee Kong Chian School of Medicine.
Dr Tan has authored more than 500 peer-reviewed papers and book chapters on clinical and neuroimaging studies, functional genomics and experimental therapeutics in Movement Disorders.
He has served as an editor in Parkinsonism related disorders, European Journal of Neurology and Journal of Parkinson's disease, among several others. He has received various national and international accolades including the David Marsden lectureship and Yoshi Mizuno lectureship awards.
Dr Tan has broad research interest including epidemiology, neuroimaging, clinical and functional genomics and experimental therapeutics in Parkinson's disease, essential tremor and other movement disorders.

Chair:
Atsushi Takeda
National Hospital Organization, Sendai Nishitaga Hospital
Yoshio Tsuboi
Department of Neurology, School of Medicine, Fukuoka University

1. The use of patient iPSCs for translational research of neurodegenerative diseases

Speaker:
Haruhisa Inoue, MD, PhD
Center for iPS Cell Research and Application (CiRA), Kyoto University
RIKEN

Abstracts:

Induced pluripotent stem cells (iPSCs) have the ability to proliferate infinitely and differentiate into cells of various organs in the body, including the brain. However, the analysis of neurodegenerative diseases including Parkinson's disease and related disorders using patient-derived cells has been limited, as it is difficult to collect living neurons from patients, and cells have already degenerated or disappeared in postmortem pathological tissues. The advent of iPSCs has made it possible to generate disease models by differentiating patient iPSCs into neural cells and analyzing their phenotype. These models are now being used in the research and development of therapeutics, including the elucidation of pathological conditions and the screening of compounds for drug discovery.

iPSC technology is progressing rapidly, converging with emerging technologies, including organoids. Brain organoids are three-dimensional cell culture systems derived from iPSCs that can be used to analyze physiological and pathological processes in development and disease, and, with a view to clinical application, to study patient-specific cellular responses to therapeutic agents. One of the latest technological advances in the organoid field is to improve the regional specificity of cells leading to the analysis of regionally atypical cell types.

In this symposium, I will talk about the research of neurodegenerative diseases using patient iPSCs toward their clinical applications.

Biosketch:

Haruhisa Inoue received his M.D. from Kyoto University in 1992. He completed a residency in clinical neurology at Kyoto University Hospital and at Sumitomo Hospital. After obtaining his Ph.D. degree from Kyoto University in 2000, he held postdoctoral positions at RIKEN Brain Science Institute and Harvard Medical School.
He is a pioneer in the field of iPSC-based drug discovery and, currently, is head of the Department of Fundamental Cell Technology at the Center for iPSC Research and Application (CiRA) of Kyoto University and a principal investigator at RIKEN.

Key articles (Up to 5):

1. Kondo T, Hara N, Koyama S, Yada Y, Tsukita K, Nagahashi A, Ikeuchi T, Ishii K, Asada T, Arai T, Yamada R, Japanese Alzheimer's Disease Neuroimaging Initiative (J-ADNI), Alzheimer's Disease Neuroimaging Initiative (ADNI), **Inoue H**. Dissection of the polygenic architecture of neuronal Aβ production using a large sample of individual iPSC lines derived from Alzheimer's disease patients. Nature Aging 2: 125–139, 2022.

2. Suong D, Imamura K, Inoue I, Kabai R, Sakamoto S, Okumura T, Kato Y, Kondo T, Yada Y, Klein WL, Watanabe A, **Inoue H**. Induction of inverted morphology in brain organoids by vertical-mixing bioreactors. Communications Biology 4(1): 1213, 2021.
3. Imamura K, Yada Y, Izumi Y, Morita M, Kawata A, Arisato T, Nagahashi A, Enami T, Tsukita K, Kawakami H, Nakagawa M, Takahashi R, **Inoue H**. Prediction model of amyotrophic lateral sclerosis by deep learning with patient induced pluripotent stem cells. Annals of Neurology 89(6): 1226-1233, 2021.
4. Kikuchi T, Morizane A, Doi D, Magotani H, Onoe H, Hayashi T, Mizuma H, Takara S, Takahashi R, **Inoue H**, Morita S, Yamamoto M, Okita K, Nakagawa M, Parmar M, Takahashi J. Human iPSC-derived dopaminergic neurons function in primate Parkinson's disease models. Nature 584(7669): 592-596, 2017.
5. Shi Y*, **Inoue H***, Wu J, Yamanaka S. Induced pluripotent stem cell technology: a decade of progress. Nature reviews Drug Discovery 16(2): 115-130, 2016. (*Correspondence)

2. Gene-based PD drug development

Speaker:
Hiroyuki Ishiura, MD, PhD
Department of Neurology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences

Abstracts:

Parkinson's disease can be classified into monogenic form and polygenic form. The molecular pathogenesis of monogenic familial Parkinson's disease is being elucidated, and several treatments based on the pathogenesis are being proposed. Genome-wide association studies have been conducted for elucidating polygenic form of Parkinson's disease and many disease susceptibility genes have been identified, which is expected to elucidate the molecular pathogenesis and develop therapeutic methods. In this presentation, I would like to discuss the findings from the genetics of Parkinson's disease and the current status of therapeutic development.

Biosketch:

Dr. Hiroyuki Ishiura graduated from the Faculty of Medicine at the University of Tokyo in 2002. After engaging in internal medicine and neurology clinical training, he graduated from the Graduate School of Medicine at the University of Tokyo and obtained a Ph.D. degree in 2011 with a thesis paper on genetic analysis of hereditary spastic paraplegia. After he worked as a post-doc with a Research Fellowship on Young Scientists in 2011, he became an assistant professor at the Department of Neurology at the University of Tokyo Hospital in 2012. He took up a professorship at the Department of Neurology at Okayama University in 2022. His research interest is neurogenetics.

Key articles (Up to 5):

1. Ishiura H, et al. Recent advances in CGG repeat diseases and a proposal of fragile X-associated tremor/ataxia syndrome, neuronal intranuclear inclusion disease, and oculophryngodistal myopathy (FNOP) spectrum disorder. J Hum Genet 2023; 68: 169-174.
2. Ishiura H, et al. Noncoding CGG repeat expansions in neuronal intranuclear inclusion disease, oculopharyngodistal myopathy and an overlapping disease. Nat Genet 2019; 51: 1222-1232.
3. Ishiura H, et al. Expansions of intronic TTTCA and TTTTA repeats in benign adult familial myoclonic epilepsy. Nat Genet 2018; 50: 581-590.
4. Ishiura H, et al. The TRK-fused gene is mutated in hereditary motor and sensory neuropathy with proximal dominant involvement. Am J Hum Genet 2012; 91: 320-329.
5. Ishiura H, et al. C9ORF72 repeat expansion in amyotrophic lateral sclerosis in the Kii peninsula of Japan. Arch Neurol 2012; 69: 1154-1158.

Chair:
Kazunori Ito
IWAMIZAWA NEUROLOGY CLINIC

Masahiko Tomiyama
Department of Neurology, Hirosaki University Graduate School of Medicine

1. Biomarker analysis in prodromal cohort of Lewy body disease

Speaker:
Masahisa Katsuno, MD, PhD
Department of Neurology, Nagoya University Graduate School of Medicine

Abstracts:

Lewy body disease including Parkinson's disease (PD) and dementia with Lewy body (DLB) share not only imaging biomarkers including MIBG myocardial scintigraphy and dopamine transporter scintigraphy (DaT SPECT), but prodromal signs such as constipation, REM sleep behavior disorder (RBD), and hyposmia, which precede the onset of motor or cognitive symptoms by as early as 20 years. We created a high-risk cohort of Lewy body disease by conducting a questionnaire survey of annual health checkup examinees without neurological symptoms using self-reported questionnaires on prodromal Symptoms. Subjects ≥50 years of age with ≥2 core prodromal symptoms (dysautonomia, hyposmia, and RBD), were classified as high-risk. Among 11,452 subjects ≥50 years of age, 759 (6.6%) were classified as high-risk. These subjects had worse values of BDI-II and ESS, in addition to SCOPA-AUT, SAOQ, and RBDSQ. At the second stage of investigation using imaging and fluid biomarkers, about one-third of high-risk subjects showed deficit in MIBG and/or DaT SPECT. In plasma biomarker analysis, AD-related biomarker levels were not elevated in the high-risk group, but NfL levels were higher in the high-risk, PD, and DLB groups than in the low-risk group. NfL elevation was associated with metaiodobenzylguanidine scintigraphy abnormalities in the high-risk group. We have been conducting a placebo-controlled randomized clinical trial of zonisamide for the high-risk subjects with imaging deficits as a preventive therapy (jRCTs041190126).

Biosketch:

Dr. Masahisa Katsuno received his M.D. in 1995 and his Ph.D. in Neurology in 2003, both from Nagoya University in Nagoya, Japan. Following a postdoctoral fellowship at Japan Foundation for Aging and Health, he became an Associate Professor of Institute of Advanced research, Nagoya University, at 2006. From July 2015, he has been the Professor/Chair of Department of Neurology, Nagoya University. He also serves as the Professor/Chair of Department of Clinical Research Education, and the Chief Coordinator of the Doctoral Program for World-leading Innovative & Smart Education (WISE) in Nagoya University Graduate School of Medicine.

Key articles (Up to 5):

1. Yokoi K, Iribe Y, Kitaoka N, et al. Parkinsonism Relat Disord. 2023; 113: 105411.
2. Hattori M, Hiraga K, Satake Y, et al. NPJ Parkinsons Dis. 2023; 9(1): 67.
3. Hattori M, Tsuboi T, Yokoi K, et al. J Neurol. 2020; 267(5): 1516-1526.

2. Movement disorder's treatment from the perspective of community

Speaker:
Tetsuya Maeda, MD, PhD
Division of Neurology and Gerontology, Department of Internal Medicine,
School of Medicine, Iwate Medical University

Abstracts:

In 2022, the results of cinpanemab and prasinezumab have been launched. These could not show the favorable primary outcome, but the publishments mean that the development of disease modifying therapy has begun and come to emerge in Parkinson's disease (PD). The investigators described the lack of appropriate enrollment criteria detecting candidates as one of the reasons in the discussions. Therefore, it is important to establish a methodology to detect optimal candidates for the future success. We have been conducting a prospective cohort study since 2016 targeting community-dwelling people aged 65 years or older to clarify the onset of neurological diseases and their risk factors. As a criteria detecting pre-motor phase of PD, we developed a self-assessment questionnaire referring the research criteria of prodromal PD conducted by the International Parkinson and Movement Disorder Society. As a verification process, we evaluated people already living with PD using this questionnaire by adapting it to their condition and the information obtained during their first visit to our clinic and reinforced at enrollment. The probability was an average of over 0.8. We continue our verification prospectively in our clinic. Using this questionnaire, the crude prevalence rate of premotor PD in our cohort was 5,034.5 per 100,000 persons, where the crude prevalence rate of PD was almost equivalent to the previously reported prevalence rate in Japan.

We hope to contribute to the establishment of screening criteria that will help detect people with a higher risk of developing PD or other neurological diseases through our cohort study. We advocate for broad screening in routine health examinations, but this requires non-invasive screening tools that do not rely on specialized tests or nuclear imaging that constrain the sample size.

Biosketch:

Tetsuya Maeda, MD, PhD (Iwate, Japan) is a Professor and Chairman of "Neurology and Gerontology" in Iwate Medical University. He graduated from Hirosaki University in 1993 and completed his clinical residency and research fellowship in Neurology. His research interests have been focused on the movement disorders, particularly L-dopa metabolism in serotoninergic neurons in Parkinson's disease. He has served on the Japanese Society of Neurology Guideline Committee for the treatment of Parkinson's disease (Chair, Prof. Nobutaka Hattori) from 2014 to 2017.

Key articles (Up to 5):

1. Lang AE, et al. Trial of Cinpanemab in Early Parkinson's Disease. N Engl J Med 2022; 387(5): 408-420. doi: 10.1056/NEJMoa2203395.
2. Pagano G, et al. Trial of Prasinezumab in Early-Stage Parkinson's Disease. N Engl J Med 2022; 387(5): 421-432. doi: 10.1056/NEJMoa2202867.
3. Heinzel S, et al. Update of the MDS research criteria for prodromal Parkinson's disease. Mov Disord 2019; 34(10): 1464-1470. doi: 10.1002/mds.27802.
4. Taguchi K, et al. A cross-sectional study of Parkinson's disease and the prodromal phase in community-dwelling older adults in eastern Japan. Clin Park Relat Disord 2022; 7: 100147. doi: 10.1016/j.prdoa.2022.100147.
5. Taguchi K, et al. Prodromes and probabilities in people living with Parkinson's disease: a retrospective study. JMDD 2021; 31(1): 1-11 [in Japanese].

Chair:
Tadashi Ichikawa
Saitama Prefectural Rehabilitation Center

Shinji Saiki
Department of Neurology, Institute for Medicine, University of Tsukuba

1. Parkinson's disease treatment from the viewpoint of levodopa blood levels

Speaker:
Noriko Nishikawa, MD, PhD
Juntendo University School of Medicine, Tokyo, Japan.

Abstracts:

The gold standard of Parkinson's disease (PD) treatment is dopamine replacement therapy, whose mainstay is levodopa (LD). The unstable absorption and short half-life of LD, and progressive degenerative loss of dopaminergic innervation lead to appearance of motor complications such as wearing-off and dyskinesia. In the early stage of PD, dopamine replacement therapy is applied to adequately ameliorate PD symptoms and to control these motor complications as much as possible. In the advanced stages, the goal of treatment is to adequately control such motor complications and maintain drug-responsive on-time, which leads to the maintenance of the level of activities of daily living and quality of life.

There are two types of LD drug effects: the one drug effect that improves symptoms immediately after administration (SDR: Short Duration Response) and the other one obtained from sustained and stable administration (LDR: Long Duration Response). SDR is closely related to the blood concentration of LD while on the other hand LDR is associated with more complex pharmacodynamic mechanisms that it requires days to weeks till the effect is accumulated after LD initiation. Its formulation should be designed for provision of continuous stimulation, as fasting or high single doses can cause steep concentration rise and pulsatile stimulation can induce dyskinesia. The concomitant use of peripheral COMT inhibitors raises the AUC and the trough value of LD. LDP/CDP (foslevodopa/foscarbidopa), launched last year, maintain stable blood levels for 24 hours, contributing to shorter off-time for patients.

Even if the pharmacokinetics of LD cannot be actually measured, familiarity with the pharmacological characteristics of LD and designing prescriptions with its hemodynamics in mind is a step toward the best possible medication for each individual patient.

Biosketch:

Juntendo University School of Medicine, Tokyo, Japan.(April 2020 - present)
National Center of Neurology and Psychiatry, Tokyo, Japan (January 2018 - March 2020)
Ehime University, Ehime, Japan (April 2005 - December 2017)
Shinshu University, Nagano, Japan (May 2000 - March 2005)

Key articles (Up to 5):

1. Parkinson's disease, Levodopa, Pharmacokinetics, Foslevodopa/foscarbidopa

2. ACP in Movement Disorders

Speaker:
Genko Oyama, MD, PhD, FAAN
Department of Neurology, Juntendo University School of Medicine

Abstracts:

Advanced Care Planning (ACP) involves clarifying a patient's wishes for future medical care and planning in advance for times when the patient may be unable to make decisions. Movement diseases such as Parkinson's disease, Huntington's disease, and Multiple System Atrophy are progressive, affecting the patient's physical and cognitive functions over time. Therefore, initiating ACP earlier is crucial for ensuring a high quality of life and a dignified end-of-life experience. However, ACP practices for patients with movement disorders are often inadequate due to several factors, including a lack of knowledge about ACP among healthcare providers, patients, and their families, as well as healthcare providers' time constraints. The attitudes towards ACP also vary significantly across different cultures and societies, affecting its implementation.

For effective implementation of ACP in movement disorders, educating and raising awareness among healthcare providers, patients, and their families is essential. ACP must be tailored to each patient's specific medical condition, values, and cultural background. Personalized care plans can enhance acceptance by patients and their families. Initiating ACP discussions before the disease progresses is vital, rather than waiting until it has advanced. This proactive approach increases the patient's opportunities for self-determination and decreases uncertainties regarding future medical interventions. Since ACP honors the patient's right to self-determination, it should also emphasize creating legal documents, such as living wills and designating a healthcare proxy. Furthermore, leveraging digital tools and online platforms can facilitate the sharing of information, education, and support for decision-making regarding ACP.

ACP in movement disorders is a critical process for patients, necessitating education, awareness, early intervention, and a personalized approach to enhance its quality and adoption. It is hoped that healthcare providers, patients, and their families will collaborate to comprehend the significance of ACP and actively participate in the process.

Biosketch:

Concurrent appointments
Associate professor, Department of Neurology, Department of Neurodegenerative and Demented Disorders, Department of Home medical care System based on Information and Communication Technology, Department of Drug Development for Parkinson's Disease, Department of Patient Reported Outcome-Based Integrated Data Analysis in neurological disorders, Department of Monitoring Motor Symptoms with Digital System, Department of Research and Therapeutics for Movement Disorders, and, Department of Research for Parkinson's Disease, Department of Medical Metaverse, AI incubation farm, Juntendo University Graduate School of Medicine
Courtesy Associate Professor, Department of Neurology, University of Florida
Education and Postgraduate training
1996-2002: Saitama Medical School, Saitama, Japan (M.D.)
2002-2006: Residency in Neurology at Juntendo University Hospitals, Tokyo, Japan
2006-2010: Juntendo University Faculty of Medicine (Ph.D.), Japan
2009-2011: Research fellow, Center for Movement Disorders & Neurorestoration, University of Florida, FL, USA
Employment
2011-2014: Assistant professor, Department of Neurology, Juntendo University School of Medicine, Tokyo, Japan

2014-present: Associate professor, Department of Neurology, Juntendo University School of Medicine, Tokyo, Japan

Others

Board Certified Member of the Japanese Society of Internal Medicine
Fellow of the Japanese Society of Internal Medicine
Board Certified Member and Councilor of the Japanese Society of Neurology
Councilor of the Japanese Society of Neurological Therapeutics
Board Certified Member of the Japan Society for Stereotactic and Functional Neurosurgery
LEAP steering Committee member and Neurosurgery SIG Steering Committee member of the Movement Disorder Society
Fellow of the American Academy of Neurology
Associate Editor of Frontier in Neurology

Abstracts

2nd Day
17 Mar 2024 (Sunday)

（大塚製薬株式会社）

Chair:
宇川 義一
福島県立医科大学医学部・ヒト神経生理学講座

パーキンソン病の在宅医療

Speaker:
織茂 智之
上用賀世田谷通りクリニック 院長

Abstracts:

近年、高齢発症のパーキンソン病（Parkinson disease：PD）の人が増加してきており，今後在宅医療が必要なPDの人がますます増加することが予想される。これまで在宅療養期のPDの人の診療は主に非脳神経内科医に委ねていたが、訪問診療医は抗PD薬をほとんど調整せず、そのために症状が悪化してしまうことをしばしば経験してきた。2011年から我々脳神経内科医がPDの人の訪問診療を行ったところ、レボドパ換算用量相当量（LEDD）が増加し、運動症状の悪化が抑制された（織茂智之ほか. Jpn J Rehabil Med, 2019）。このような流れを受け、我々は新たに2021年4月から上用賀世田谷通りクリニックでPDなどの神経疾患の人の訪問診療を開始した。2023年12月までに訪問診療を行った神経疾患の人は145人で、PDは86人（年齢80.6歳、罹病期間12.8年、Hoehn-Yahr 4.0）であった。このうち31人が訪問診療を終了した（死亡15人、その他特養入所など）。基本的にLEDDは増加しており、Hoehn-Yahrの進行は抑制されている。PDの人へのアンケート調査によると、メリットでは通院の負担軽減など（80%）、デメリットでは検査や処置に限界がある（10%）であり、満足度は高かった。最近、家族と訪問看護師らの協力のもとに、2人のPDの人にホスレボドパ・ホスカルビドパ持続皮下注を施行した。いずれもオフ時間が非常に短縮し、ADLが改善した。在宅医療を経験して以下のことを学んだ。1）外来診察時とは異なり普段の状態がわかる、2）家庭内でどのように生活をしているかがわかる、3）家庭内の住居環境がわかる、4）きめ細かな診察や薬物投与ができる、5）ゆっくり話を聞くことができる、6）家庭内での介護のキーパーソン、介護の状態がわかる、7）訪問看護師、訪問理学療法士などさまざまな医療スタッフの意見を聞くことができる。これはすなわち多職種連携である。在宅療養期のPDの人においても、脳神経内科医によるきめ細かな訪問診療と多職種連携を行えば、運動症状・非運動症状の悪化を抑制し、本人・家族の満足度が高くなる。

略歴:

1980年4月　東京医科歯科大学神経内科医員
1983年1月　関東逓信病院神経内科医員
1994年1月　関東中央病院神経内科医長
2001年4月　関東中央病院神経内科部長
2017年4月　関東中央病院脳神経内科統括部長
2021年4月　上用賀世田谷通りクリニック院長

主要論文（5報以内）：

1. 織茂智之, 嶋田聖子, 吾妻玲欧, ほか. パーキンソン病の在宅医療. Jpn J Rehabil Med 2019; 56: 213-17.
2. Ikeda M, Mori E, Orimo S, et al. Efficacy of adjunctive therapy with zonisamide versus increased dose of levodopa for motor symptoms in patients with dementia with Lewy bodies: The randomized, controlled, non-inferiority DUEL Study. J Alzheimers Dis 2023; 95: 251-64.
3. Maruoka H, Hattori T, Hase T, et al. Aberrant morphometric networks in Alzheimer's disease have hemispheric asymmetry and age dependence. Eur J Neurosci 2023; Dec 17. doi: 10.1111/ejn.16225.
4. Ebina J, Mizumura S, Ishii N, et al. Reduced ^{123}I-MIBG uptake in the parotid and submandibular glands in patients with Parkinson's disease identified using a quantitative semi-automatic method. J Neurol 2023; 270: 4385-92.
5. Hattori T, Ohara M, Yuasa T, et al. Correlation of callosal angle at the splenium with gait and cognition in normal pressure hydrocephalus. J Neurosurg 2023; 139: 481-91.

（住友ファーマ株式会社）

Chair:
花島 律子
鳥取大学医学部脳神経医科学

パーキンソン病の脳ネットワーク

Speaker:
坪井 崇, MD, PhD
名古屋大学神経内科学

Abstracts:

本セミナーでは、パーキンソン病（PD）における振戦、発声・発話障害、ジスキネジアについて、脳ネットワークの観点からレビューする。PDの振戦は、安静時振戦・姿勢時振戦・運動時振戦として観察され、患者ごとに異なる組み合わせで発生する。振戦では大脳基底核と小脳－視床－大脳皮質ネットワークの関与が明らかにされており、振戦の発生と維持のメカニズムを説明するdimmer-switch modelが提唱されている。さらに、ドパミン系以外にもセロトニン、ノルアドレナリンなどが振戦の発生に関与すると考えられている。脳深部刺激療法（DBS）から得られた脳内の過剰に同期した神経活動（oscillation）の解析は、振戦の病態解明に貢献してきた。Oscillationには治療マーカーとしての役割も期待されている。振戦に対する薬物治療として、レボドパ、ドパミンアゴニスト、MAO-B阻害薬、ゾニサミドなどに有効性が期待できる。

PD患者の約60～90%に運動低下性構音障害が合併するとされる。背景にある病態には、発話に関連する筋群の固縮や無動に留まらず、聴覚フィードバックや運動プログラミングなどのより高次なレベルの異常も関連していると考えられている。また、PDでは吃音も頻繁に発生する。学習された自動化されたシークエンスの実行破綻によるものとされ、ドパミン欠乏による大脳基底核の障害を基盤としつつ、高次機能障害にも影響を受ける。発声・発話障害はDBSの最も一般的な刺激誘発性合併症でもある。PD固有の発声・発話障害に加えてDBS誘発性構音障害が発生することで、フェノタイプは複雑化する。患者ごとの病態に合わせた治療が求められるため、フェノタイプの正確な認識が重要である。

ジスキネジアは大きくpeak dose dyskinesiaとdiphasic dyskinesiaに分類されるが、infusion therapy下ではより複雑で重度なジスキネジアも起こりうる。GPi DBSには強力なジスキネジア抑制作用があり、淡蒼球視床路が重要と考えられている。また、この淡蒼球視床路はlesioning thrapyのターゲットとしても注目されている。

略歴:

2005年3月　名古屋大学医学部卒業
2005年4月　安城更生病院にて初期研修・後期研修
2010年4月　名古屋大学神経内科学大学院
2015年4月　名古屋大学医学部附属病院神経内科　医員
2018年4月　フロリダ大学のMovement disorders center, research fellow
2020年12月　名古屋大学医学部附属病院脳神経内科　助教

主要論文（5報以内）：

1. **Tsuboi T**, Charbel M, Peterside DT, et al. Pallidal Connectivity Profiling of Stimulation-induced Dyskinesia in Parkinson's Disease. Mov Disord 2021; 36(2): 380-388.
2. **Tsuboi T**, Wong JK, Eisinger RS, et al. Comparative connectivity correlates of dystonic and essential tremor deep brain stimulation. Brain 2021; 144(6): 1774-1786.
3. **Tsuboi T**, Jabarkheel Z, Zeilman PR, et al. Longitudinal follow-up with VIM thalamic deep brain stimulation for dystonic or essential tremor. Neurology 2020; 94(10): e1073-e1084.
4. **Tsuboi T**, Cauraugh JH, Wong JK, Okun MS, Ramirez-Zamora A. Quality of life outcomes after globus pallidus internus deep brain stimulation in idiopathic or inherited isolated dystonia: a meta-analysis. J Neurol Neurosurg Psychiatry 2020; 91(9): 938-944.
5. **Tsuboi T**, Watanabe H, Tanaka Y, Ohdake R, Yoneyama N, Hara K, et al. Distinct phenotypes of speech and voice disorders in Parkinson's disease after subthalamic nucleus deep brain stimulation. J Neurol Neurosurg Psychiatry 2015; 86: 856–64.

Japanese Session

（アッヴィ合同会社）

Chair:
大熊 泰之
順天堂大学医学部附属静岡病院

デバイス補助療法の未来

Speaker:
下 泰司
順天堂大学医学部附属練馬病院

Abstracts:

本邦におけるパーキンソン病に対して、主に3種類のデバイスを用いた治療を行うことができる。脳深部刺激療法（DBS）、レボドパカルビドパ持続経腸投与（LCIG）、ホスレボドパ/ホスカルビドパ持続皮下注（ヴィアレブ®）である。これらの治療方法は運動合併症に対して効果があることは証明されているが、問題点がないわけではない。いくつかを挙げると、
①いずれも、それほど治療導入における侵襲性は高くないが、それでもDBSやLCIG は外科的な処置が必要となり、特にDBSの導入には特別な機器、手技が必要となる。
②デュオドーパ、ヴィアレブは導入後も、患者自身または介護者による機器の操作が必要であるが、その操作性は決して簡便ではない。
③特にDBSにおいてデバイスの発展が著しいが、それに伴って機器を操作する側が必要とする知識も増えており、それらをupdateをすることが医療従事者にとって困難となってきている。さらにデバイスの複雑化に伴い、特に外来では、機器の調整に費やす診療時間が長くなっている。
④機器特有のトラブルが生じ得る。
⑤LCIGやヴィアレブの治療継続のための費用。
等が挙げられる。今後、これらの点が改善されれば、デバイス補助療法はさらに普及するものと思われるが、一朝一夕には困難である。本シンポジウムではこれらの問題点も踏まえて今後のデバイス補助療法の未来を予想してみたいと思う。

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