多発性硬化症および視神経脊髄炎に関する国際会議

Sendai Conference 2026

会　期

2026.7/4(土)

9:00~17:00

会　場

TKPガーデンシティ仙台

〒980-6130　仙台市青葉区中央1-3-1

主　催

NPO法人 日本多発性硬化症ネットワーク

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ALEXION AstraZeneca Rare Disease　Tanabe Pharma　CHUGAI 中外製薬 Roche ロシュ グループ　NOVARTIS　Biogen

NPO法人 日本多発性硬化症ネットワーク
JAPAN MULTIPLE SCLEROSIS NETWORK

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Sendai Conference 2026

Date: 4 July, 2026
Venue: Hall 30B, TKP Garden City Sendai
(AER 30F, 1-3-1 Chuo, Aobaku, Sendai)

Time Schedule

9:00～ 9:05	Opening Remarks
9:05～10:05	Oral session 1
10:10～11:00	Sponsored Session 1 (Sponsored by Novartis Pharma K.K.)
11:00～11:10	Coffee Break
11:10～12:00	Sponsored Session 2 (Sponsored by Chugai Pharmaceutical Co., Ltd.)
12:00～12:10	General Membership Meeting of NPO
12:10～12:20	Photo Session
12:20～13:00	Lunch & Poster viewing
13:00～13:50	Sponsored Session 3 (Sponsored by Biogen)
13:55～14:55	Oral session 2
14:55～15:10	Coffee Break
15:10～16:00	Sponsored Session 4 (Sponsored by Alexion Pharma G.K.)
16:00～16:10	Coffee Break
16:10～17:00	Sponsored Session 5 (Sponsored by Tanabe Pharma)
17:00	Closing Remarks (& Award ceremony)

Sendai Conference 2026 Program

9:00～ 9:05 Opening Remarks

OR Dr. Kazuo Fujihara

9:05～10:05 Oral session 1 (Chair: Dr. Tatsuro Misu & Dr. Tomoko Okamoto)

OS1-1 Dr. Naoki Yamamoto (Tohoku University)
Re-evaluation of IPMOGAD criteria by MOG-IgG titer in consecutive patients with suspected CNS inflammatory diseases

OS1-2 Dr. Shogo Yoshida (Keio University)
Outcome of early initiation of complement C5 inhibitors in anti-AQP4 antibody-positive NMOSD: Case series and theoretical considerations

OS1-3 Dr. Kotaro Iida (Kyushu University)
Neuroprotective effects of BK channel activation in a mouse model of NMOSD via suppression of astrocytic inflammation

OS1-4 Dr. Hiroki Masuda (Chiba University)
Longitudinal Comparison of Brain Atrophy Between NMOSD and Healthy Controls: A Japanese–German MRI Study With Exploratory Analysis of Biologic Therapy

10:10～11:00 Sponsored Session 1 (Chair: Dr. Juichi Fujimori)

SS-1 Victoria M. Leavitt (Associate Professor of Neuropsychology, Department of Neurology, Columbia University, USA)
Innovative Digital Tools for Monitoring Disease Activity in Multiple Sclerosis
(Sponsored by Novartis Pharma K.K.)

11:00～11:10 Coffee Break

11:10～12:00 Sponsored Session 2 (Chair: Dr. Yusei Miyazaki)

SS-2 Eoin Paul Flanagan (Marilyn A. Park & Moon S. Park Director, Center for MS & Autoimmune Neurology|Chair, Division of MS and Autoimmune Neurology|Professor of Neurology|Mayo Clinic, Rochester, MN, USA)
MOGAD: From Clinical Characterization to Pathogenesis and Treatment—Lessons Learned from NMOSD(Sponsored by Chugai Pharmaceutical Co., Ltd.)

12:00～12:10 General Membership Meeting of NPO

12:10～12:20 Photo Session

12:20～13:00 Lunch & Poster viewing

13:00～13:50 Sponsored Session 3 (Chair: Dr. Chiyoko Nohara)

SS-3 Anneke van der Walt (Department of Neuroscience, School for Translational Medicine, Monash university, Melbourne, Australia / MS and Neuroimmunology Service, Alfred Hospital, Bayside Health, Melbourne Australia)
Ageing in MS: Pathophysiological and Treatment Considerations
(Sponsored by Biogen)

13:55～14:55 Oral session 2 (Chair: Dr. Yoshiki Takai & Dr. Kazumasa Yokoyama)

OS2-1 Dr. Koji Sekiguchi (Keio University)
Fingolimod to Ofatumumab Switching With Natalizumab Bridging in Relapsing MS

OS2-2 Dr. Itsuki Sano (Osaka University)
Association Between the Immune Semaphorin Sema4A and Response to B-Cell Therapy in Patients with Multiple Sclerosis

OS2-3 Dr. Miwako Fujisawa (Kanmon Medical Center)
Intrinsic Blood-Brain Barrier Dysfunction Contributes to Multiple Sclerosis Pathogenesis

OS2-4 Dr. Youwei Lin (National Center Hospital, National Center of Neurology and Psychiatry)
Novel mode of action and therapeutic efficacy prediction of plasmapheresis in multiple sclerosis (MS)

14:55～15:10 Coffee Break

15:10～16:00 Sponsored Session 4 (Chair: Dr. Jin Nakahara)

SS-4 Dr. Sarosh R. Irani (Professor of Neurology, Professor of Neuroscience, Senior Associate Consultant, Departments of Neurology and Neurosciences, Mayo Clinic, Florida)
Optimizing NMOSD Outcomes: From Pathophysiology to Early Intervention and Long-term C5 Inhibitor Therapy Management
(Sponsored by Alexion Pharma G.K.)

16:00～16:10 Coffee Break

16:10～17:00 Sponsored Session 5 (Chair: Dr. Noriko Isobe)

SS-5 Orhan Aktas, MD (Professor for Molecular Neurology & Acting Chair, Department of Neurology, Heinrich Heine University Düsseldorf, Germany)
B cell Depletion therapy in AQP4-IgG Seropositive NMOSD: German NEMOS Cohort Experience(Sponsored by Tanabe Pharma)

17:00 Closing Remarks (& Award ceremony)

CR Dr. Ichiro Nakashima

Poster Session (Venue: Hall 30A)

P-1 Dr. Hiroshi Kuroda (Fukushima Medical University / Southern TOHOKU Research Institute for Neuroscience)
Utility of blood neutrophil to diagnose bacterial infections under satralizumab treatment for AQP4+NMOSD: a report of two cases

P-2 Dr. Yoshizawa Koki (Chiba University)
Brain Volume in Japanese Patients with MOGAD: A Comparison with Healthy Controls

P-3 Dr. Kyoka Shiroma (Kobe University)
Cerebrospinal Fluid Central Memory T Cells Are Associated with Disease Severity in Japanese Patients with Neuromyelitis Optica Spectrum Disorder

P-4 Dr. Yuji Tomizawa (Juntendo University)
Patient Understanding and Readiness for Shared Decision-Making in Neuromyelitis Optica Spectrum Disorder

P-5 Dr. Akihiro Nakajima (Niigata University)
Autoimmune neutropenia in a patient with NMOSD and MG

P-6 Dr. Haruhiko Motegi (Jikei University)
Disease Stabilization with Ofatumumab in an Elderly Patient with Multiple Sclerosis: A Case Report

P-7 Dr. Jun Shinmi (National Center Hospital, National Center of Neurology and Psychiatry)
Clinical significance of the frequency of plasmablasts among B cells in autoimmune encephalitis

P-8 Dr. Akinobu Hori (Kyoto University)
Unraveling the Role of Microglia in Multiple Sclerosis through Disease Susceptibility Genes

Oral Session 1

Chair: Tatsuro Misu
(Tohoku University Hospital)
Tomoko Okamoto
(Department of Neurology, National Center Hospital, National Center of Neurology and Psychiatry)

OS1-1 Re-evaluation of IPMOGAD criteria by MOG-IgG titer in consecutive patients with suspected CNS inflammatory diseases

Naoki Yamamoto[1], Yoshiki Takai[1], Yuki Matsumoto[1], Toshiyuki Takahashi[2], Naoya Yamazaki[1], Kimihiko Kaneko[1], Mizuki Otomo[1], Naohiro Sakamoto[1], Shu Umezawa[1], Chihiro Namatame[1], Hirohiko Ono[1], Shuhei Nishiyama[1], Hiroshi Kuroda[3,4], Kazuo Fujihara[3,4], Tatsuro Misu[1], Masashi Aoki[1]

1. Department of Neurology, Tohoku University Graduate School of Medicine
2. Department of Neurology, National Hospital Organization Yonezawa National Hospital
3. Multiple Sclerosis & Neuromyelitis Optica Center
4. Department of Multiple Sclerosis Therapeutics, Fukushima Medical University

Introduction: Studies to evaluate the International MOGAD Panel proposed criteria (IPMOGAD criteria) by serum MOG-IgG titer in patients with suspected CNS inflammatory diseases outside MS and AQP4-IgG+NMOSD are limited.

Method: This retrospective cross-sectional study included consecutive patients tested for MOG-IgG at Tohoku University in 2021. Patients with insufficient data or alternative diagnoses, primarily MS or AQP4-IgG+NMOSD, were excluded. For supporting clinical/MRI features (SF) evaluation, acute disseminated encephalomyelitis (ADEM)-like lesions and MOG antibody-associated cortical encephalitis pattern (MOGCEP), defined as lesions extending along the cortical surface, were included. Odds ratios for each SF across serum MOG-IgG titers were estimated. CDE-negative diseases were reviewed in detail.

Results: Of the 1816 patients from whom serum samples were received, we analyzed 547 patients (99 with optic neuritis (ON), 171 with myelitis, 8 with ADEM, 64 with cerebral focal deficits, 49 with brainstem or cerebellar deficits, 26 with cerebral cortical encephalitis, 64 with combined CDEs, and 66 with CDE-negative diseases). Serum MOG-IgG titers were grouped into the following four: seronegative (n=358), 1:16–1:64 (n=75), 1:128–1:256 (n=32), and ≥1:512 (n=82). Logistic regression demonstrated significantly higher prevalence of longitudinally extensive myelitis, H sign, conus lesion, ADEM-like lesions, and cerebral cortical lesions at ≥1:512, and of longitudinal ON, perineural optic sheath enhancement, and MOGCEP at 1:128–1:256 and ≥1:512. 14 CDE-negative patients were MOG-IgG–positive in serum and/or CSF (1 with NMDAR encephalitis, 5 with encephalitis/meningoencephalitis, 1 with seizure, 3 with leukodystrophy, 1 with combined central and peripheral demyelination, and 3 with asymptomatic brain lesions).

Conclusions: In the present cohort, SFs clearly associated with serum MOG-IgG titers were identified. Certain clinical phenotypes such as encephalitis/meningoencephalitis and leukodystrophy may warrant consideration for future criteria expansions.

Oral Session 1

Chair: Tatsuro Misu
(Tohoku University Hospital)
Tomoko Okamoto
(Department of Neurology, National Center Hospital, National Center of Neurology and Psychiatry)

OS1-2 Outcome of early initiation of complement C5 inhibitors in anti-AQP4 antibody-positive NMOSD: Case series and theoretical considerations

Shogo Yoshida, Koji Sekiguchi, Jin Nakahara

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

Background: Complement C5 inhibitors (C5IT) significantly reduce relapses in anti-AQP4 antibody-positive neuromyelitis optica spectrum disorders (AQP4+NMOSD). Recently, potential additional benefit of early initiation of C5IT for the recovery after the attack has been discussed. We aimed to preliminary evaluate the clinical impact of early initiation of C5IT for AQP4+NMOSD in our university hospital.
Methods: We retrospectively collected and analyzed 20 AQP4+NMOSD case series who were treated for acute attacks during January 2015 and December 2025 in our hospital. Eight cases to whom C5IT (eculizumab or ravulizumab) was initiated within 60 days from the attack were compared with 12 cases to whom standard-of-care (SoC) treatments were utilized. The primary outcome measure was the change in Expanded Disability Status Scale (EDSS) scores during 6–12 months post-attack: Outcomes were considered "good" if patients achieved full clinical recovery (EDSS=0), improved by ≥1 EDSS score for cases with nadir scores of EDSS≤ 3, or improved by ≥2 points for cases with nadir scores of >3.
Results: Numerically higher patients exhibited "good" outcome in the C5IT group compared with the SoC group, albeit not statistically significant (75% vs. 50%; Odds ratio 2.8; P = 0.373). In particular, three out of eight patients in the C5IT group were refractory to conventional acute therapies (e.g. intravenous methylprednisolone and/or plasma exchange) while demonstrating clinically recovery following C5IT.
Conclusions: Treatment selection bias may have influenced the results. Nonetheless, our case series do not demonstrate negative clinical impact by the early initiation of C5IT, and some particular cases were in favor of the potential benefit. Prospective controlled studies are warranted to draw a final conclusion.

Oral Session 1

Chair: Tatsuro Misu
(Tohoku University Hospital)
Tomoko Okamoto
(Department of Neurology, National Center Hospital, National Center of Neurology and Psychiatry)

OS1-3 Neuroprotective effects of BK channel activation in a mouse model of NMOSD via suppression of astrocytic inflammation

Kotaro Iida[1], Takuya Matsushita[2], Satoshi Nagata[1], Ezgi Ozdemir Takase[1], Keisuke Mizutani[1], Siqi Song[1], Kaoru Kashu[1], Takayuki Fujii[1], Mitsuru Watanabe [1], Katsuhisa Masaki[1,3], Ryo Yamasaki[4], Noriko Isobe[1]

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3. Department of Neurology, Hamanomachi Hospital
4. Department of Neurology and Geriatric Medicine, Ehime University Graduate School of Medicine

Objective: In genome-wide association study conducted in Japanese neuromyelitis optica spectrum disorders (NMOSD) patients, a single nucleotide polymorphism in the *KCNMA1* (potassium calcium-activated channel subfamily M alpha 1) gene was associated with disease disability. *KCNMA1* encodes the BK (Big potassium) channel, which is expressed in astrocytes. We hypothesized that BK channels are related to disease severity via regulating inflammatory astrocytes and evaluated the effects of BK channels on astrocytes and a mouse model of NMOSD.

Methods: Primary mouse astrocytes were treated with A1 cocktail (IL-1α, TNFα, and C1q) or aquaporin-4 antibodies (AQP4-ab). C3 expression and NF-κB nuclear translocation rate of astrocytes were evaluated by immunofluorescence staining after treatments with BK channel activator NS19504 or DMSO. We also quantified IL-6 production in the supernatant of astrocyte cultures. Reverse transcription quantitative polymerase chain reaction (RT-qPCR) was performed to evaluate changes in *IL-6* expression levels caused by AQP4-ab following treatment with NS19504 or DMSO. In an animal model, we administered vehicle or NS19504 intraperitoneally to NMOSD model mice, which were induced by intracerebral injection with AQP4-ab and human complement. Motor functions were evaluated by the balance beam test, and the AQP4 loss area was measured by immunofluorescence staining.

Results: In astrocyte cultures, C3 expression and NF-κB nuclear translocation induced by A1 cocktail or AQP4-ab were reduced by NS19504 treatment compared to the control. IL-6 production in the supernatant caused by A1 cocktail was also reduced by NS19504 treatment. Although IL-6 in the supernatant was not detectable after AQP4-ab treatment, RT-qPCR analysis revealed that NS19504 reduced *IL-6* expression levels (all comparisons, $p < 0.05$). In the animal model, NS19504 reduced the number of paw slips at beam tests and the AQP4 loss area compared to the vehicle.

Conclusion: BK channel activation may ameliorate the severity of NMOSD by modulation of neurotoxic astrocytes.

Oral Session 1

Chair: Tatsuro Misu
(Tohoku University Hospital)
Tomoko Okamoto
(Department of Neurology, National Center Hospital, National Center of Neurology and Psychiatry)

OS1-4 Longitudinal Comparison of Brain Atrophy Between NMOSD and Healthy Controls: A Japanese–German MRI Study With Exploratory Analysis of Biologic Therapy

Hiroki Masuda,[1] Lina Anderhalten,[2,3] Masahiro Mori,[1] Tadashi Shiohama,[4,5] Norihide Maikusa,[6,7] Shigeki Hirano,[1] Akiyuki Uzawa,[1] Mayumi Muto,[1,8] Ryohei Ohtani,[1,9] Tomohiko Uchida,[9] Reiji Aoki,[1] Hitomi Kitagawa,[10] Yoshiyuki Hirano,[10] Japanese Alzheimer's Disease Neuroimaging Initiative (J-ADNI)†, Friedemann Paul,[2,3] and Satoshi Kuwabara[1]

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†A list of authors and their affiliation appears at the end of the paper.

Background: Differences in brain atrophy rates between patients with aquaporin-4 IgG-positive neuromyelitis optica spectrum disorder (AQP4Ab+NMOSD) and healthy controls (HCs), as well as the impact of biologic agents (BIO) on brain atrophy, have not been fully examined.
Methods: In total, 72 patients with AQP4Ab+NMOSD identified at Chiba University Hospital or in the Berlin Registry of Neuroimmunological Entities (Chiba, 63; Berlin, 9) and 52 age- and sex-matched HCs (Chiba, 47; Berlin, 5) were included. Only patients without relapses between the baseline and follow-up MRI scans were included. Regional brain volumes were normalised to the intracranial volume. Patients who continuously used BIOs (satralizumab, eculizumab, ravulizumab, inebilizumab or rituximab) between the two MRI scans were included in the BIO subgroup, whereas those who continuously received non-BIO preventive treatments, such as steroids or immunosuppressants, during the same period comprised the non-BIO subgroup. We applied a longitudinal combined association test to correct for MRI scanner differences.
Results: Patient age and the interval between MRI scans did not differ between the groups. The NMOSD group exhibited a lower whole-brain volume than the HC group at follow-up ($P < 0.001$) and a significantly higher whole-brain atrophy rate ($P = 0.009$). Patients with smaller subcortical grey matter (SGM) volumes at follow-up MRI exhibited greater clinical disability ($\rho = -0.27$, $P = 0.022$), a higher number of relapses before baseline ($\rho = -0.28$, $P = 0.016$) and older age at onset ($\rho = -0.46$, $P < 0.001$). In the BIO subgroup (n=15), early initiation of treatment ($P = 0.013$) and a higher relative duration of BIO exposure ($P = 0.028$) were associated with lower annualized SGM atrophy rates.
Conclusions: This study suggested progressive silent brain atrophy in patients with AQP4Ab+NMOSD and that early BIO initiation might prevent the progression of brain atrophy.

Sponsored Session 1

Chair: Juichi Fujimori
(Professor, Department of Neurology,Tohoku Medical and Pharmaceutical University, Sendai, Miyagi, Japan)

SS-1 Innovative Digital Tools for Monitoring Disease Activity in Multiple Sclerosis

Victoria M. Leavitt, PhD, FAAN

Associate Professor of Neuropsychology, Department of Neurology, Columbia University, USA.

Detecting early functional decline, which may signify progression or relapse in adults with multiple sclerosis (MS), is a key challenge for clinicians. Precise, accurate, and reliable measurement tools are essential for early recognition and appropriate treatment of disease-specific changes. One of the most intractable symptoms of MS is cognitive impairment, which patients frequently describe but clinicians struggle to capture in the context of a regular clinic visit. Moreover, our current gold standard cognitive tests often fail to align with MRI measures of disease burden, gold standard measures of disease progression such as motor function, and patient self-report, making it difficult for clinicians to know whether and how to modify a patient's treatment based on cognitive complaints. Another challenge is the practical barrier to performing frequent cognitive assessments in the clinic. Accessible, precise cognitive measurement tools are urgently needed. Digital tools represent a promising opportunity by potentially enabling more precise and personalized measurements. In this talk, Dr. Leavitt will introduce a novel digital tool designed in her laboratory to measure cognitive changes in adults with MS. The Language and Memory Test (LMT) is a quick and easy app-based test that has been tested in 15 countries on 5 continents, and has the potential to dynamically inform tailored treatment decisions and support more informed and more frequent monitoring of MS disease activity. Given the practical challenges of conducting a full spectrum of functional tests in the clinic, digital solutions are gaining momentum as a practical and potentially superior option to traditional tools.

CURRICULUM VITAE

Victoria M. Leavitt is a clinical neuropsychologist and cognitive neuroscientist who directs the Leavitt Laboratory in the Department of Neurology at Columbia University Irving Medical Center in New York City. After completing her bachelor's degree at Cornell University in Ithaca, New York, she earned her PhD from the City University of New York under the mentorship of John J. Foxe. Through the support of an NIH-funded pre-doctoral grant, she conducted her dissertation research employing EEG to study basic sensory processing deficits in schizophrenia at St. Vincent's Hospital in Dublin. She subsequently completed a National Multiple Sclerosis Society-funded postdoctoral fellowship at the Kessler Foundation before joining the faculty of Columbia University, where she currently holds the position of Associate Professor.

The primary focus of her laboratory's research is developing novel measurement tools and precision treatments for cognitive impairment in adults with multiple sclerosis. Dr. Leavitt serves on the editorial board of the journal Neurology and is the recipient of grants from the National Institutes of Health, the United States Department of Defense, and the National Multiple Sclerosis Society. Most recently, the Leavitt Laboratory received gifts from over 400 individual donors in response to a patient-led fundraising effort to support the development of new digital tools for MS.

Chair: Yusei Miyazaki
(Department of Neurology, National Hospital Organization Hokkaido Medical Center)

SS-2 MOGAD: From Clinical Characterization to Pathogenesis and Treatment—Lessons Learned from NMOSD

Eoin Paul Flanagan, M.B., B.Ch.

Marilyn A. Park & Moon S. Park Director, Center for MS & Autoimmune Neurology|Chair, Division of MS and Autoimmune Neurology|Professor of Neurology|Mayo Clinic, Rochester, MN, USA

The discovery of aquaporin-4-IgG as the first biomarker of an acquired CNS inflammatory demyelinating disease was paradigm shifting. It enabled neuromyelitis optica spectrum disorder (NMOSD) to be distinguished from multiple sclerosis, supported development of disease-specific diagnostic criteria, and catalyzed major advances in understanding NMOSD pathogenesis. These insights were subsequently translated into clinical trials of targeted therapies, leading to multiple highly efficacious approved treatments for AQP4-IgG–positive NMOSD. The later discovery of myelin oligodendrocyte glycoprotein-IgG and recognition of MOG antibody-associated disease (MOGAD) as a distinct disease entity established MOGAD as the second antibody-defined inflammatory CNS demyelinating disease with its own diagnostic criteria. Although MOGAD shares some clinical and radiologic features with NMOSD, important differences in disease biology, attack phenotype, relapse risk, recovery, and treatment response are increasingly recognized. Applying lessons learned from AQP4-IgG–positive NMOSD to MOGAD has accelerated clinical characterization, mechanistic investigation, and therapeutic development. These advances are now informing targeted clinical trials in MOGAD, several of which are beginning to report results, marking an important transition from disease definition toward pathogenesis-based treatment.

CURRICULUM VITAE

Dr Eoin Flanagan is a Professor of Neurology, The Marilyn A. Park and Moon S. Park Director of The Center for Multiple Sclerosis and Autoimmune Neurology, Chair of the Division of MS and Autoimmune Neurology and Program Director of the Autoimmune Neurology Fellowship at Mayo Clinic, Rochester, MN. He completed medical school at University College Dublin in Ireland and completed neurology residency, fellowships in neuroimmunology and a Master's in Clinical and Translational Science at Mayo Clinic. He has been Principal Investigator on an NIH RO1 grant studying MOGAD and was a co-author of its 2023 diagnostic criteria. He also has expertise in autoimmune encephalitis, myelitis, MS, NMOSD and paraneoplastic neurologic disorders.

Chair: Chiyoko Nohara
(Tokyo Metropolitan Ebara Hospital)

SS-3 Ageing in MS: Pathophysiological and Treatment Considerations

Anneke van der Walt

Department of Neuroscience, School for Translational Medicine, Monash university, Melbourne, Australia
MS and Neuroimmunology Service, Alfred Hospital, Bayside Health, Melbourne Australia

Multiple sclerosis (MS) has traditionally been considered a disease of young adults, yet more than half of people living with MS today are aged 50 years or older. This demographic shift demands a fundamental rethinking of how we understand, monitor, and treat MS across the lifespan.

The pathophysiology of MS in older adults is shaped by the converging forces of immunosenescence, inflammageing, and reproductive ageing. Immunosenescence drives a progressive dysregulation of both adaptive and innate immune responses, while the accompanying state of chronic low-grade inflammation exacerbates neurodegeneration, impairs remyelination, and reduces synaptic plasticity. In females, the menopausal decline in oestrogen and progesterone coincides with accelerating brain atrophy and disability accumulation, independent of disease duration. These biological changes contribute to an accelerated ageing phenotype in MS, with brain age estimated to exceed chronological age by approximately a decade.

Diagnosing MS in older adults presents distinct challenges. Cerebral small vessel disease, cervical spondylotic myelopathy, and other age-associated conditions share overlapping clinical and radiological features with MS, increasing misdiagnosis risk. Late-onset MS is more likely to present with progressive phenotypes and faster disability accrual, yet often goes unrecognised or inadequately treated.

Treatment decision-making in this population requires careful individualisation. While high-efficacy disease-modifying therapies remain beneficial for controlling focal inflammatory activity, their risk profiles are amplified by age-related immunosenescence, comorbidities, and frailty.

The optimal timing and strategies for treatment de-escalation or discontinuation remain poorly defined, with existing evidence limited primarily to lower-efficacy agents.
This presentation will synthesise current evidence on the pathophysiology, diagnosis, and treatment of MS in older adults and highlight critical knowledge gaps.

CURRICULUM VITAE

A/Prof van der Walt completed her undergraduate training in South Africa before relocating to Australia. She completed specialist training in neurology in Melbourne followed by a PhD in Neuroscience in 2013 under the supervision of Professors Trevor Kilpatrick and Helmut Butzkueven at the University of Melbourne.
She currently serves as the Director of the Multiple Sclerosis, Neuroimmunology Unit and Neuro-ophthalmology Service, Alfred Health, Melbourne. She leads the MS and Neuro-ophthalmology Research group in the Department of Neuroscience, School for Translational Medicine, Monash University. She is the Chief Operating Officer of the MSBase Foundation, which oversees the research and operational programs of the MSBase Registry. The MSBase registry is an international multiple sclerosis outcomes registry in more than 40 countries and contains more than 150,000 patient records. Prof Van der Walt has published over 230 papers since completing her PhD.
Her main research focuses on the development and implementation of digital, neuroimaging, visual, and other biomarkers of subclinical progression and ageing in the MS clinic. In addition, she is passionate about advancing understanding of the long-term safety of MS treatments, especially for women and older people with MS. Her work is funded by the National Health and Medical Research Council of Australia and MS Australia.
Her detailed profile can be accessed here: https://www.monash.edu/medicine/ccs/neuroscience/research/van-der-walt-group

Oral Session 2

Chair: Yoshiki Takai
(Tohoku University Hospital)
Kazumasa Yokoyama
(Tohsei Center for Neurological Diseases)

OS2-1 Fingolimod to Ofatumumab Switching With Natalizumab Bridging in Relapsing MS

Koji Sekiguchi, Jin Nakahara

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

Background: Rebound inflammatory activity after fingolimod (FTY) cessation is a clinical concern in relapsing-remitting multiple sclerosis (RRMS), particularly during transition to anti-CD20 therapy.
Objective: To describe outcomes of natalizumab (NAT) bridging before ofatumumab (OFA) initiation after FTY cessation.
Methods: We retrospectively reviewed a single-center case series of RRMS patients who discontinued FTY, received NAT bridging for at least 5 months, and then initiated OFA. Outcomes were clinical relapse, MRI activity, confirmed EDSS worsening, and progressive multifocal leukoencephalopathy (PML).
Results: Twelve patients (83% female) underwent FTY-NAT-OFA sequencing. Relapse rates decreased during FTY treatment and remained 0 after FTY cessation with NAT bridging. No clinical relapses or MRI activity occurred within 90 days after FTY cessation. During subsequent follow-up, one asymptomatic MRI event occurred. No PML was observed.
Conclusion: In this cohort, NAT bridging before OFA initiation after FTY cessation was associated with no observed early (within 90 days) clinical or radiological disease activity. NAT bridging may be a practical sequencing option for selected patients, but larger comparative studies are needed to clarify effectiveness, safety, and optimal duration.

Oral Session 2

Chair: Yoshiki Takai
(Tohoku University Hospital)
Kazumasa Yokoyama
(Tohsei Center for Neurological Diseases)

OS2-2 Association Between the Immune Semaphorin Sema4A and Response to B-Cell Therapy in Patients with Multiple Sclerosis

Itsuki Sano, Toru Koda, Tatsusada Okuno

Department of Neurology, The University of Osaka Graduate School of Medicine

Multiple sclerosis (MS) treatment options have expanded substantially in recent years, including the introduction of ofatumumab (OFB), an anti-CD20 monoclonal antibody targeting B cells. Semaphorin 4A (Sema4A), a member of the semaphorin family, is a neural guidance molecule that has also been implicated in inflammatory immune responses. Our group previously demonstrated that serum Sema4A levels are elevated in approximately 30% of patients with MS. Furthermore, we reported that patients with high Sema4A levels tend to exhibit a poor response to interferon-β (IFN-β) therapy, whereas fingolimod (FTY) remains effective in this subgroup.

In the present study, we investigated the relationship between serum Sema4A levels and therapeutic response to OFB in patients with MS. Clinical and laboratory data were retrospectively collected from patients with MS who had been treated with OFB. Serum Sema4A levels were measured using enzyme-linked immunosorbent assay (ELISA), and patients were categorized into high- and low-Sema4A groups. Nineteen patients were classified into the high-Sema4A group and 29 into the low-Sema4A group. Clinical characteristics and therapeutic outcomes were compared between the two groups. Treatment efficacy was evaluated based on the annualized relapse rate, changes in Expanded Disability Status Scale (EDSS) scores, and radiological disease activity before and after OFB treatment. Statistical analyses were performed to assess differences between the groups.

No significant difference in treatment response to OFB was observed between the high- and low-Sema4A groups. These findings suggest that OFB may show therapeutic efficacy regardless of serum Sema4A status.

Oral Session 2

Chair: Yoshiki Takai
(Tohoku University Hospital)
Kazumasa Yokoyama
(Tohsei Center for Neurological Diseases)

OS2-3 Intrinsic Blood-Brain Barrier Dysfunction Contributes to Multiple Sclerosis Pathogenesis

Miwako Fujisawa[1,4],Sarah Guimbal[1], Chiara Stüdle[1], Pelin Kasap[1], Amandine Mathias[2], Renaud du Pasquier[2], Kinya Matsuo[3], Hideaki Nishihara[3] , Britta Engelhardt[1]

1. Theodor Kocher Institute, University of Bern, Switzerland
2. Laboratory of Neuroimmunology, University of Lausanne, Switzerland
3. Department of Neurotherapeutics, Yamaguchi University, Japan
4. Department of Neurology, Kanmon Medical Center, Japan

Background: Multiple sclerosis (MS) is considered an autoimmune disease of the central nervous system (CNS). Blood-brain barrier (BBB) breakdown is amongst the earliest pathological hallmarks observed in MS. The mechanisms leading to BBB dysfunction are incompletely understood and are generally thought to be a consequence of the autoimmune neuroinflammatory process in MS. We have challenged this view as we observed that human induced pluripotent stem cell (hiPSC) derived brain microvascular endothelial cells (BMECs) from persons with MS (pwMS) display impaired barrier properties and an inflammatory phenotype when compared to their counterparts from healthy controls (HC).

Methods: Here we established additional hiPSCs from a total of 6 HC, 2 persons with radiologically isolated syndrome (RIS) - as a preclinical stage of MS - who later developed MS, and 10 persons with MS and differentiated them into BMECs using the extended endothelial cell culture method (EECM). Phenotype and functional properties were characterized by immunostaining, permeability measurements and transendothelial electrical resistance (TEER). Their transcriptional profile was investigated by bulk RNA sequencing (RNAseq).

Results: RIS- and MS-derived EECM-BMECs display impaired barrier properties when compared to HC-derived EECM-BMECs. Transcriptional profiling distinguished MS and RIS-derived EECM-BEMCs from those derived from HC. For example, when compared to HC-derived EECM-BMECs, RIS- and MS-derived EECM-BMECs display reduced expression levels of CLDN5 which is accompanied by interrupted junctional localization of claudin-5 protein. In addition, we found modulation of the Semaphorin-4D (SEMA4D) signalling pathway in MS-versus HC-derived EECM-BMECs and could show that soluble SEMA4D decreased SEMA4D mRNA expression in EECM-BMECs.

Conclusion: Our observations underscore that intrinsic alterations in brain endothelial cells manifested at the genetic or epigenetic, transcriptional and ultimately phenotypic level cause or contribute to altered BBB function already in pwRIS, which in combination with additional risk factors is crucial for the development of clinical MS.

Oral Session 2

Chair: Yoshiki Takai
(Tohoku University Hospital)
Kazumasa Yokoyama
(Tohsei Center for Neurological Diseases)

OS2-4 Novel mode of action and therapeutic efficacy prediction of plasmapheresis in multiple sclerosis (MS)

Youwei Lin[1,2,3], Kimitoshi Kimura[4], Tomoko Okamoto[1,3], Yuji Takahashi[1], Takashi Yamamura[2,3]

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2. Department of Immunology, National Institute of Neuroscience, NCNP, Tokyo, JAPAN
3. Multiple Sclerosis Center, National Center Hospital, NCNP, Tokyo, JAPAN
4. Department of Neurology, Kyoto University Graduate School of Medicine, Kyoto, JAPAN

MS patients initially present relapse of symptoms affecting central nervous system, and some of them later follow a chronic progressive course with accumulation of disability.

Nowadays disease-modifying drugs with remarkable efficacy to prevent relapses has expanded treatment options for MS, enabling control of disease activity in many cases and suppression of disease progression in some cases. Nevertheless, there are still refractory cases, especially those with insufficient remission after acute treatment for relapse.

Plasmapheresis, a treatment for acute relapses and exacerbations of MS, is performed for patients who have failed to steroid pulse therapy, and its main effect is to regulate humoral immunity by removing plasma components, including autoantibodies. However, no specific autoantibodies have been identified in MS, the mechanism and the patients in which plasmapheresis is expected to be effective in MS have not been clarified.

We have been promoting combined immunotherapy, including plasmapheresis, based on the hypothesis that residual symptoms from insufficient remission are not sequelae but smoldering states due to inadequate treatment, which may lead to chronic progression. In the process, we have found that IFNγ-producing Th1 cells are predictive biomarkers for therapeutic efficacy of plasmapheresis (especially IAPP), and that IAPP suppresses the function of Th1 cells, and also decreases the frequency of CD11c-positive B cells, and reduces the amount of immunoglobulins in all subclasses.

The fact that IAPP depletes immunoglobulins regardless of the subclasses, not just IgG1 and IgG3, demonstrates a novel mode of action that goes beyond removal of plasma components by the adsorption properties of the column to modulation of cellular function. The mechanism that plasmapheresis can regulate immune cell function by removing etiological agents or disease-related factors is an advantage of plasmapheresis alone, we believe that plasmapheresis can be useful as an alternative or combination therapy for treating intractable cases involving with complex pathologies.

Chair: Jin Nakahara
(Department of Neurology, Keio University School of Medicine)

SS-4 Optimizing NMOSD Outcomes: From Pathophysiology to Early Intervention and Long-term C5 Inhibitor Therapy Management

Sarosh R Irani BMBCh MA (Oxon) DPhil FRCP FEAN

1.Professor of Neurology and Neuroscience - Mayo Clinic, Florida
2.Associate Editor - Brain
3.Medical Research Council, Senior Clinical Fellow – University of Oxford

The discovery of autoantibodies directed at neuroglial surface targets has transformed neurology, defining clinically distinctive immunotherapy-responsive syndromes.

In this lecture, I will focus on pathogenic autoantibodies against the water channel, aquaporin 4 (AQP4), discovered in patients with a syndrome known as neuromyelitis optica spectrum disorder (NMOSD). Patients with AQP4-antibody mediated NMOSD can now choose from a series of proven medications which induce B cell depletion, IL6R inhibition and terminal complement inhibition. Each of these reduce relapse rates to various extents. This intervention is key as relapses are the main source of disability in patients with NMOSD.

My lecture will explore clinically-relevant concepts around relapses and these medications, biomarkers for NMOSD, and how these relate to the underlying pathophysiology of astrocyte damage and loss of immune tolerance. I will utilize these observations to highlight cellular sources which produce AQP4-antibodies, both in the periphery and the CNS – within patient tissue, CSF, bone marrow and lymph node compartments. These insights will mechanistically address the potential clinical-serological paradox, hypothesizing why AQP4-antibodies may persist despite clinical remission. Finally, I will review triggers of tolerance failure, including thymic mechanisms, infections and iatrogenic therapies.

Our increasing understanding of CNS autoantibody-associated diseases holds promise for further improved diagnostic and therapeutic paradigms, ultimately leading to improvements in patient outcomes.

CURRICULUM VITAE

EDUCATION AND QUALIFICATIONS

2023 FANA (Fellow of the American Neurological Association)
2018 FRCP (Fellow of the Royal College of Physicians)
2018 FEAN (Fellow of the European Academy of Neurology)
2018 FRCP (Fellow of the Royal College of Physicians)
2010 DPhil in Clinical Neurology
2003 BM BCh, BA (Oxon) Oxford University, Corpus Christi College

CLINICAL AND RESEARCH CAREEER SUMMARY

I am an international leader in both clinical and scientific research regarding Autoimmune Neurology, in particular autoantibody mediated diseases of the CNS. I led discovery of LGI1 and CASPR2 antibodies, their associated phenotypes, immunology and genetic associations, and my group has advanced key clinical and scientific observations around NMDAR- and AQP4-antibody associated diseases. I am currently a Professor of Neurology and Neurosciences and lead the Mayo Florida Autoimmune Neurology Group. I have generated $£20 million in grants from diverse sources and attracted and managed a team of, in all, 1200 scientists, clinicians and students, including 12 completed PhDs and 10 successfully pursuing independent academic careers. I have been an invited speaker at >100 international meetings, have a H-Index of 74, and have published >250 PubMed-cited papers including several senior author, highly cited, seminal articles in Nature, PNAS, Science Advances, Lancet journals, Brain, Annals of Neurology and JAMA Neurology, alongside several invited editorials.

PRIZES

2024 Cozzarelli Prize, to recognize recently published PNAS papers of outstanding quality
2021 International Society of Neuroimmunology (ISNI) Mid-career clinical science award
2019 Royal College of Physicians Graham-Bull Prize in Clinical Science; Goulstonian Lectureship

KEY RECENT PUBLICATIONS

1. Kleeman S…..Irani SR, Furukawa H, Jankowitz T. Ectopic NMDAR expression in cancer unmasks germline-encoded autoimmunity. Nature 2026 Mar 25.
2. Al-Diwani A….Irani SR. The distinctive psychopathology of NMDAR-antibody encephalitis compared with primary psychoses: an international, multicentre, retrospective phenotypic analysis. Lancet Psychiatry. 2026 Jan;13(1):47-61.
3. Sun B… Irani S.R. Permissive central tolerance plus defective peripheral checkpoints license pathogenic memory B cells in CASPR2-antibody encephalitis. Science Advances. 2025;11(16):eadr9986.
4. Theorell J, .. Irani SR. Ultrahigh frequencies of peripherally matured LGI1- and CASPR2-reactive B cells characterize the cerebrospinal fluid in autoimmune encephalitis. Proc Natl Acad Sci U S A. 2024;121(7):e231104912
5. Damato V…Irani SR. Rituximab abrogates aquaporin-4-specific germinal center activity in patients with neuromyelitis optica spectrum disorders. Proc Natl Acad Sci U S A. 2022;119(24):e2121804119.

Chair: Noriko Isobe
(Professor, Department of Neurology, Graduate School of Medical Sciences, Kyushu University)

SS-5 B cell Depletion therapy in AQP4-IgG Seropositive NMOSD: German NEMOS Cohort Experience

Orhan Aktas

Department of Neurology, Medical Faculty and University Hospital, Heinrich Heine University Düsseldorf, Düsseldorf, Germany, with the German Neuromyelitis Optica Study Group (NEMOS)

Preventing relapses in neuromyelitis optica spectrum disorder (NMOSD) remains a central therapeutic goal. Inebilizumab (INE), a humanized anti-CD19 monoclonal antibody approved in Germany for AQP4-IgG+ NMOSD since 2022 and for IgG4-related disease since 2026, offers broader B-cell targeting compared with rituximab (RTX), a chimeric anti-CD20 antibody long used in NMOSD. While RTX depletes mature CD20+ B cells, INE additionally targets CD19+ plasmablasts and subsets of short-lived plasma cells, potentially enabling more sustained suppression of pathogenic antibody responses.

Using data from the German Neuromyelitis Optica Study Group (NEMOS) registry, we conducted a retrospective, multicenter, real-world analysis of adult NMOSD patients treated with INE and contextualized these findings with data from RTX-treated patients. Outcomes included clinical efficacy (EDSS, annualized attack rate), laboratory parameters (immunoglobulin levels, leukocyte and lymphocyte counts), and infection rates. Multivariate regression was applied to identify infection risk factors. In a subgroup, peripheral blood mononuclear cells were analyzed by CyTOF using two 50-marker panels to characterize B- and T-cell phenotypes and functional states. Results of the ongoing analysis will be presented, suggesting high efficacy of INE in relapse prevention and, deeper and broader B-cell depletion.

CURRICULUM VITAE

Orhan Aktas, MD
Professor for Molecular Neurology & Acting Chair, Department of Neurology
Heinrich Heine University Düsseldorf, Germany

Orhan Aktas, MD, is Professor of Molecular Neurology and Acting Chair of the Department of Neurology at Heinrich Heine University Düsseldorf, Germany. His main research interests are in the field of neuroimmunology, including Multiple Sclerosis (MS), Neuromyelitis Optica Spectrum Disorder (NMOSD), and MOG-IgG-associated Disease (MOGAD).

Professor Aktas has authored numerous publications in leading journals and has served as principal investigator or co-investigator in major international clinical trials for MS and NMOSD. He is Co-Leader of the Biomarkers Focus Area for the International Panel for NMOSD Diagnosis (IPND, 2025), a member of the Guthy Jackson Charitable Foundation International Clinical Consortium, Scientific Advisor to The MOG Project, Ambassador for The Sumaira Foundation, and a founding member and country coordinator of the German NEMOS study group.

He has received several prestigious awards, including the Hermann Oppenheim Award for Multiple Sclerosis and a Heisenberg Professorship from the German Science Foundation, and is an active referee for international research organizations.

P-1 Utility of blood neutrophil to diagnose bacterial infections under satralizumab treatment for AQP4+NMOSD: a report of two cases

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2. Multiple Sclerosis and Neuromyelitis Optica Center, Southern TOHOKU Research Institute for Neuroscience, Koriyama, Japan.
3. Department of Neurology, Southern TOHOKU Research Institute for Neuroscience Southern TOHOKU General Hospital, Koriyama, Japan.

Background: Satralizumab is a biologic blocking interleukin-6 receptor, used for relapse prevention of aquaporin-4 antibody-positive neuromyelitis optica spectrum disorder (AQP4+NMOSD). The drug inhibits pyrexia and C-reactive protein (CRP) production; may mask bacterial infections. Here we report clinical and laboratory findings of two patients with AQP4+NMOSD who developed afebrile bacterial infections under satralizumab treatment, focusing on utility of blood neutrophil for the diagnosis.

Case report: Case 1. A 47-year-old female with AQP4+NMOSD under 28-month satralizumab treatment developed afebrile abdominal pain with normal white blood cell (WBC) count (6530/mm^3), neutrophil count (5780/mm^3), and CRP level (<0.03 mg/dL). Abdominal CT scan exhibited a swollen appendix with fecal pellets. She was diagnosed with acute appendicitis and underwent laparoscopic appendectomy following antibiotic administration. Case 2. A 55-year-old female with AQP4+NMOSD under 19-month satralizumab treatment developed afebrile back pain with normal WBC (6070/mm^3), neutrophil (3750/mm^3), and CRP (<0.03 mg/dL). Abdominal CT scan exhibited an enlarged gallbladder suggesting acute cholangitis with biliary stones. She underwent endoscopic therapy following antibiotic administration.

In the two patients, the neutrophil count and neutrophil to lymphocyte ratio (NLR) decreased during satralizumab treatment whereas the neutrophil change ratio (NCR), defined as the ratio of present to previous neutrophil counts, did not. At the time of infections, these parameters were elevated compared to the confidence intervals derived from the values during non-infectious periods.

Conclusions: Patients with AQP4+NMOSD under satralizumab treatment may develop afebrile bacterial infections without CRP elevation. In such conditions, elevation of neutrophil count, NLR, and NCR may be a clue to diagnosis.

P-2 Brain Volume in Japanese Patients with MOGAD: A Comparison with Healthy Controls

Yoshizawa Koki[1], Masuda Hiroki[1], Aoyama Shinji[1], Ohtani Ryohei[2], Muto Mayumi[3], Uzawa Akiyuki[1], Hirano Shigeki[1], Mori Masahiro[1]

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3. Department of Neurology, Chiba Rosai Hospital/ 2-16 Tatsumidai-higashi, Ichihara-shi, Chiba, Japan

Introduction: This study aimed to compare brain volumes between Japanese patients with myelin oligodendrocyte glycoprotein antibody–associated disease (MOGAD) and healthy controls (HCs).
Methods: Twenty-eight Japanese patients with MOGAD in the remission phase and 20 Japanese HCs were included. Image analyses were performed using Statistical Parametric Mapping (SPM) 25, and statistical analyses were conducted using JMP. Lesion filling based on fluid-attenuated inversion recovery (FLAIR) images was applied to both groups. Brain volume ratios were compared using the Mann–Whitney U test. Voxel-based morphometry (VBM) analysis was performed to identify regional differences ($P < 0.001$ (uncorrected), cluster-level FWE-corrected $P < 0.05$). Correlations between brain volume ratios and disease duration or number of attacks in the MOGAD group were assessed using Spearman's rank correlation coefficient.
Results: Age and sex ratio did not differ between the two groups. In the MOGAD group, the median disease duration was 4.9 years and the median number of attacks was 2. The median gray matter volume ratio was significantly lower in the MOGAD group than in HCs (0.45 vs. 0.49, $P < 0.001$). The median white matter volume ratio was significantly higher in the MOGAD group than in HCs (0.30 vs. 0.29, $P = 0.020$). No significant difference was found in the total-brain volume ratio between the MOGAD group and HCs (0.76 vs. 0.78, $P = 0.43$). VBM analysis revealed significant atrophy in the bilateral thalamus and temporal lobes in the MOGAD group. No significant correlations were observed between brain volume ratio and either the number of attacks or disease duration in the MOGAD group.
Conclusion: Japanese patients with MOGAD exhibited a reduced gray matter volume ratio compared with HCs, with significant atrophy in the bilateral thalamus and temporal lobes, whereas the white matter volume ratio was significantly higher compared with HCs.

P-3 Cerebrospinal Fluid Central Memory T Cells Are Associated with Disease Severity in Japanese Patients with Neuromyelitis Optica Spectrum Disorder

Kyoka Shiroma[1], Atsushi Hara[2], Ryosuke Takeda[1], Asato Tsuji[1], Ritsu Akatani[1], Shusuke Koto[1], Norio Chihara[1]

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2. Hyogo Prefectural Harima-Himeji General Medical Center, Kobe, Japan.

Background: Neuromyelitis optica spectrum disorder (NMOSD) is an autoimmune astrocytopathy characterized by relapsing inflammatory attacks of the optic nerves and spinal cord. Despite advances in diagnosis and treatment, clinical severity varies widely among patients. The immunological factors associated with severe neurological disability remain incompletely understood. We investigated whether lymphocyte subset profiles in peripheral blood and cerebrospinal fluid (CSF) are associated with disease severity in Japanese patients with NMOSD.

Methods: We retrospectively studied 13 Japanese patients with NMOSD admitted to our hospital between 2018 and 2023. Peripheral blood mononuclear cells and CSF cells were obtained during inflammatory attacks. Blood samples from healthy controls and CSF samples from patients with idiopathic normal pressure hydrocephalus or multiple sclerosis were used as controls. T- and B-cell subsets were analyzed by flow cytometry, and patients were categorized into mild and severe groups according to clinical disability and functional outcome.

Results: Age, sex, baseline Expanded Disability Status Scale score, disease duration, and relapse number were comparable between the mild and severe groups. In contrast, CSF immune profiling showed significantly higher proportions of CD4+ central memory T cells in the severe group than in the mild group (mean 39.12 vs. 10.01, p=0.0196). CD8+ central memory T cells were also increased in severe cases (mean 22.30 vs. 5.11, p=0.0159). These differences were not observed in peripheral blood. Plasmablasts and double-negative B cells in either compartment were not significantly associated with severity.

Conclusion: Increased central memory T-cell frequencies in CSF may represent compartmentalized CNS immune activation and may help identify patients with more severe NMOSD.

P-4 Patient Understanding and Readiness for Shared Decision-Making in Neuromyelitis Optica Spectrum Disorder

Yuji Tomizawa[1], Isamu Takai[1], Hanna Okada[1], Cossu Davide[1], Yasunobu Hoshino[1], Kazumasa Yokoyama[2], Taku Hatano[1]

1. Department of Neurology, Faculty of Medicine, Juntendo University
2. Tohsei Center for Neurological Diseases

Background and Objective: In the management of intractable neurological diseases, including neuromyelitis optica spectrum disorder (NMOSD), the importance of shared decision-making (SDM) has been increasingly recognized to improve patients' quality of life (QOL) and long-term outcomes. High-quality SDM requires that patients have an adequate understanding of their disease and available treatment options. This study aimed to exploratorily evaluate the current status of disease and treatment understanding among patients with NMOSD.

Methods: A questionnaire survey regarding disease understanding was conducted among patients with NMOSD attending our institution. The questionnaire consisted of two domains: "Disease and Symptoms" and "Treatment." It included closed-ended questions assessing disease- and treatment-related knowledge, as well as visual analogue scales (VAS) evaluating perceptions toward therapeutic interventions. The survey results were retrospectively collected and analyzed.

Results: Responses were obtained from 24 patients with aquaporin-4 antibody-positive (AQP4-Ab-positive) NMOSD. Patients were divided into two groups according to the total scores for disease and treatment understanding. The high-understanding group showed a trend toward a higher rate of biologic agent use. In addition, willingness to actively participate in treatment decision-making, assessed using the VAS, was significantly higher in the high-understanding group.

Discussion and Conclusion: Disease and treatment understanding among patients with NMOSD may be associated with treatment selection and willingness to participate in shared decision-making. Assessing patient understanding may be useful for patient support during treatment introduction and for implementing SDM in clinical practice. However, the questionnaire used in this study was exploratorily developed, and establishment of a standardized method for evaluating disease understanding specific to NMOSD patients will be required in future studies.

P-5 Autoimmune neutropenia in a patient with NMOSD and MG

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3. Medical Education Center, Graduate School of Medical and Dental Sciences, Niigata University

Background: Autoimmune neutropenia is a subtype of neutropenia characterized by the immune-mediated destruction of neutrophils and is often associated with several underlying autoimmune diseases. On the other hand, drug-induced neutropenia has been reported in patients with neuromyelitis optica spectrum disorders (NMOSD) receiving disease-modifying therapy (DMT), such as satralizumab (anti-interleukin-6 receptor antibody) or B-cell depleting drugs, although it is often mild and self-limited. We report a case in which anti-neutrophil antibody testing contributed to the diagnosis and elucidation of the pathogenesis of autoimmune neutropenia.

Case summary: We report a 33-year-old female patient diagnosed with acetylcholine receptor antibody-positive myasthenia gravis (MG) at 19 years old, followed by aquaporin-4 antibody-positive NMOSD at 21 years old. Treatment with eculizumab/ravulizumab (anti-C5 antibodies), prednisolone (5 mg/day), and tacrolimus successfully controlled disease activity in both NMOSD and MG after flares. The patient subsequently remained relapse-free for 6 years. However, the white blood cell count dropped to 1060/μL, with neutropenia (130/μL) developing during treatment without infectious complications. No abnormalities were detected on bone marrow examination. Anti-neutrophil antibodies were detected, indicating the concomitant of autoimmune neutropenia. Her neutropenia did not improve sufficiently with granulocyte-colony-stimulating factor, but responded to intravenous methylprednisolone and an increased prednisolone dose (10 mg/day). After the patient was switched from ravulizumab to inebilizumab (anti-CD19 antibodies), the neutrophil count increased (4,530/μL), and both NMOSD and MG have remained relapse-free for 13 months.

Conclusion: Not only DMTs but also anti-neutrophil antibodies could cause neutropenia in patients with NMOSD. Sustained improvement and no relapses of NMOSD/MG since switching from ravulizumab to inebilizumab with the use of glucocorticoids could indicate that neutropenia in this case should be caused by autoimmune etiologies. Testing for antineutrophil antibodies is useful for elucidating the pathogenesis of neutropenia and for determining treatment strategies, including switching to an alternative DMT.

P-6 Disease Stabilization with Ofatumumab in an Elderly Patient with Multiple Sclerosis: A Case Report

Haruhiko Motegi, Teppei Komatsu, Masahiro Mimori, Motohiro Okumura, Hiromasa Matsuno, Asako Onda, Kenichiro Sakai, Yasuyuki Iguchi

Department of Neurology, The Jikei University School of Medicine

Background: The management of multiple sclerosis (MS) in elderly patients presents significant clinical challenges due to immunosenescence and an elevated risk of treatment-related adverse events. As a result, clinicians frequently hesitate to initiate high-efficacy disease-modifying therapies (DMTs) in this population.
Methods: The clinical course and treatment outcomes of a 77-year-old female patient with highly active MS who achieved disease stabilization following the initiation of ofatumumab are described.
Results: The patient initially developed myelitis at age 67, presenting with numbness and weakness in the right upper extremity. At age 73, she experienced right-finger numbness and was admitted to the hospital. Brain and spinal MRI revealed periventricular and spinal cord lesions. Cerebrospinal fluid analysis demonstrated positive oligoclonal bands (4 bands) and an IgG index of 0.53, resulting in a diagnosis of MS (Expanded Disability Status Scale: 2). The anti-JC virus (JCV) antibody index was elevated at 3.27, and the baseline Processing Speed Test (PST) score was 41 (Z-score: 0.48). Dimethyl fumarate was initially prescribed but discontinued due to adverse skin symptoms. The patient subsequently experienced two relapses within one year. Due to high disease activity, ofatumumab was introduced despite advanced age. After initiation, the patient continued ofatumumab for 4 years and achieved complete clinical stability with no further relapses, and cognitive function, as evaluated by the PST, remained stable.
Conclusions: This case demonstrates that ofatumumab can safely and effectively achieve disease stabilization and preserve cognitive function in an elderly patient with highly active MS. High-efficacy DMTs should be considered based on disease activity rather than excluded solely due to chronological age, particularly when other options are limited by tolerability or high JCV seropositivity.

P-7 Clinical significance of the frequency of plasmablasts among B cells in autoimmune encephalitis

Jun Shinmi[1],Tomoko Okamoto[1,2],Wakiro Sato[2,3,4], Youwei Lin[1,2], Kyoko Kanazawa[1], Hotake Takizawa[1], Shinji Oda[1],Yuka Hama[1],Tasuku Ishihara[1],Shuho Namatame[1],Takashi Yamamura[2,3],Yuji Takahashi[1]

1. Department of Neurology, National Center Hospital, National Center of Neurology and Psychiatry
2. Center of Multiple Sclerosis, National Center Hospital, National Center of Neurology and Psychiatry
3. Department of Immunology, National Institute of Neuroscience, National Center of Neurology and Psychiatry
4. Translational Medical Center, National Center of Neurology and Psychiatry

Objective: The frequency of plasmablasts among B cells (PB), which are antibody-producing cells, is known to be elevated in autoimmune diseases. We investigated the clinical significance of PB in autoimmune encephalitis (AE).

Methods: Among patients in whom PB was measured at our institution, we included those who met the "probable" criteria of the Graus criteria for AE, excluding patients with NMOSD and MOGAD. We examined the associations between PB levels, disease classification, and clinical course.

Results: A total of 11 AE patients (age at PB measurement: 24–64 years) were analyzed. The disease classifications, number of patients, and PB (%) were as follows: combined central and peripheral demyelination (CCPD), 2 patients (31.2% [patient positive for anti-myelin antibody], 2.19%); anti-VGluT2 antibody-positive encephalitis, 1 patient (17.8%); anti-Flotillin antibody-positive encephalitis, 1 patient (14.5%); Sjögren's syndrome with central nervous system involvement, 1 patient (11.6%); Hashimoto's encephalopathy, 2 patients (11.3%, 2.1%); anti-Sez6l2 antibody-associated encephalitis, 1 patient (7.4%); Bickerstaff brainstem encephalitis, 1 patient (4.1%); chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS), 1 patient (2.0%); and others, 1 patient (25.9%). Seven of the 11 patients showed elevated PB levels (defined as greater than the mean + 2 standard deviations of healthy controls [21 individuals]: ≥5.4%). Among these 7 patients with elevated PB, AE-associated antibodies were subsequently identified in 6 patients (86%). In the patient with anti-myelin antibody-positive CCPD, who showed the highest PB level, intensive immunotherapy including IVMP, PE, and IVIg was administered. PB improved from 31.3% to 13.5%, accompanied by clinical improvement.

Conclusion: Elevated PB levels were observed in 64% of AE patients. In the high-PB group, the antibody-positive rate was high (86%), suggesting that PB may reflect antibody-mediated immune mechanisms. PB may serve as a useful biomarker for diagnosis, disease activity assessment, and evaluation of treatment response in AE.

P-8 Unraveling the Role of Microglia in Multiple Sclerosis through Disease Susceptibility Genes

Akinobu Hori[1], Shinya Hirata[1], Hiroki Tanaka[1], Takakuni Maki[1], Ryosuke Takahashi[2, 3], Riki Matsumoto[1], Kimitoshi Kimura[1, 2]

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2. Department of Therapeutics for Multiple System Atrophy, Kyoto University Graduate School of Medicine
3. Kyoto University Office of Research Acceleration

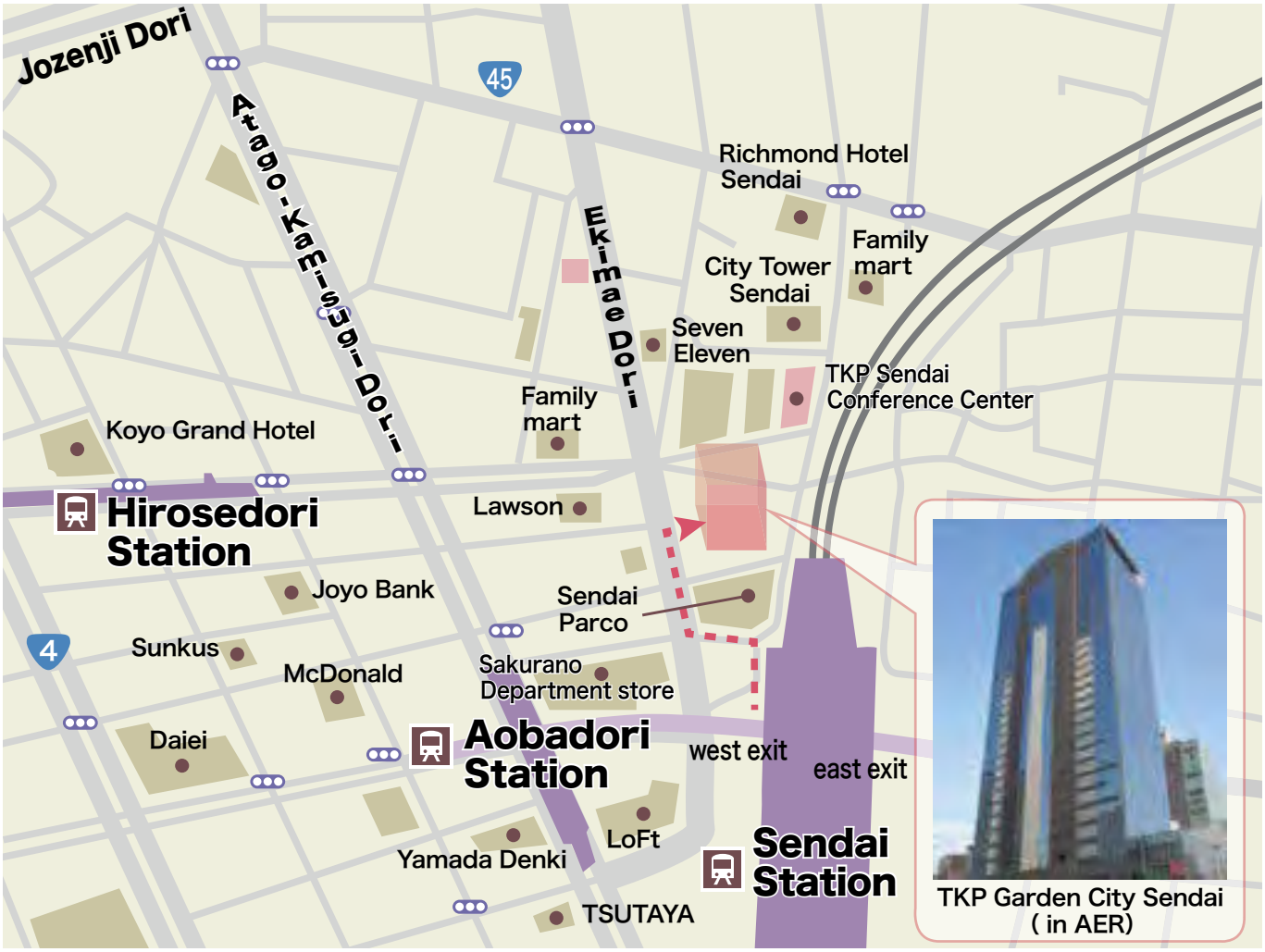
Objective: Multiple sclerosis (MS) is a multifactorial disease influenced by both genetic and environmental factors. Genome-wide association studies (GWAS) have prioritized 551 MS susceptibility genes, highlighting the key role of immune cells, including microglia. Progression independent of relapse activity (PIRA) has recently attracted attention as an important component of chronic disability progression in MS. Paramagnetic rim lesions (PRLs), which reflect iron-enriched proinflammatory microglia at the edge of chronic active lesions, are associated with poor prognosis and PIRA, suggesting that sustained microglial activation may contribute to chronic progression.

Methods: From the 551 genes, we extracted those enriched in microglia using public mouse and human brain RNA-seq datasets. Candidate genes were knocked out in BV2 cells, a mouse microglial cell line, using the CRISPR-Cas9 system. Subsequently, the effects of these genetic modifications were evaluated on microglial functions.

Results: We found 35 out of the 551 genes that were enriched in microglia compared to other cell types in the central nervous system. Monoclonal cell lines lacking each susceptibility gene (21 genes, 1–3 cell lines for each) were established. We also developed assays based on myelin debris stimulation to evaluate changes in phagocytic function and ROS production. Several specific gene-KO BV2 clones showed altered myelin debris phagocytosis, ROS production, or both.

Conclusion: We identified 35 microglia-enriched genes among 551 MS susceptibility genes prioritized by GWAS and generated monoclonal specific gene-KO BV2 clones. Functional screening showed that several KO clones altered myelin debris phagocytosis and/or myelin debris-induced ROS production. Candidate genes will be validated using independent KO clones, mouse primary microglia, and iPSC-derived microglia, followed by in vivo studies for the final candidate genes. These findings may clarify microglial mechanisms underlying MS progression and inform future therapeutic strategies.

Access



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