9th Congress of the Pan-Asian Committee for Treatment and Research in Multiple Sclerosis (PACTRIMS)
Thursday 27-Saturday 29 October 2016, Bangkok, Thailand
MedImmune is the global biologics research and development arm of AstraZeneca, a global, innovation-driven biopharmaceutical business that focuses on the discovery, development and commercialization of small molecule and biologic prescription medicines. MedImmune is pioneering innovative research and exploring novel pathways across key therapeutic areas, including respiratory, inflammation and autoimmunity; cardiovascular and metabolic disease; oncology; neuroscience; and infection and vaccines.

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XXIII World Congress of Neurology
September 16–21 2017
Kyoto, Japan
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Abstract Submission Deadline: April 6 2017
Early Registration Deadline: June 14 2017

Defining the Future of Neurology
WELCOME NOTE

Dear Friends and Colleagues,

Welcome to Bangkok, the city of Angels. We are very pleased to host you in this mystical and magical city at our 9th PACTRIMS congress. For those of you who have been attending our past congresses, welcome back and for those of you are with us for the first time, we hope this congress will be rewarding and enjoyable.

The MS community has made notable progress over the last decade. We strongly believe that PACTRIMS has also played a significant contribution to the medical education of MS in this part of the world. Over the last 8 years, we have brought together top researchers and reputable key note speakers to participate in our congress. This year is no different and our Scientific Program Committee led by Dr. Junichi Kira have once again put together a most compelling and exciting program for you.

Some of the key lectures are from guests such as Amit Bar-Or, Ludwig Kappos, Jacqueline Palace, Wim Van Hecke, Anthony Traboulsee, Achim Gass, Ho Jin Kim, Naraporn Prayoonwiwat, Stephen Reddel, Takakuni Maki, Izumi Kawachi, Masoud Etemadifar, Yuko Shimizu and Yaou Liu.

PACTRIMS congresses also value highly the opportunity afforded to delegates to be able to interact socially both in the evenings and at the day 2 luncheon. We, together with the Local Organising Committee have therefore prepared an exciting social program for you to complement the Scientific Program. We hope you will enjoy your stay in this beautiful city of Bangkok while learning more about the advances in the knowledge and practice of MS and NMOSD.

We are indebted to those who have worked tirelessly to prepare this meeting for us, especially Kays Asia, Pharma and industry and the PACTRIMS subcommittees and on behalf of all we wish you a most enjoyable, satisfying and memorable meeting.

Sincerely,

Takahiko Saida                William Carroll           Naraporn Prayoonwiwat
President              Vice President & Treasurer     Local Organising Chairman
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**PROGRAMME OVERVIEW**

**Thursday, 27 October 2016**

**Grand Ballroom Level 2**

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<th>Session</th>
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<tr>
<td>13:00-14:30</td>
<td><strong>European Charcot Foundation Symposium</strong>&lt;br&gt;<strong>Progressive MS</strong>&lt;br&gt;Chairpersons: Giancarlo Comi (Italy) &amp; William Carroll (Australia)&lt;br&gt;1. Introductory Remarks about International Progressive MS Alliance — William Carroll (Australia)&lt;br&gt;2. Progressive MS in Asia — Kazuo Fujihara (Japan)&lt;br&gt;3. Pathogenesis — Hans-Peter Hartung (Germany)&lt;br&gt;4. Treatment in Progressive MS — Giancarlo Comi (Italy)</td>
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<tr>
<td>14:30-15:00</td>
<td><strong>Coffee Break</strong></td>
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<td>15:00-15:15</td>
<td><strong>Opening Ceremony</strong>&lt;br&gt;1. Welcome Address by the Chairman, 2016 Local Organising Committee — Naraporn Prayoonwiwat (Thailand)&lt;br&gt;2. Opening Address by the President, PACTRIMS — Takahiko Saida (Japan)&lt;br&gt;3. Special Remarks by the Deputy Director General of the Department of Medical Services, Ministry of Public Health — Pannet Pangputhipong (Thailand)</td>
</tr>
<tr>
<td>15:15-17:15</td>
<td><strong>Opening Lecture Series</strong>&lt;br&gt;<strong>B Cell-Targeted Therapy Unravels the Critical Roles of B Cells in Demyelinating Disease</strong>&lt;br&gt;Chairperson: Naraporn Prayoonwiwat (Thailand)&lt;br&gt;1. The Expanding Role of B Cells in CNS Demyelinating Disease — Amit Bar-Or (Canada)&lt;br&gt;<strong>Opening Lecture-1</strong>&lt;br&gt;2. B Cell Therapies in MS — Ludwig Kappos (Switzerland)&lt;br&gt;<strong>Opening Lecture-2</strong>&lt;br&gt;3. B Cell Therapies in Neuromyelitis Optica Spectrum Disorder — Ho Jin Kim (Republic of Korea)&lt;br&gt;<strong>Opening Lecture-3</strong></td>
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<tr>
<td>17:15-17:30</td>
<td><strong>Coffee Break</strong></td>
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<td>17:30-19:00</td>
<td><strong>MAGNIMS Teaching Session</strong>&lt;br&gt;<strong>Using MRI to Diagnose MS and Related Disorders</strong>&lt;br&gt;Chairpersons: Jacqueline Palace (United Kingdom) &amp; Kazuo Fujihara (Japan)&lt;br&gt;1. MS MRI Features and Its Differentiation from Vascular Disease and Aging — Olga Ciccarelli (United Kingdom)&lt;br&gt;2. Differentiating the Imaging Features of MS from NMOSD and ADEM — Jacqueline Palace (United Kingdom)&lt;br&gt;3. Case Examples of Other MS Mimics — Kazuo Fujihara (Japan)</td>
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<tr>
<td>19:30-21:00</td>
<td><strong>Welcome Reception @ Flow Restaurant, 1F, Millennium Hilton Bangkok</strong></td>
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Friday, 28 October 2016

Grand Ballroom Level 2

<table>
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<tr>
<th>Time</th>
<th>Session/Activity</th>
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| 8:30-10:00 | **MedImmune Sponsored Symposium**  
* B Cell Biology in NMOSD: From Pathology to Innovative Therapeutics |
| 10:00-10:30 | Coffee Break |

### Oral Presentation-1 (10:30-11:26)

**Multiple Sclerosis**  
Chairperson: Allan Kermode (Australia)

- **[O-1] [14min]** Evaluation of 2016 MAGNIMS MRI Criteria for Dissemination in Space in Patients with A Clinically Isolated Syndrome  
  — Hyun Jae-Won (Republic of Korea)

- **[O-2] [14min]** A Prospective, Observational Study on the Progression of Clinically Isolated Syndrome (CIS) to Multiple Sclerosis for at least 4-year period  
  — Long-Sun Ro (Taiwan)

- **[O-3] [14min]** The Effects of the HLA–DRB1*04:05 Allele on Intracortical Lesions Detected by 3-Dimensional Double Inversion Recovery Imaging in Japanese Patients with Multiple Sclerosis  
  — Koji Shinoda (Japan)

- **[O-4] [14min]** The Role of Genetic Susceptibility Variants in Predicting Clinical Course in Multiple Sclerosis: A Cohort Study  
  — Gongbu Pan (Australia)

### Oral Presentation-2 (11:26-12:08)

**Neuromyelitis Optica**  
Chairperson: Fu-Dong Shi (China)

- **[O-5] [14min]** Evaluation of NMOSD2015 Imaging Guideline for Differential Diagnosis of CDMS and NMOSD in Thai Patients  
  — Orasa Chawalparit (Thailand)

- **[O-6] [14min]** Predictors of Treatment Response to Immunosuppressive Therapy in Neuromyelitis Optica Spectrum Disorder  
  — Su-Hyun Kim (Republic of Korea)

- **[O-7] [14min]** Outcomes of Rituximab Therapy in Anti-Rituximab Antibody-Positive Patients with NMOSDs  
  — Lin-Jie Zhang (China)

### One Minute Oral Presentation of Selected Posters (12:08-12:30)

Chairperson: Makoto Matsui (Japan)

- **[O-8]** Distinct Repertoires of CD4 and CD8 T Cells in Multiple Sclerosis Patients with and without Deletion-type Copy Number Variations  
  — Guzaiali Maimaitijiang (Japan)

- **[O-9]** Deep Learning of Joint Myelin-T1w MRI Features on Normal-Appearing Brain Tissues Distinguishes Multiple Sclerosis from Healthy Controls  
  — Yougjin Yoo (Canada)

- **[O-10]** Clinico-Radiological Phenotype and Number of Lesions on MRI Influences Medication Choice in Multiple Sclerosis  
  — Patrick Aouad (Australia)

- **[O-11]** Disease Modifying Treatments in MS: Clinical Outcomes of Induction and Escalation Strategies  
  — Owain Hedd William (United Kingdom)

- **[O-12]** The Incidence of Demyelination Syndromes in Children in Singapore – Predilection for Optic Nerve and Spine  
  — Simon Ling (Singapore)

- **[O-13]** Accuracy of the Fluorescence-activated Cell Sorting Assay for the Aquaporin-4 Antibody (AQP4-Ab): Comparison with the Commercial AQP4-Ab Assay Kit  
  — Sung Min Kim (Republic of Korea)

- **[O-14]** The Effect of Body Mass Index on Disease Outcomes in Neuromyelitis Optica Spectrum Disorder with Aquaporin4-Igg Preliminary Results of Multicenter Study in Korea  
  — Sung Min Kim (Republic of Korea)

- **[O-15]** Processing Speed, Cognitive Flexibility and Mood Disturbances in Neuromyelitis Optica Spectrum Disorder  
  — Anna Combres (Canada)
[O-16] q-Space Myelin Map Analysis of Brain Lesions in Neuromyelitis Optica-Spectrum Disorders: A Preliminary Study
— Jin Nakahara (Japan)

[O-17] Cytokine/Chemokine Profile in MOG-Ab+ Disorder
— Kimihiko Kaneko (Japan)

[O-18] CDS9 Deficiency in Astrocytes Contributes to Central Nervous System Restricted Lesion Development in Neuromyelitis Optica
— Yaping Yan (China)

[O-19] Reconditioning Brain Microenvironment Facilitates the Protection of Astrocytes in A Mouse Model of Neuromyelitis Optica Spectrum Disorder
— Kai-Bin Shi (China)

[O-20] Experimental Autoimmune Encephalomyelitis (EAE) is Ameliorated in Mice with Gray Matter (GM) Astrocyte-Specific Inducible Conditional Connexin 43 Knock-Out (Cx43cKO)
— Hayato Une (Japan)

12:30-13:30 Lunch @ Flow Restaurant, 1F, Millennium Hilton Bangkok & Poster Viewing

13:30-14:25 Presidential Seminar
Chairpersons: Alvin Seah (Singapore) & Ernest Willoughby (New Zealand)
1. How to Optimise MS/NMOSD Diagnosis and Treatment in the Developing Regions of the World
   — Naraporn Prayoonwiwat (Thailand)
2. Management of Immunosuppression and Immunomodulation in MS/NMOSD
   — Stephen Reddel (Australia)

14:25-14:35 Coffee Break

14:35-16:05 Cutting Edge Workshop
Glial Pathology in Demyelinating Disease
Chairperson: Jun-ichi Kira (Japan)
1. Novel Roles of Perivascular and Circulating Oligodendrocyte Precursor Cells in the Damaged Brain
   — Takakuni Maki (Japan)
2. Axo-glial Pathology of Anterior Visual Pathways in NMO
   — Izumi Kawachi (Japan)

[O-21] [15min] Elevated Cerebrospinal Fluid — CRMP5 As A Biomarker of Damage to Astrocyte Foot Process and Growth Corn in AQP4-Igg-Seropositive NMOSD
— Shuhei Nishiyama (Japan)

[O-22] [15min] Investigation of Microscopic Tissue Changes in Multiple Sclerosis: A Sodium (\(^{23}\)Na) MRI Study
— Achim Gass (Germany)

16:05-17:00 Coffee Break & Poster Round

17:00-18:30 Teva Sponsored Symposium
The Changing Treatment Landscape in MS, Immunosuppression vs Immunomodulation

20:00-22:30 Presidential Dinner @ The Grand Chaophraya Cruise & After-cruise Cocktail at Flow Restaurant, 1F, Millennium Hilton Bangkok

Friday, 28 October 2016

Thonburi Ballroom, Level M (Breakout Session)

14:35-16:05 PACTRIMS Educational Seminar
Chairpersons: Kazuo Fujihara (Japan) and Lekha Pandit (India)
1. Diagnosis and Treatment of RIS and CIS
   — Masoud Etemadifar (Iran)
2. Management of Asian MS and NMOSD Patients During Pregnancy and Postpartum
   — Yuko Shimizu (Japan)
3. The Measurement and Interpretation of AQP4 and MOG Antibodies
   — Jacqueline Palace (United Kingdom)

16:05-18:35 MS Patients’ Activity in Thailand and other Southeast & South Asian Countries and Pacific Countries
### Saturday 29 October, 2016

**Grand Ballroom Level 2**

<table>
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<tr>
<td>10:00-10:30</td>
<td><strong>Coffee Break &amp; Poster Review</strong></td>
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</table>
| 10:30-12:30| **Main Symposium**  
Advances in Neuroimaging for Demyelinating Disease: Novel Techniques and Optimisation  
Chairperson: Yaou Liu (China)  
1. Implementation of Novel MRI Techniques in MS and NMOSD  
   — Wim Van Hecke (Belgium)  
2. Atrophy and NEDA: Experience of Western and Asian MS/NMO Patients in Vancouver  
   — Anthony Traboulsee (Canada)  
3. How to Optimise the Use of MRI in MS  
   — Achim Gass (Germany)  
4. How to Optimise the Use of MRI in MS/NMOSD in Asia  
   — Yaou Liu (China) |
| 12:30-12:40 | **Closing and Award Ceremony**  
1. Award Ceremony  
   — Jun-ichi Kira (Japan)  
2. Closing Remarks by the Vice President, PACTRIMS  
   — William Carroll (Australia) |
MSPARIS 2017
7TH JOINT ECTRIMS – ACTRIMS MEETING
25–28 OCTOBER 2017
PARIS, FRANCE
SAVE THE DATE
INVITED LECTURE

Opening Lecture Series

B Cell-Targeted Therapy Unravels the Critical Roles of B Cells in Demyelinating Disease

L-1
The Expanding Role of B Cells in CNS Demyelinating Disease
Amit Bar-Or (Canada)
Department of Neurology and Neurosurgery, Montreal Neurological Institute and Hospital - The Neuro, McGill University, Quebec, Canada

While MS has traditionally been thought of as principally a T-cell-mediated disease, the substantial impact of selective B cell targeting on disease activity underscores key roles for B cells at least in the relapsing biology of MS. Of note, this contribution of B cells invokes important antibody-independent functions of B cells including their potential to act as either pro-inflammatory or anti-inflammatory mediators, thereby influencing disease-relevant T cell responses. Contrasting results of different treatments targeting B cells in patients (in spite of predictions of therapeutic benefits from animal models) call for a better understanding of the multiple roles that distinct human B cell responses likely play in MS. Most recently, the implication of a GM-CSF expressing inflammatory disease with high-efficacy therapy will result in question arising whether more effective early control of efficacy and safety outcomes observed in these studies, the and clinically relevant benefits of this treatment. In view of the in PP MS have been completed and show statistically significant comparing Ocrelizumab with IFNB1a sc and one against placebo. In the meantime, phase 3 studies in RR MS the results of a phase 2 study with Ocrelizumab, a humanized MAB, therapies increased considerably and was further enhanced by neurodegeneration.

L-2
B Cell Therapies in MS
Ludwig Kappos (Switzerland)
Neurologic Clinic and Polyclinic, Departments of Medicine, Clinical Research, Biomedicine and Biomedical Engineering, University Hospital Basel, Basel, Switzerland

The traditional view of MS pathophysiology is that it is predominantly a T-cell-mediated disease. But clinical and experimental evidence does also suggest an important role of B cells that are thought to exert their influence on the pathogenesis of MS through antigen presentation, autoantibody production, cytokine regulation, and formation of ectopic lymphoid follicle-like aggregates in meningeal tissue, which may cause cortical neurodegeneration.

After a first proof of concept study in RR MS with the Anti-CD20 Monoclonal Antibody(MAB) Rituximab, interest in B-Cell targeting therapies increased considerably and was further enhanced by the results of a phase 2 study with Ocrelizumab, a humanized MAB, also targeting CD20. In the meantime, phase 3 studies in RR MS comparing Ocrelizumab with IFNB1a sc and one against placebo in PP MS have been completed and show statistically significant and clinically relevant benefits of this treatment. In view of the efficacy and safety outcomes observed in these studies, the question arises whether more effective early control of inflammatory disease with high-efficacy therapy will result in longer term and more complete prevention of MS-associated disability. This needs to be elucidated in further studies.

Phase 3 studies with the fully humanized anti-CD20 MAB Ofetunumb have started and other B-cell targeting principles are entering Phase 1 and 2 studies. Enhancement of disease activity in a phase 2 trial with the B-cell targeting recombinant protein Atacicept warns that the line to therapeutic success may be finer than anticipated.

L-3
B Cell Therapies in Neuromyelitis Optica Spectrum Disorder
Ho Jin Kim (Republic of Korea)
Department of Neurology, Research Institute and Hospital of National Cancer Center, Goyang, Republic of Korea

Neuromyelitis optica spectrum disorder (NMOSD) is a devastating autoimmune disease characterized by severe and relapsing episodes of optic neuritis, longitudinally extensive transverse myelitis, and less commonly, brain and brainstem syndromes. Although rare, NMOSD has gained increasing attention since the discovery of a unique biomarker autoantibodies that target aquaporin-4 (AQP4). While its pathogenesis has not been fully elucidated, NMOSD is now considered an AQP4 antibody-mediated astrocytopathic disease in which clinical and neuromaging findings, and therapeutic responses are distinct from MS.

Disabling sequelae of NMOSD result from incomplete recovery from acute attacks, rather than from a supervening progressive course, which is the usual case in multiple sclerosis (MS). Accordingly, the primary treatment goal is the prevention of relapse. To date, there are no prospective randomized clinical trials offering class I evidence to direct therapy. However, various immunosuppressive drugs have been reported to be effective in the attenuation of attack severity as well as in reducing relapse episodes. Among those, B cell targeted therapy showed the strongest evidence to support its use in NMOSD, demonstrating long-term efficacy and an acceptable safety profile.

In this talk, I’ll discuss about the specific therapies for NMOSD aiming to suppress and/or modulate B cells or downstream effector mechanisms.

L-4
How to Optimise MS/NMOSD Diagnosis and Treatment in the Developing Regions of the World
Naraporn Prayoonwiwat (Thailand)
Division of Neurology, Department of Medicine, Faculty of Medicine Siriraj Hospital, Bangkok, Thailand

Multiple sclerosis (MS) is an immune-mediated demyelinating disorder of the central nervous system that affects people of both sexes since they are young, at their productive lives. A cure for MS has not been achieved but several modalities of treatment involving immunomodulation or “disease-modifying therapy” (DMT) have shown significant impacts in retarding the disease progression. As it had been shown that axonal damages occur early in the disease course. Therefore, the earlier the diagnosis of MS and DMT started, the better chance of preventing neuronal loss. Currently, the use of magnetic resonance imaging (MRI) has...
Although individual immunomodulatory agents affect the immune system in different ways, there are common themes in patient risk. Not all of these will occur within the limited time frame of a two-year trial. Themes include reactivation of existing infections including herpes viruses, mycobacterial and JC virus infections, vaccine preventable disease, cardiovascular and metabolic risk. Immune dysregulation may play important roles for pathogenesis. We recently reported that the anterior visual pathway involvement in NMO is characterized by the followings, compared to multiple sclerosis (MS): (i) longitudinally extensive optic neuritis; (ii) loss of AQP4 immunoreactivity on Müller cells with no deposition of complement in the retinas, and (iii) densely packed AQP4 astrocytes with complement activation in optic neuritis lesions, (ii) severe visual impairment and worse prognosis for optic neuritis; 3) unique AQP4 dynamics including (i) loss of AQP4 immunoreactivity on astrocytes with complement activation in optic neuritis lesions, (ii) loss of AQP4 immunoreactivity on Müller cells with no deposition of complement in the retinas, and (iii) densely packed AQP4 immunoreactivity on astrocytes in gliosis of secondary antero/retrograde degeneration in the optic nerves and retinal nerve fiber layer (RNFL); and 4) more severe neurodegeneration including (i) axonal accumulation of degenerative mitochondria and transient receptor potential melastatin 4 channel with complement-dependent astrocyte pathology in optic neuritis lesions, (ii) mild loss of horizontal cells, and (iii) RNFL thinning and loss of ganglion cells with abundance of AQP4+ astrocytes, indicating secondary retrograde degeneration after optic neuritis. These findings are consistent with a new concept in which severe neurodegeneration via abnormal AQP4 dynamics in astrocytes/Müller cells and/or inflammatory signals is prominent in NMO. Unique axo-glial pathology is present in NMO.

L-6
Novel Roles of Perivascular and Circulating Oligodendrocyte Precursor Cells in the Damaged Brain
Takakuni Maki (Japan)
Department of Neurology, Kyoto University Graduate School of Medicine, Kyoto, Japan
Recent research advances have revealed that oligodendrocyte precursor cells (OPCs) have several underestimated roles in the brain. In addition to a well-known role of providing mature oligodendrocytes which form myelin sheaths and promote saltatory conduction, OPCs have been shown to regulate neuronal and vascular systems in more direct ways than previously recognized. I will try to introduce novel roles of perivascular and circulating OPCs which connect systemic circulation and brain in the normal and pathological conditions.

L-7
Axo-glial Pathology of Anterior Visual Pathways in NMO
Izumi Kawachi (Japan)
Department of Neurology, Brain Research Institute, Niigata University, Niigata, Japan
Neuromyelitis optica (NMO) is an inflammatory autoimmune disorder of the CNS, and aquaporin-4 (AQP4) autoantibodies play important roles for pathogenesis. We recently reported that the anterior visual pathway involvement in NMO is characterized by the followings, compared to multiple sclerosis (MS): (i) longitudinally extensive optic neuritis; (ii) loss of AQP4 immunoreactivity on Müller cells with no deposition of complement in the retinas, and (iii) densely packed AQP4 immunoreactivity on astrocytes in gliosis of secondary antero/retrograde degeneration in the optic nerves and retinal nerve fiber layer (RNFL); and 4) more severe neurodegeneration including (i) axonal accumulation of degenerative mitochondria and transient receptor potential melastatin 4 channel with complement-dependent astrocyte pathology in optic neuritis lesions, (ii) mild loss of horizontal cells, and (iii) RNFL thinning and loss of ganglion cells with abundance of AQP4+ astrocytes, indicating secondary retrograde degeneration after optic neuritis. These findings are consistent with a new concept in which severe neurodegeneration via abnormal AQP4 dynamics in astrocytes/Müller cells and/or inflammatory signals is prominent in NMO. Unique axo-glial pathology is present in NMO.

L-5
Management of Immunosuppression and Immunomodulation in MS/NMOSD
Stephen Reddel (Australia)
Department of Neurology, Concord Repatriation General Hospital, New South Wales, Australia
New immunotherapies for neurological inflammatory diseases such as MS and NMOSD present significant challenges in clinical risk management. Indeed, the clinical practice evaluation of risks with differing treatments for MS is probably more complex and time consuming than the evaluation of efficacy. Although individual immunomodulatory agents affect the immune system in different ways, there are common themes in patient risk. Not all of these will occur within the limited time frame of a two-year trial. Themes include reactivation of existing infections including herpes viruses, mycobacterial and JC virus infections, vaccine preventable disease, cardiovascular and metabolic risk. Immune dysregulation may also result in autoimmune and immune reconstitution inflammatory syndromes. Managing these risks requires a systematic approach. An online immunosuppression screening tool may help reduce omissions in individual patient-specific risk assessment.

Cutting Edge Workshop
Glial Pathology in Demyelinating Disease
Okuda and is applied to the incidental brain magnetic resonance imaging (MRI) finding of white matter lesions suggestive of MS demonstrating dissemination in space in subjects with a normal neurologic examination and without historical accounts of typical MS symptoms. Although some patients with RIS will go on to develop clinical symptoms of MS, an as yet undetermined proportion will have radiographic progression only, no progression, or will be found to have alternate diagnoses. Sensitivity and specificity of the RIS diagnostic criteria in predicting progression to MS is as yet uncertain, and the benefits of treatment of RIS with DMT remains entirely speculative. Considerations then evaluating the diagnosis of RIS include the regional MS prevalence, quality and experience of the MRI scanning centers and reading radiologists, and expertise of the treating neurologists in performing a thorough MS history and workup including CSF analysis, evoked potentials, and neurocognitive testing. Data recently published by okuda provide supportive evidence that a significant number of RIS subjects evolve to a first clinical symptom. An age .37 y; male sex, and spinal cord involvement appear to be the most important independent predictors of symptom onset. Some MS expert prefer treat high risk RIS patients especially those with positive oligoclonal bands in CSF.

A CIS is defined as an acute or sub-acute episode of neurological dysfunction due to inflammatory demyelination that last more than 24 hours. A CIS is clinically indistinguishable from relapses that occurs in MS except that they are isolated at least clinically in time and in most patients in space. According to revised 2011 MC Donald criteria more than 80% of CIS patients converted to MS. However, a proportion of patients have a monophasic illness and the diagnosis remains CIS even with long term follow up. These patients with isolated, idiopathic demyelinating event account less than 20% of CIS patients. Accurate prediction of which patients with CIS will have future neurological event and convert to MS is very important. In addition to treatment of acute and severe of attacks in CIS, prophylactic treatment limited to high risk CIS.

For childbirth and pregnancy among patients with neuromyelitis optica spectrum disorder (NMOSD), although the relapse rate does decrease during pregnancy, this decrease is not as pronounced as that seen in the third trimester in MS, and the relapse rate 3 months after childbirth tends to be higher than that for MS. NMOSD is also associated with higher risk for miscarriage.

L-10
The Measurement and Interpretation of AQP4 and MOG Antibodies
Jacqueline Palace (United Kingdom)
Nuffield Department of Clinical Neurosciences, Oxford University, Oxford, UK

Over the past decade the discovery of pathogenic aquaporin 4 (AQP4) and myelin oligodendrocyte glycoprotein (MOG) antibodies (Ab) has broadened the clinical phenotype of neuromyelitis optica (NMO) and demonstrated overlap between NMO and acute disseminated encephalomyelitis (ADEM). AQP4-Abs are associated with NMO, longitudinally transverse myelitis (LETM) and optic neuritis (ON) as well as brain and brainstem syndromes and rarely in children an ADEM like picture. These are all now categorised under the diagnostic label NMO spectrum disorder (NMOSD). MOG-Abs are associated with the NMOSD and ADEM clinical phenotypes and are particularly common in children.

The initial NMO antibody was identified using indirect immunofluorescence on mouse tissue and showed a distinctive IgG staining pattern. Subsequent dual immunostaining with AQP4-specific rabbit IgG demonstrated that the antibodies were binding to AQP4. Since more sensitive assays have been developed; the highest sensitivities yielded by assays detecting IgG binding to live cells expressing recombinant AQP4 with quantitative flow cytometry or visual observation (CBA). The cell based assays (fixed or live) are currently the most commonly used in clinical practice for diagnostic testing. Of the two isoforms of AQP4, the M23 isoform (which aggregates to produce orthogonal antibodies) has broadened the clinical phenotype of multiple sclerosis. Since the development of assays detecting antibodies to conformationally intact extracellular MOG, it is clear such antibodies are associated with distinct non-MS clinical phenotypes. The current reliable diagnostic assays use live CBA techniques.

As with other auto-antibodies it is clear that antibody titre is not a reliable indicator of severity across populations but within an individual it can be helpful. Antibodies titres usually reduce with immunosuppressive treatments and can often increase with relapses. However, fluctuations can occur without clinical correlates. Patients with low positive AQP4-Ab titres can become negative with treatment and can later become positive during a relapse. Although untreated AQP4- Ab disease is a relapsing condition, some MOG-Ab patients have a monophasic course (up to around half). Not surprisingly it appears that relapse is more likely in those in whom the MOG antibodies remain. Although MOG-Ab disease is a more recently described condition, it may turn out to be more common than AQP4-Ab disease, and this is definitely so in children. In addition to the different age

L-9
Management of Asian MS and NMOSD Patients During Pregnancy and Postpartum
Yuko Shimizu (Japan)
Department of Neurology, Tokyo Women’s Medical University School of Medicine, Tokyo, Japan

The age of onset of multiple sclerosis (MS) is between the 20s and 40s, and as this is the fertile age range for women, childbirth and pregnancy among MS patients are issues encountered on a daily. To ease the anxieties felt by patients, it is important for medical professionals to have the correct knowledge about pregnancy and childbirth, so they can guide and support women in the process leading up to safe delivery. Although the activity of MS remains stable during pregnancy because immunological tolerance of the fetus within the mother’s body comes into effect, there is characteristically a high risk of relapse during the puerperal period. Stabilizing the disease activity before pregnancy helps to reduce the risk of relapse after childbirth; it is essential to start patients with high disease activity on treatment with a disease-modifying therapy (DMT) before pregnancy to maintain remission. A DMT that has little effect on the fetus is desirable for this purpose.

For childbirth and pregnancy among patients with neuromyelitis optica spectrum disorder (NMOSD), although the relapse rate does decrease during pregnancy, this decrease is not as pronounced as that seen in the third trimester in MS, and the relapse rate 3 months after childbirth tends to be higher than that for MS. NMOSD is also associated with higher risk for miscarriage.
spectrum affected, the marked female predominance and increased association with other auto-antibody conditions noted in AQP4-Ab disease is not seen in MOG-Ab disease.

Main Symposium

Advances in Neuroimaging for Demyelinating Disease: Novel Techniques and Optimisation

L-11 Implementation of Novel MRI Techniques in MS and NMOSD
Wim Van Hecke (Belgium)
Radiology Department, Antwerp University Hospital, Edegem, Belgium

Over the past decades, new MRI techniques have been developed and applied to a wide range of brain disorders, including Multiple Sclerosis (MS) and Neuromyelitis Optica Spectrum Disorder (NMOSD). In contrast to the classical MR images and use of MRI, these new techniques allow for quantification, including volumetric measures of lesions and brain structures, as well as measures of structural and functional connectivity, vasculature and metabolic changes. The introduction of these new MRI biomarkers has provided insights into disease mechanisms and specific pathological changes in patients with MS and NMOSD. The ultimate goal is the clinical use of these techniques for an improved diagnosis, prognosis and follow-up of individual patients with MS and NMOSD. However, translating these novel MRI techniques from a research setting and a group level to a clinical setting and an individual patient level is a challenging task. Standardisation of the image acquisition, a robust quality assurance and obtaining reliable measures with a very low error are of paramount importance in this context.

L-12 Atrophy and NEDA: Experience of Western and Asian MS/NMO Patients in Vancouver
Anthony Traboulsee (Canada)
University of British Columbia, British Columbia, Canada

Acute inflammation of the central nervous system, and subsequent incomplete recovery from this injury contributes to permanent disability in both Multiple Sclerosis (MS) and Neuromyelitis Optica Spectrum Disorder (NMOSD). Although the mechanism and severity of inflammation differ between the two disorders (demyelination in MS and astrocytopathy in NMOSD), prevention of these attacks or relapses is the primary therapeutic goal in the early management. Therapies for relapsing forms of MS must demonstrate efficacy on multiple measures that mostly reflect their anti-inflammatory role. These measures include clinical relapses (annualized relapse rate, relapse severity, and proportion of patients who are relapse free), and brain MRI surrogates of acute inflammation (contrast enhancing lesions on T1 weighted MRIs and/or new T2 lesions on FLAIR or equivalent weighted MRIs). No evidence of disease activity (NEDA) summarizes these key inflammatory outcomes and includes a disability progression measure as well. Over two years, only 10% of untreated patients will reach NEDA. In contrast, between 10-30% of patients on first line therapies and 30-50% of patients on high efficacy therapies will achieve NEDA over two years. Because MS populations perform differently across clinical trials, caution is needed when comparing any outcome for the different therapies, especially in the absence of a randomized comparator group.

Disability progression occurs in MS, independent of acute relapses, characterized by a gradual change in the physical disability scale (EDSS). Once this becomes evident over one or two years of clinical follow up, patients become classified as having progressive MS (Secondary Progressive MS; SPMS) with or without relapses. While the mechanisms of acute relapses and new MRI lesions is well understood, the same can not be said about progression. Various mechanisms have been proposed, including sequestered low grade inflammation throughout the normal appearing brain tissue (both grey and white), and premature neuronal failure and degeneration. Clinically, this is monitored as sustained progression of disability (a 0.5 to 1 step increase in the EDSS score sustained over 2 to 6 months minimum) in the absence of decline due to relapses.

The imaging surrogate for neurodegeneration or progression is brain atrophy. The annual rate of brain atrophy in MS is 10 times greater than seen in healthy control cohorts, involving white matter, grey matter, spinal cord, and retinal nerve fibre layers. The process of tissue loss (atrophy) is evident as early as the first signs of MS (clinically isolated syndrome; CIS) and the rate is relatively constant throughout the disease course. Brain atrophy is the most advanced tool available for assessing the impact of MS therapies on preventing irreversible tissue loss. High efficacy therapies have recently shown a significant and sustainable impact on this measure as well as demonstrating clinical stability.

Less is known about the value of routine (annual) MRI of the brain and spinal cord in evaluating NMOSD patients to detect clinical silent disease activity, and if expressing disease stability as NEDA is meaningful. Clinical progression, thought to be rare in NMOSD in the absence of relapses, requires systematic studies that include broader outcomes such as cognition and imaging outcomes such as OCT, brain and spinal cord atrophy to ensure that we are not missing a clinically silent disease process that could have long term consequences. Many of these studies are currently underway as part of clinical trials of new NMOSD therapies.

L-13 How to Optimise the Use of MRI in MS
Achim Gass (Germany)
Department of Neurology, University Hospital Mannheim, University of Heidelberg, Heidelberg, Germany

Based on the insights from MRI studies into the pathophysiology of MS MRI is a key investigation and biomarker in MS. Besides its importance in the diagnosis and differential diagnosis of MS it is an established marker of inflammatory disease activity in Phase II and Phase III studies. This has also lead to the use of monitoring inflammatory disease activity to guide therapeutic management of MS patients. MRI is also used for safety surveillance as it is the most sensitive tool to detect progressive multifocal encephalopathy (PML) early as a potential complication of immunosuppressive therapy. MAGNIMS guidelines as well as several national guidelines have recently underlined the need of optimised imaging and reporting strategies. Besides established conventional MRI markers an optimised approach includes the best possible use of the individual MRI system at hand. Many MRI
systems nowadays can provide 3D T2-weighted MRI, double inversion recovery or susceptibility weighted sequences in very reasonable acquisition times. All of those can be of great use in individual patients. The same needs to be emphasized in regard to spinal cord or optic nerve MRI, that are also highly sensitive to the pathological changes in MS and can be particularly helpful to guide clinical decision making. Future developments will include more assistance from software for the detection of new lesions and the visualisation and quantification of brain volume changes.

L-14
How to Optimise the Use of MRI in MS/NMOSD in Asia
Yaou Liu (China)
Department of Radiology, Xuanwu Hospital, Capital Medical University, Beijing, China
MRI is very sensitive and robust in detecting brain, spinal cord and optic nerve alteration in MS and NMO. In Asia, NMO, which predominantly involves optic nerve and spinal cord, has higher prevalence than in western world. The imaging characteristics of Asian MS and NMO patients are not identical to the western patients. We need to optimize the use of MRI in MS/NMOSD in Asia to investigate patients and for clinical trials. This lecture will include:
1. Imaging characteristics (brain, spinal cord and optic nerve) including lesions, white matter diffusion changes, gray matter atrophy, and functional alterations of Asian patients especially NMO patients.
2. The basic MRI techniques for imaging NMO and MS patients in Asia.
3. The advanced MRI techniques (e.g. functional MRI in spinal cord) for imaging Asian patients highlighting spinal cord and optic nerve imaging.
4. A summary and future perspective of imaging Asian MS/NMO patients.
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**Oral Session 1**

**Multiple Sclerosis**

**[O-1]**

**Evaluation of 2016 MAGNIMS MRI Criteria for Dissemination in Space in Patients with A Clinically Isolated Syndrome**

J.-W. Hyun,¹ S.-Y. Huh,¹ W. Kim,² M. S. Park,³ S.-W. Ahn,⁴ J.-Y. Cho,² B.-J. Kim,⁵ S.-H. Lee,² S.-H. Kim,¹ H. J. Kim¹

Departments of Neurology & Radiology, National Cancer Center, Goyang, Departments of Neurology, Konin University College of Medicine, Busan,¹Department of Neurology, The Catholic University of Korea College of Medicine, Seoul,² Department of Neurology, College of Medicine, Yeungnam University College of Medicine, Daejeon,³ Department of Neurology, Chung-Ang University Hospital, Chung-Ang University College of Medicine, Seoul,⁴ Department of Neurology, Ilsan Paik Hospital, Inje University College of Medicine, Goyang,⁵ Department of Neurology, Korea University Medical Center, Seoul, Korea

**Background & Objective:** The magnetic resonance imaging in multiple sclerosis (MAGNIMS) group, which is a European collaborative research network, recently proposed MRI criteria for the diagnosis of multiple sclerosis (MS). We compared the validity of the 2010 McDonald and 2016 MAGNIMS MRI criteria for dissemination in space (DIS) to predict the conversion of clinically definite MS (CDMS) in patients with a clinically isolated syndrome (CIS).

**Methods:** Between 2006 and 2016, we enrolled 170 patients who had the first clinical event suggestive of MS from 7 referral hospitals in Korea. Patients were classified into two groups based on the main outcome at the last follow-up: CDMS converters, who experienced a second attack, and non-converters.

**Results:** Of 170 (109 women, 61 men) patients with a mean follow-up duration of 54 months (range, 7-148), 86 (51%) converted to CDMS after a mean of 17 months from onset. The sensitivity, specificity, accuracy, positive and negative predictive values of the 2010 McDonald criteria were 70.9%, 63.1%, 67.1%, 66.3%, 67.9% and those for the 2016 MAGNIMS criteria were 88.4%, 45.2%, 67.1%, 62.3%, 79.2%, respectively. When we excluded 45 patients who underwent disease modifying therapy before the second clinical event among the non-converters, the specificity was increased to 92.3% and 82.1% for the 2010 McDonald and the 2016 MAGNIMS criteria, respectively.

**Conclusion:** The 2016 MAGNIMS MRI criteria for DIS showed higher sensitivity but lower specificity than the 2010 McDonald criteria, to predict conversion to CDMS in patients with a CIS.

**[O-2]**

**A Prospective, Observational Study on the Progression of Clinically Isolated Syndrome (CIS) to Multiple Sclerosis for at Least 4-year Period**

Long-Sun Ro¹, Chih-Chao Yang², Rong-Kuo Lyu¹, Kon-Ping Lin³, Tsung-Chang Tsai², Shiang-Ru Lu², Li-Chieh Huang³, Ching-Piao Tsai³

¹Chang Gung Memorial Hospital (CGMH), Taoyuan City, Taiwan (R.O.C.)
²National Taiwan University Hospital (NTUH), Taipei City, Taiwan (R.O.C.)
³Taipei Veterans General Hospital (TVGH), Taipei City, Taiwan (R.O.C.)
⁴China Medical University Hospital (CMUH), Taichung City, Taiwan (R.O.C.)
⁵Kaohsiung Medical University Hospital (KMUH), Kaohsiung City, Taiwan (R.O.C.)
⁶Merck Biopharma (Taiwan), Taipei City, Taiwan (R.O.C.)

**Background:** In Taiwan, a retrospective study conducted in 2006 showed that the conversion rate of optic neuritis (ON) to Multiple Sclerosis (MS) was 14.7% over a 4-year follow-up period. Here, we described the progression of MS and disease characteristics in a prospective and observational manner.

**Objective:** To observe the progression of MS in patients with first episode of neurological event and to determine status of anti-aquaporin-4 (AQP4) immunoglobulin G (IgG) antibody and disease characteristics of MS patients.

**Method:** The enrolled subjects participated in clinic visits for anti-AQP4 IgG detection, telephone follow-up to assess health status, and examination in the event of a relapse. Subject were considered as reaching the end of trial participation if diagnosed with MS or had other explanations for their symptoms.

**Results:** Twenty-two of the 152 enrolled patients (14.5%) converted to MS from first episode of CIS, and 5 patients to NMO (3.3%). The mean ± SD period of conversion to MS was 1.1 ± 1.1 years. Only one MS patient (4.5%) was positive for AQP4-antibody. The mean length of longest spinal cord lesion in MS and NMO patients was 2.0 ± 0.8 sections versus 3.5 ± 0.7 sections, respectively. No significant association was found between baseline demographics/disease characteristics and progression to MS.

**Conclusions:** The conversion rate was similar to that of in a retrospective study in Taiwan. In our study, some of subjects not diagnosed with MS or NMO may be diagnosed with NMO spectrum disorders according to diagnostic criteria.

**[O-3]**

**The Effects of the HLA-DRB1*04:05 Allele on Intracortical Lesions Detected by 3-Dimensional Double Inversion Recovery Imaging in Japanese Patients with Multiple Sclerosis**

K Shinoda¹, T Matsushita¹, Y Nakamura¹, K Masaki¹, R Yamasaki¹, O Togao², A Hiwatashi² and J-I Kirita³

¹Department of Neurology, Neurological Institute, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan
²Department of Clinical Radiology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

**Background:** We are not aware of previous reports on the use of 3-dimensional double inversion recovery (3D-DIR) images to examine cortical lesions (CLS) in Asian patients with multiple sclerosis (MS).

**Objectives:** To elucidate the frequency of CLS, and their association with HLA-DRB1 and DPB1 alleles in Japanese MS patients.

**Methods:** 3D-DIR MRI was performed in 92 Japanese MS patients, with clinical information including HLA-DRB1 and DPB1 genotypes obtained retrospectively.
Results: Total CLs, intracortical lesions (ICLs), and leukocortical lesions (LCLs) were detected in 39.1%, 26.1%, and 28.3% of MS patients respectively. CLs were present in 29.7% of relapsing-remitting MS (RRMS) patients and 77.8% of secondary progressive MS (SPMS) patients. MS patients with ICLs had a significantly higher frequency of SPMS (p=0.0016), and greater Expanded Disability Severity Scale (EDSS) scores than those without ICLs (p=0.0038). Similar trends were observed with total CLs and LCLs. The numbers of CLs, ICLs, and LCLs positively correlated with EDSS scores (CLs: r=0.1318, p<0.0001, ICLs: r=0.3206, p=0.0018, LCLs: r=0.4071, p<0.0001). The frequency and number of ICLs were significantly higher in HLA-DRB1*15:01 carriers than in non-HLA-DRB1*15:01 carriers (p=0.014, p=0.0036, respectively), but significantly lower in HLA-DRB1*04:05 carriers than in non-HLA-DRB1*04:05 carriers (p=0.023, p=0.025, respectively). Multivariate logistic regression analysis revealed that HLA-DRB1*04:05 was negatively associated with ICLs (Odds ratio 0.273, p=0.0297), but that sex, disease duration, EDSS, RRMS, SPMS, or HLA-DRB1*15:01 were not.

Conclusions: ICLs are associated with greater disease severity and secondary progression in Japanese patients with MS, and are partly suppressed by the presence of the HLA-DRB1*04:05 allele.

[O-4] The Role of Genetic Susceptibility Variants in Predicting Clinical Course in Multiple Sclerosis: A Cohort Study
Gongbu Pan,1 Steve Simpson, Jr,1 Ingrid van der Mei,1 Jac C. Charlesworth,2 Robyn Lucas,1 Anne-Louise Ponsonby,1 Yuan Zhou,1 Feitong Wu,1 AusLong/Ausimmune Investigator Group,3 Bruce V. Taylor1
1Menzies Institute for Medical Research, University of Tasmania, Hobart, Australia
2National Centre for Epidemiology and Population Health, Research School of Population Health, The Australian National University, Canberra, Australia
3Murdock Children’s Research Institute, University of Melbourne, Melbourne, Australia
A full list of members of the AusLong/Ausimmune Investigator Group is provided in the Acknowledgments

Background: The genetic drivers of multiple sclerosis (MS) clinical course are essentially unknown with limited data arising from severity and clinical phenotype analyses in genome-wide association studies (GWAS).

Objective: This study aimed to determine whether susceptibility variants are associated with MS clinical course.

Methods: Prospective cohort study of 279 participants recruited 2003-6 with a first clinical diagnosis of central nervous system (CNS) demyelination. 116 MS risk-associated single nucleotide polymorphisms (SNPs) were assessed as predictors of conversion to clinically definite MS (CDMS), relapse, and annualised disability progression (EDSS) up to 5-year review (ΔEDSS). Survival analysis was used to test for predictors of CDMS & relapse, and linear regression for disability progression. The top seven SNPs predicting CDMS/relapse and disability progression were evaluated as a cumulative genetic risk score (CGRS).

Results: We identified two non-HLA (rs12599600 & rs1021156) and one HLA (rs9266773) SNP predicting both CDMS and relapse risk. Additionally, three non-HLA SNPs predicted only CDMS; one HLA and two non-HLA SNPs predicted only relapse; and seven non-HLA SNPs predicted ΔEDSS. The CGRS significantly predicted CDMS and relapse in a significant, dose-dependent manner: those having >5 risk genotypes had a 6-fold greater risk of CDMS and relapse compared to those with <2. The CGRS for ΔEDSS was also significant: those carrying >6 risk genotypes progressed at 0.48 EDSS points per year faster compared to those with <2, and the CGRS model explained 32% of the variance in disability in this study cohort.

Orasa Chawalparit,1 Siri-on Tritragarn,1 Sinwin Piaypittayanan1, Smatom Thakolwiboont,1 Jiraporn Jitprapaikulson1, Chanon Ngamsombut1, Narapon Prayoonwivat,1 Siriraj Neuroimmunology Research Group1
1Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Objective: To evaluate the NMOSD2015 imaging guideline for distinguishing clinical diagnosed multiple sclerosis and NMOSD in Thai patients.

Materials and Methods: The patients were recruited from database of patients attending MS clinic at Siriraj Hospital. The diagnosis of NMOSD was concluded from the result of serosensitive test for anti-AQP4 antibody. For the MS patients, diagnosis was performed after excluding seropositive cases, and then NMOSD 2015 seronegative criteria and McDonald 2010 clinical criteria were used for the final conclusion. The retrospective review of MRI was done according to imaging criteria in NMOSD2015.

Results: There were 86 cases with seropositive NMOSD, 16 cases with seronegative NMOSD, and 28 cases with final diagnosis of MS. For brain MRI, the findings suggestive MS rather than NMOSD were Dawson’s finger sign, cortical gray lesion, and lesions involving periventricular-ITL. Involvement of corpus callosum was found more in MS, whereas bridging pattern was found more in NMOSD. For optic pathway involvement, negative MRI was found more in NMOSD cases. When abnormal MRI, involvement of posterior half optic nerve and chiasm were found more in NMOSD cases. About the spinal MRI, lesion involving cervical cord with extension to medullar was found more in NMOSD than MS. The LETM, centrally located and swelling were found more in NMOSD. For brain MRI, the findings suggestive MS rather than NMOSD were Dawson’s finger sign, cortical gray lesion, and lesions involving periventricular-ITL. Involvement of corpus callosum was found more in MS, whereas bridging pattern was found more in NMOSD. For optic pathway involvement, negative MRI was found more in NMOSD cases. When abnormal MRI, involvement of posterior half optic nerve and chiasm were found more in NMOSD cases. About the spinal MRI, lesion involving cervical cord with extension to medullar was found more in NMOSD than MS. The LETM, centrally located and swelling were found more in NMOSD.

Conclusion: Only some brain MRI features were more conclusive for NMOSD in Thai patients. Spinal cord lesions were still more helpful for differential diagnosis between MS and NMOSD.

[O-6] Predictors of Treatment Response to Immunosuppressive Therapy in Neuromyelitis Optica Spectrum Disorder
Su-Hyun Kim, Jae-Won Hyun, Hyo-Jin Jo, AeRan Joung, Ho Jin Kim
Department of Neurology, Institute and Hospital of National Cancer Center, Korea

Background: Azathioprine (AZA) and myecophenolate mofetil (MMF) were the most commonly used first-line therapy in neuromyelitis optica spectrum disorder (NMOSD). Some patients...
reviewed the medical records of 117 patients, who were initially treated with AZA or MMF at least for 6 months. Non-response to immunosuppressive therapy was defined as the presence of either more than two relapses or one severe relapse despite the therapy over 6 months.

**Results:** Of 117 patients, 41(35%) patients were classified into the non-responders over a median 36 months of AZA or MMF therapy (range, 6-193 months). Non-responders exhibited higher frequency of definite NMO phenotype (p=0.007), higher frequency of severe attack before therapy (p<0.001), and higher pre-annualized relapse rate (ARR) (p=0.011) compared to the responders. Logistic regression analysis identified the severe attack history before therapy (p=0.001) and high pre-ARR (p=0.005) as an independent risk factor for non-response. The frequency of disability worsening after immunotherapy was higher (47% vs. 3%, p <0.001) in the non-responders than the responders. Of 41 non-responders, 36 (88%) switched to rituximab therapy: 32 (89%) patients were classified into the responders and only 4 (11%) patients remained the non-responders over median 32 months of rituximab therapy.

**Conclusion:** Patients with severe attack history and high ARR prior to initiation of therapy may have a risk of suboptimal response to AZA or MMF therapy.

**[O-7] Outcomes of Rituximab Therapy in Anti-Rituximab Antibody-Positive Patients with NMO/SDS**

Zhang LJ, MD, Li T, MD, Yang CS, MD, Zhang C, MD, Li YJ, MD, Shi F, MD, PhD, Yang L, MD, PhD

1Department of Neurology, Tianjin Neurological Institute, Tianjin Medical University General Hospital, 154 Anshan Road, Heping District, Tianjin 300052, P. R. China.

2Department of Neurology, Tianjin Medical University General Hospital, 154 Anshan Road, Heping District, Tianjin 300052, P. R. China.

**Objective:** We aimed to clarify the effect of deletion-type CNVs on the repertoires of CD4 and CD8 T cells in peripheral blood mononuclear cells (PBMCs) in patients with MS.

**Methods:** PBMCs were collected from 15 MS patients with and 14 without the deletion-type CNVs in remission phase. Samples were stained with surface markers to assess naive/memory cells and intracellular cytokines after stimulation by phorbol 12-myristate 13-acetate and ionomycin, and analyzed by FACSVersace flow cytometer.

**Results:** In MS patients with deletion-type CNVs, the frequency of activated CD4 T cells (HLA-DR+), effector CD8 T cells (CCR7-CD45RA-), effector memory CD8 T cells (CCR7-CD45RA-), and naive CD8 T cells (CCR7+CD45RA+) were significantly decreased (p=0.030, p=0.011, respectively). Although the frequency of interleukin (IL)-4, IL-17, and granulocyte-macrophage colony-stimulating factor (GM-CSF)-producing cells were comparable, IFN-γ-producing cells were significantly increased in CD4 and CD8 T cells in MS patients with deletion-type CNVs than those without them (p=0.025, and p=0.030 respectively).

**Conclusion:** Our results suggest that the presence of deletion-type CNVs is associated with the development of activated CD4 T cells, effector/effecto memory CD8 T cells, and IFN-γ-producing CD4/CD8 T cells further work is needed to confirm these findings.

**[O-9] Deep Learning of Joint Myelin-T1w MRI Features on Normal-Appearing Brain Tissues Distinguishes Multiple Sclerosis from Healthy Controls**

Y. Yoo, L. W. Tang, T. Brosch, D.K.B. Li, S. Kolind, I. Vavasour, A. Rauscher,
A Trabousee, R Tam
University of British Columbia, Vancouver, BC, Canada

Background: Myelin water imaging is a quantitative magnetic resonance imaging (MRI) technique that measures myelin content and can potentially allow demyelinating diseases such as multiple sclerosis (MS) to be detected earlier. Current methods for analyzing myelin-specific images typically use global or regional mean myelin measurements to detect abnormalities in normal-appearing brain tissue, but ignore finer spatial patterns that may be also characteristic of MS.

Objective: To determine whether machine learning can improve identification of non-lesional myelin reductions that can potentially improve the early detection of MS pathology.

Methods: Myelin (3D GRASE sequence) and T1-weighted (T1w) (gradient echo sequence) images were acquired from 55 remitting-relapsing MS patients (EDSS median (range): 4 (0-5); age: 45 (30-60)) and 44 normal controls (age: 45 (30-60)). Unsupervised deep learning, a machine learning method using artificial neural networks, was used to extract latent spatial myelin-T1w features. The deep-learned myelin-T1w features were compared with the traditional regional mean MRI measurements for automatically distinguishing MS from normal controls in normal-appearing brain tissue. An 11-fold cross-validation was employed to evaluate the classification accuracy.

Results: The deep-learned myelin-T1w features produced a significantly (p=0.0041) higher classification accuracy rate than the regional mean MRI measurements: 87.9% (SD=8.4) vs. 70.7% (SD=12.8).

Conclusion: Deep learning has strong potential for identifying visually indistinct MRI features that are more sensitive to MS pathology in normal-appearing brain tissue. Applications of this approach could include augmenting clinical assessment criteria to improve the speed and accuracy of differential diagnosis, predicting clinical progression and changes in disease status.

[O-10] Clinico-Radiological Phenotype and Number of Lesions on MRI Influences Medication Choice in Multiple Sclerosis

P Aouad1, A Fontes-Villaba1, Y Lee2, A Kirby2 and J Parratt2
1University of Sydney, Sydney, NSW, Australia
2Royal North Shore Hospital, Sydney, NSW, Australia

Background: Groups suggest that MRI characteristics are useful in categorising multiple sclerosis (MS) and are associated with level of disability.

Objective: To determine whether clinico-radiological phenotype and lesion number influence medication choice and to measure patient disability.

Methods: Data from 194 patients with relapsing forms of MS were retrospectively analysed and separated into two groups, higher potency (HP) and lower potency (LP) based on the predominant medication prescribed between 2013 and 2016. Patients were then categorised into brain-stem/cerebellar MS (bcMS), spinal predominant MS (sMS), generalised MS (gMS) and deep white matter MS (dWMs) phenotypes. The number of MRI lesions were calculated and the proportion of phenotypes and mean number of MRI lesions in HP and LP groups were compared. The MSSS was compared between potency groups.

Results: Of the total 194 patients there were 97 in both the HP and the LP medication groups. Within the HP group 54% were categorised as gMS compared with 40% on LP medications (p = 0.06). Mean number of total lesions on MRI was 30 ± 18 for HP the group compared with 25 ± 17 LP (p = 0.06). Those patients prescribed high potency medications had a mean MSSS of 3.2 ± 2.6, compared with 1.9 ± 1.4 in the LP group (p = 0.02).

Conclusions: In our clinic HP medications are more frequently prescribed to patients with gMS and high lesion load. Patients prescribed HP medications are more disabled, but overall outcomes are good when compared to the natural history of MS.

[O-11] Disease Modifying Treatments in MS: Clinical Outcomes of Induction and Escalation Strategies

OH Williams1,2, KE Harding1,2, A Rimmer1, MD Willis1,2, TP Pickersgill1, F Joseph1, M Wardle1, NP Robertson1,2
1Institute of Psychological Medicine and Clinical Neuroscience, Cardiff University, UHW, Cardiff, UK
2Department of Neurology, Royal Gwent Hospital, Newport, UK

Background: It is currently unclear whether aggressive induction or stepwise escalation of DMTs provides optimum long-term outcomes for patients with MS.

Objective: To Compare outcomes in routine clinical practice amongst unmatched patient groups receiving either initial mononoclonal induction, injectable DMT only or escalation from injectable DMT.

Methods: 382 patients were identified from a population-based cohort, with a mean follow up post-treatment of 6.5 years. Time to disability end points (EDSS) were examined using survival analysis.

Results: Annual relapse rate pre- and post-treatment of the induction strategy (21%) demonstrated a 89% reduction from 2.20(±1.82) to 0.24(±0.40); injectable DMT only (58%) had a 77% reduction from 1.07(±0.89) to 0.24(±0.29); escalation strategy (21%) had the lowest reduction by 54% from an elevated baseline of 1.63(±1.66) to 0.75(±0.42). Time to EDSS4 was shorter for induction against both injectable and escalation strategies (5.4 vs 9.5 vs 7.8 years, p=0.0002). Time to EDSS6 was similar for the treatment strategies respectively (11.4 vs 14.9 vs 12.8 years, p=0.12).

Conclusions: Patients requiring escalation could be identified as having higher disease activity prior to treatment initiation. Escalation strategy demonstrated relatively worse relapse outcomes, suggesting that a window of therapeutic opportunity for aggressive treatments may be lost by delaying administration. The finding of similar times to EDSS6 regardless of DMT choice suggests that aggressive induction in patients with higher disease activity at onset prevents disability accrual on the same rapid trajectory; therefore, slowing the rate of disability progression to EDSS6 to that of patients with less aggressive disease.


Ling SR1, Hoh SY1, Lin J2, Thomas T2
1Neuroinflammatory Disease, UHW, Cardiff, UK
2NHMRC Clinical Trials Centre University of Sydney, Sydney, NSW, Australia

Results: Of the total 194 patients there were 97 in both the HP and the LP medication groups. Within the HP group 54% were categorised as gMS compared with 40% on LP medications (p = 0.06). Mean number of total lesions on MRI was 30 ± 18 for HP the group compared with 25 ± 17 LP (p = 0.06). Those patients prescribed high potency medications had a mean MSSS of 3.2 ± 2.6, compared with 1.9 ± 1.4 in the LP group (p = 0.02).

Conclusions: In our clinic HP medications are more frequently prescribed to patients with gMS and high lesion load. Patients prescribed HP medications are more disabled, but overall outcomes are good when compared to the natural history of MS.
Background: Inflammatory demyelinating disorders of the central nervous system can be monophasic or recurrent. In Southeast Asian patients with recurrent disease, neuromyelitis optica (NMO) is thought to be more common. Paediatric Neurologists in Singapore had anecdotally noted an increase in children with NMO, optic neuritis (ON) and transverse myelitis (TM) over the last decade compared to acute disseminated encephalomyelitis (ADEM).

Objective: The objective of our study was to characterise the spectrum of demyelinating disorders in children in Singapore, calculate their incidence and analyse patterns over time.

Methods: Retrospective case review performed at KK Women’s & Children’s Hospital, Singapore National University Hospital Singapore (NUH) covering the period January 2004 to December 2015. Children age less than 18 years with diagnoses of ADEM, ON, TM, clinically isolated syndrome (CIS), MS or NMO were included. Official Singapore Census child population data was used and incidence compared between periods 2004-2009 and 2010-2015.

Results: 78 cases were identified. 26 ADEM, 16 TM, 21 ON, 7 NMO, CIS 3, MS 5. Median length of follow up was 4.8 years. Comparing the two time periods, incidence (per 100,000 person-years) of ADEM decreased from 0.025 to 0.0159, ON increased 0.013 to 0.019 and NMO increased 0.003 to 0.008. TM incidence was unchanged at 0.013.

Conclusions: This is the first report of incidence of demyelination disorders in children in Singapore. Although small case numbers limit the study, there appears to be a predilection for optic nerve and spinal cord disease in Southeast Asian children.

Accuracy of the Fluorescence-activated Cell Sorting Assay for the Aquaporin-4 Antibody (AQP4-Ab): Comparison with the Commercial AQP4-Ab Assay Kit

Ji Won Yang1, Sung Min Kim2, Byung-Jo Kim2, Ohyun Kwon1, Jung-Hwan Oh3, Sa-Yoon Kang4, Kee-Hong Park5, Sung-Rae Cho6, Kyung Seok Park6.
1Department of Neurology, Gachon University, Gil Medical Center, Incheon, Korea
2Department of Neurology, Seoul National University Hospital, Seoul, Korea
3Department of Pathology, Seoul National University College of Medicine, Seoul, Korea
4Department of Neurology, Chung Ang University College of Medicine, Jeju, Korea
5Department of Neurology, Gyeongsang National University School of Medicine
6Department of Neurology, Seoul National University Bundang Hospital, Seongnam

Background and Objective: We aimed to evaluate the accuracy of the FACS assay in detecting the AQP4-Ab compared with the commercial cell-based assay (C-CBA) kit.

Methods: The optimal cut off values of FACS assay was tested using 1123 serum samples from patients with inflammatory demyelinating diseases and negative controls. The accuracy of FACS assay and C-CBA were compared in consecutive 225 samples that were collected between January 2014 and June 2014.

Results: With a cut-off value of MFIi of 3.5, the receiver operating characteristic curve for the FACS assay showed an area under the curve of 0.876. Among 225 consecutive sera, the FACS assay and C-CBA had a sensitivity of 77.3% and 69.7%, respectively, in differentiating the sera of definite NMO patients from sera of controls without IDD or of MS. Both assay had a good specificity of 100% in it. The overall positivity of the C-CBA among FACS-positive sera was 81.5%; moreover, its positivity was low as 50% among FACS-positive sera with relatively low MFlis.

Conclusions: Both the FACS assay and C-CBA are sensitive and highly specific assays in detecting AQP4-Ab. However, in some sera with relatively low antibody titer, FACS-assay can be a more sensitive assay option. In real practice, complementary use of FACS assay and C-CBA will benefit the diagnosis of NMO patients, because the former can be more sensitive among low titer sera and the latter are easier to use therefore can be widely used.

The Effect of Body Mass Index on Disease Outcomes in Neuromyelitis Optica Spectrum Disorder with Aquaporin4-IgG: Preliminary Results of Multicenter Study in Korea

Sung-Min Kim1, Byung-Jo Kim2, Yoo-Whan Kim3, Ohyun Kwon1, Jung-Hwan Oh4, Sa-Yoon Kang4, Kee-Hong Park5, Sung-Rae Cho6, Kyung Seok Park6.
1Department of Neurology, Seoul National University Hospital, Seoul, Korea
2Department of Neurology, Korea University Medical Center, Korea University College of Medicine
3Department of Neurology, College of Medicine, Eulji University
4Department of Neurology, Cheju National University School of Medicine, Jeju, Korea
5Department of Neurology, Gyeongsang National University School of Medicine
6Department of Neurology, Seoul National University Bundang Hospital, Seongnam

Background: Recent studies showed that the body mass index (BMI) can be associated with the prognosis of diverse inflammatory diseases as multiple sclerosis, rheumatoid arthritis, psoriasis, and Hashimoto’s thyroiditis.


Methods: Demographics, clinical and radiological outcomes were assessed among 88 NMOSD-AQP4 patients from the multicentre cohort of 4 referral hospitals in Korea. The BMI of patients were assessed at disease onset and longitudinally at each relapse. The BMI, obtained within 1 month of their disease onset and before the use of steroid treatment, was defined as the BMI-naïve.

Results: At disease onset, the BMI-naïve of female patients were negatively associated with their EDSS at disease onset (p = 0.002), longer consecutive spinal cord lesions on MRI (p < 0.001), and higher mortality (p = 0.041), compared to the other females. Moreover, the multivariable shared-frailty analysis revealed that the BMI were negatively associated with the risk of relapse, independent of gender, age, and oral steroid use (p = 0.042).

Conclusion: Low BMI can be a risk factor in NMOSD with AQP4-Ab. Because it was associated with a high disability at onset, higher mortality, and poor clinical/radiological outcomes of patients. These effect of BMI was independent of the age, gender, and use of oral steroid.

A. Combes1,2, K. McMullen1, S. Kolind1,2, R. Carruthers1, A. Traboulsee3
1Neurology, Medicine, University of British Columbia, Vancouver, Canada
2Neuroimaging, Institute of Psychiatry, Psychology & Neuroscience, King’s College London, London, UK
3Radiology, Medicine, University of British Columbia, Vancouver, Canada

Background: Cognitive impairment is present in around half of neuromyelitis optica spectrum disorder (NMOSD) patients. Psychometric tasks relying on speed of information processing have great sensitivity in the detection of cognitive impairment in this population. Reports of mood disturbances are fewer, although cognition and mood are interrelated. Both remain to be fully characterised in NMOSD.

Objective: To assess mood disturbances and cognitive performance in an NMOSD group.

Methods: 21 NMOSD patients and 14 matched healthy controls completed the Symbol Digits Modalities Test (SDMT), verbal fluency test, Trail Making Test (TMT) A&B, Centre for Epidemiology Studies Depression Scale, Fatigue Severity Scale, and State-Trait Anxiety Inventory (trait anxiety referring to a propensity to experience high levels of anxiety).

Results: We found higher levels of fatigue (p < .01) and a trend level increase in trait anxiety (p = .06) in NMOSD compared to controls. There was no difference in depression scores (p = .36). NMOSD patients performed significantly worse than controls on the SDMT (p = .03) and TMT even when accounting for motor speed (p = .04). Both groups performed comparably on the verbal fluency test, with similar numbers of correct responses (p = .13) and errors (p = .26) between groups.

Conclusions: Processing speed and cognitive flexibility are affected in NMOSD, in line with known executive function deficits. Trait anxiety may be heightened in some patients, suggesting a preliminary observation that not all T2 signals are attributable to demyelination. Of note, a spindle-like lesion relatively specific to NMOSD found in cerebral cortex of the latter patient showed no evidence of demyelination by MM.

Conclusions: Brain lesions observed in NMOSD appear to be heterogeneous with respect to their myelin status. Our preliminary observations suggest a possible evolution of clinically silent brain lesions in NMOSD.

[O-17] Cytokine/Chemokine Profile in MOG-Ab+ Disorder

Kaneko K1, Sato DK1, 2, 3, Ogawa R1, Akashi TI, Takai Y1, Nishiyama S1, Takahashi T1, Misu TI, Kuroda H1, Tanaka S1, Nakashima I1, Nomura K1, Fujihara K1, 2, Aoki M1
1Department of Neurology, Tohoku University, Sendai, Japan
2Brain Institute and Hospital Sao Lucas Pontifical Catholic University of Rio Grande do Sul (PUCRS), Porto Alegre, Brazil
3Department of neurology, Sao Paulo University, Sao Paulo, Brazil
4Department of Neurology, NHO Yonezawa Hospital, Yonezawa, Japan
5Department of Neurology, Saitama Medical Center, Kawagoe, Japan
6Department of Neurology, Fukushima Medical University, Fukushima, Japan

Background: Studies of cytokine/chemokine profile in myelin oligodendrocyte glycoprotein antibody (MOG-Ab)+ disorders are limited to small-scale ones in pediatric cases.

Objective: To examine cerebrospinal fluid (CSF) cytokine/chemokine levels in MOG-Ab+ disorder in pediatric and adult patients.

Methods: We measured 27 cytokine/chemokines by multiplex fluorescent bead-based immunoassays, myelin basic protein (MBP) and glial fibrillary acidic protein (GFAP) by enzyme-linked immunosorbent assays in the CSF of MOG-Ab+ cases (n=29), aquaporin(AQP)4-Ab+ neuromyelitis optica spectrum disorder (NMOSD) (n=20), multiple sclerosis (MS) (n=21), non-inflammatory control (n=16). Samples of inflammatory diseases were collected in acute phase before treatment. Antibodies were examined using cell-based assays.

Results: No cytokine was elevated in MS compared to AQP4-Ab+ or MOG-Ab+ cases. MIP-1a, GM-CSF and IL-10 were higher in MOG-Ab+ and AQP4-Ab+ cases than in MS and control. IL-6, IL-8, IL-13 were elevated in 3 inflammatory disease groups, especially in MOG-Ab+ and AQP4-Ab+ cases. Meanwhile, G-CSF was higher in...
MOG-Ab+ cases than in AQP4-Ab+ ones, MS and control, and IL-17A was elevated in MOG-Ab+ cases as compared with MS. Serum AQP4-Ab titers correlated well with CSF-AQP4-Ab titers, CSF-IL-6, and CSF-GFAP while no correlations were seen between serum-MOG-Ab titer and such CSF-parameters as CSF-MOG-Ab titer, CSF-IL-6, and CSF-NMBP.

**Conclusion:** The cytokine profile in MOG-Ab+ cases was largely similar to AQP4-Ab+ NMOSD but was different from MS, which may have a therapeutic implication in MOG-Ab+ disease. Although there are some data supporting the pathogenicity of MOG-Ab, no good correlation between MOG-Ab and inflammatory and cell damage markers suggest additional factors may be involved in the development of MOG-Ab+ diseases.

**[O-18] CD59 Deficiency in Astrocytes Contributes to Central Nervous System Restricted Lesion Development in Neuromyelitis Optica**

Yaping Yan, PhD; Zhen Wang, MD, PhD; Kaibin Shi, MD; Wenli Zhu, MD; Fu-Dong Shi, MD, PhD

**Department of Neurology, Tianjin Neurological Institute, Tianjin Medical University General Hospital, Tianjin, 300052, China**

**Background and Objective:** Neuromyelitis optica (NMO) is an autoantibody-mediated, central nervous system (CNS) channelpathy, and in the disease, astrocytic water channel protein aquaporin 4 (AQP4) is the main target. AQP4 distributes broadly in CNS and peripheral organs, but why NMO patients develop only CNS lesions remain largely unknown. We aim to uncover the mechanisms of CNS-restricted lesion development in NMO.

**Methods:** The expression of CD59 was examined by western blot and immunofluorescent staining. IgGs purified from NMO-IgG positive patients were i.c. injected in along with human complement to induce NMO mouse model. In vivo brain overexpress CD59 or in vitro silence or block CD59 in peripheral AQP4-expressing cells to test the effect of CD59 in lesion development under treatment of IgGm IgGm and human complement. Similar experiments were performed in human AQP4-expressing cell lines.

**Results:** CD59 is co-localized with AQP4 in periphery organs but deficient on astrocytes in CNS. CD59 overexpressing in mouse brain decreased the demyelination lesion, blocked astrocyte and AQP4 loss, inhibited membrane attack complex (MAC) formation and inflammatory cells infiltration. Silencing or blocking CD59 in AQP4-expressing human tracheal epithelial cells and human skeletal muscle cells or mouse skeletal muscle cells induced more MAC formation and cytotoxicity, suggesting a protection role of CD59 under IgGm IgGm and human complement treatment.

**Conclusion:** The deficiency of CD59 in astrocytes contributes to CNS restricted lesion development in NMO and restoring the expression of CD59 in astrocytes may serve as a novel therapeutic target in the disease.

**[O-19] Reconditioning Brain Microenvironment Facilitates the Protection of Astrocytes in A Mouse Model of Neuromyelitis Optica Spectrum Disorder**

Kai-Bin Shi, MD 1; Zhen Wang, MD 1; Yuanchu Liu, MS 2; Ye Gong, MS 1; Ying Fu, MD 1; Shaowu Li, MD 2; Kristofer Wood, MS 2; Junwei Hao, MD, PhD 1; Guang-Xian Zhang, MD, PhD 1; Fu-Dong Shi, MD, PhD 1; Yaping Yan, PhD 1

1Department of Neurology, Tianjin Neurological Institute, Tianjin Medical University General Hospital, Tianjin, 300052, China;
2Department of Radiology, Beijing TianTan Hospital, Capital Medical University, Beijing, 100050, China;
3Department of Neurology, Barrow Neurological Institute, St. Joseph’s Hospital and Medical Center, Phoenix, AZ, 85013, USA;
4Department of Neurology, Thomas Jefferson University, Philadelphia, PA19107, USA.

**Objective:** A major hurdle for effective stem cell therapy is ongoing inflammation in the target organ. Here we tested a new strategy to recondition the inflammatory microenvironment in the central nervous system to promote neural stem cell therapeutic effect in a mouse model of neuromyelitis optica spectrum disorder (NMOSD), which provided a complement mediated inflammatory environment in an autoimmune context.

**Methods:** The purified serum IgG from NMOSD patients with strong NMO-IgG positivity and human complement were injected into the mice brain parenchyma to induce brain injury. The complement factor H related protein 1 (CFHR1) engineered neural stem cells (NSCs) were injected to the brain together with model induction. CFHR1 is a complement inhibitor protein. The therapeutic effects of engineered NSCs and mechanism was evaluated by the protection of astrocytes in vivo and in vitro.

**Results:** CFHR1-NSCs reduced the brain lesion volume in mice injected with NMO-IgG and human complement as detected by MRI, and decreased the demyelination area and loss of astrocytes. CFHR1-NSCs transplanted mice showed an attenuated inflammatory environment as showed by the infiltration of peripheral leukocytes and activation of microglia, together with the inhibition of formation of membrane attack complex. In vitro experiments demonstrated that it was secreted CFHR1 but not the ability to synthesize CFHR1 contribute to the protection of endogenous and NSC-derived astrocytes.

**Conclusion:** These findings suggest that manipulation of the lesion microenvironment contributes to a more effective cell replacement therapeutic strategy for autoimmune diseases of the central nervous system.

**[O-20] Experimental Autoimmune Encephalomyelitis (EAE) is Ameliorated in Mice with Gray Matter (GM) Astrocyte-Specific Inducible Conditional Connexin 43 Knock-Out (Cx43cKO)**

Hayato Une, M.D.1, Hiroo Yamaguchi, M.D., Ph.D.1, Yinan Zhao, M.D.1, Koji Shinoda, M.D., Ph.D.1, Katsushia Masaki, M.D., Ph.D.1, Magdalena Götz, M.D., Ph.D.1, Ryo Yamasaki, M.D., Ph.D.1 and Jun-ichi Kira, M.D., Ph.D.1

1Department of Neurology, Neurological institute, Graduate School of Medical Sciences, Kyushu University
2Physiological Genomics, Biomedical Center, Ludwig-Maximilians University Munich, Munich, Germany

**Background:** Multiple sclerosis (MS) is an inflammatory demyelinating disease of the central nervous system of unknown
cause. We previously reported that Cx43 expression was markedly diminished in active lesions of the white matter (WM) of autopsied MS cases. This finding suggest a possibility that Cx43 in the WM may play a role in the lesion extension.

**Objectives:** We hypothesized that acute loss of Cx43 in the WM exacerbates the demyelinating lesions while the role of GM Cx43 in demyelinating disease remains unknown. We therefore aimed to elucidate the roles of WM and GM Cx43 in EAE by generating WM and GM astrocyte-specific Cx43 inducible conditional KO mice and inducing myelin oligodendrocyte glycoprotein (MOG)-EAE.

**Methods:** We developed Cx43F/F;GLAST-CreER(T2)KI/+ mice as GM astrocyte-specific Cx43cKO mice. We induced MOG-EAE 10 days after tamoxifen injection, and analyzed the clinical course and pathology. We used Cx43F/F mice as controls.

**Results:** EAE was significantly milder in GM astrocyte-specific Cx43cKO mice from acute phase to chronic phase, as compared with control mice. Pathology demonstrated less demyelinating lesions and infiltrating cells. Infiltrating immune cells did not express Cx43 in the active demyelinating lesions of the lumbar cord in both groups. The expression level of Cx43 was similar between these two groups in the spleen and the inguinal lymph nodes.

**Conclusions:** GM astrocyte-specific Cx43cKO can reduce EAE. We consider that loss of Cx43 in GM may cause dysfunction of glymphatics through disruption of Cx43 gap junction channels, which leads to decreased MOG antigen presentation in the cervical lymph nodes.

**Cutting Edge Workshop**

**Glia Pathology in Demyelinating Disease**

**[O-21]**

**Elevated Cerebrospinal Fluid — CRMP5 As A Biomarker of Damage to Astrocyte Foot Process and Growth Corn in AQP4-IgG-Seropositive NMOSD**

Shuhei Nishiyama, Tatsuro Misu, Ichiro Nakashima, Toshiyuki Takahashi, Kazuo Fujihara, Masashi Aoki

**Department of neurology, Tohoku University Hospital, Sendai, Japan**

**Background:** NMOSD is an autoimmune neurologic disease characterized by severe optic neuritis and transverse myelitis, and associated with AQP4-IgG binding membranous AQP4 in the foot process of astrocyte. Collapsin response mediator protein 5 (CRMP5) is a membranous protein located on the filopodia in the foot process of astrocyte. It has been reported that anti-CRMP5 antibody-positive patients developed NMOSD-like symptoms, suggesting that CRMP5 could be an autoimmune target and a biomarker of astrocytic damage. However, both clinical and pathological implications of CRMP5 in the cerebrospinal fluid (CSF-CRMP5) in AQP4-IgG-seropositive NMOSD are unknown.

**Methods:** We conducted a cross-sectional study in 52 patients with inflammatory neurologic diseases (20 with AQP4-IgG-seropositive NMOSD, 3 with MOG-IgG-seropositive NMOSD, 23 with MS, 2 with Neuro-Behcet’s disease, and 4 with Neurosarcoidosis) who were diagnosed as neurological inflammatory demyelinating diseases and control patients with 7 non-inflammatory neurologic diseases (NIDC). CSF-CRMP5, GFAP, and MBP were measured by sandwich ELISA kits. The data were analyzed by Graphpad Prism.

**Results:** CSF-CRMP5 in the AQP4-IgG-seropositive NMOSD was significantly elevated (0.0975±0.0209 pg/mL, p=0.0298) than in MS (0.0043±0.0209). CSF-CRMP5 was not detected in MOG-IgG-seropositive NMOSD, Neuro-Behcet’s disease, Neurosarcoidosis, and NIDC patients. CSF-CRMP5 was mildly correlated with CSF-GFAP, but not related with CSF-MBP.

**Conclusion:** Elevated CSF-CRMP5 levels in AQP4-IgG-seropositive NMOSD could reflect damages to astrocytic foot process and growth corn caused by AQP-IgG. CSF-CRMP5 might serve as a biomarker of diagnosis and disease activity in AQP4-IgG-seropositive NMOSD.

**[O-22]**

**Investigation of Microscopic Tissue Changes in Multiple Sclerosis: A Sodium (23Na) MRI Study**

Philipp Eisele, MD; Simon Konstandin, PhD1,2,3; Martin Griebe, MD; Kristina Szabo, MD; Marc E. Wolf, MD; Angelika Alonso, MD; Christopher J. Schwarzbach, MD; Anne Ebert, PhD; Christina Roßmanith1; Christel Weiß, PhD; Melissa Ong, MD; Stefan O. Schoenberg, MD; Lothar R. Schad, PhD; Achim Gass, MD

1Department of Neurology, Universitätsmedizin Mannheim, University of Heidelberg, Theodor-Kutzer-Ufer 1 – 3, 68167 Mannheim, Germany
2MR-Imaging and Spectroscopy, Faculty 01 (Physics/Electrical Engineering), University of Bremen, NW 1 Otto-Hahn-Allee 1, 28359 Bremen, Germany
3Computer Assisted Clinical Medicine, Universitätmedizin Mannheim, University of Heidelberg, Theodor-Kutzer-Ufer 1 – 3, 68167 Mannheim, Germany
4Department for Statistical Analysis, Universität medizin Mannheim, University of Heidelberg, Ludolf-Krehl-Straße 13 – 17, 68167 Mannheim, Germany
5Institute of Clinical Radiology and Nuclear Medicine, Universitätmedizin Mannheim, University of Heidelberg, Theodor-Kutzer-Ufer 1 – 3, 68167 Mannheim, Germany

**Background:** Recent studies using sodium (23Na) imaging suggested that increased total sodium concentrations (TSC) are likely to reflect neuroaxonal damage leading to disease progression and disability.

**Objective:** To detect and quantify tissue changes in the microstructure outside macroscopically visible lesions using a multiparametric MRI protocol.

**Methods:** We performed 23Na, 1H and diffusion MRI in 14 healthy controls (HC), 18 CIS patients, 47 early RRMS (<5 years disease duration), 20 advanced RRMS and 10 SPMS.

**Results:** Normal appearing grey and white matter (GM, WM) TSC were significantly higher in advanced RRMS (GM: 46.7±3.1 mM, WM: 40.5±2.7 mM) and SPMS (GM: 52.5±5.4, WM: 46.2±5.0) vs. HC (GM: 40.1±3.3, WM: 39.9±2.4). CIS (GM: 41.5±2.7, WM: 35.6±2.2) and early RRMS (GM: 43.8±2.5, WM: 38.1±2.6). Total brain volume (TBV) and grey matter volume (GMV) and white matter (WMV) were significantly lower in advanced RRMS (TBV: 1396±68ml, GMV: 705±44ml; WMV: 684±38; WMV: 668±37) vs. HC (TBV: 1477±52, GMV: 744±48; WMV: 732±37). TBV (TBV: 1454±56, GMV: 748±35; WMV: 706±33). Strong
correlations between MRI parameters and EDSS were observed for TBV and TSC of the NAGM and NAWM.

**Conclusion:** TSC increase, loss of TBV, GMV, WMV and increased diffusion were already present in patients with CIS and more pronounced in later stages of MS. The loss of TBV, GMV, WMV and increase of TSC in NAGM and NAWM showed strong correlation with EDSS suggesting that these parameters are highly sensitive to irreversible tissue damage.

**Poster Session 1**

**CIS/Optic Neuritis/ADEM**

**[P-1]** Evaluation of 2016 MAGNIMS MRI Criteria for Dissemination in Space in Patients with A Clinically Isolated Syndrome
Departments of Neurology & Radiology, National Cancer Center, Goyang, Departments of Neurology, Kosin University College of Medicine, Busan, Department of Neurology, The Catholic University of Korea College of Medicine, Seoul. Department of Neurology, College of Medicine, Yeungnam University College of Medicine, Daeug, Department of Neurology, Chung-Ang University Hospital, Chung-Ang University College of Medicine, Seoul, Department of Neurology, Ilsan Paik Hospital, Inje University College of Medicine, Goyang, Department of Neurology, Korea University Medical Center, Seoul, Korea
Same as [O-1].

**[P-2]** A Prospective, Observational Study on the Progression of Clinically Isolated Syndrome (CIS) to Multiple Sclerosis for at Least 4-year Period
Long-Sun Ro, Chih-Chao Yang, Rong-Kuo Lyu, Kon-Ping Lin, Tsung-Chang Tsai, Shiang-Ru Lu, Li-Chieh Huang, Ching-Piao Tsai
Chang Gung Memorial Hospital (CGMH), Taoyuan City, Taiwan (R.O.C.)
National Taiwan University Hospital (NTUH), Taipei City, Taiwan (R.O.C.)
Taipei Veterans General Hospital (TVGH), Taipei City, Taiwan (R.O.C.)
China Medical University Hospital (CMUH), Taichung City, Taiwan (R.O.C.)
Kaohsiung Medical University Hospital (KMUH), Kaohsiung, City, Taiwan (R.O.C.)
Merck Biopharma (Taiwan), Taipei City, Taiwan (R.O.C.)
Same as [O-2].

**[P-3]** The Incidence of Demyelination Syndromes in Children in Singapore – Predilection for Optic Nerve and Spine
Ling SY, Hoh SY, Lin J, Thomas T
1Neurology Service, Department of Paediatric Medicine, KK Women’s & Children’s Hospital, Singapore
2Department of Neurology, KTP-National University Children’s Medical Institute, Singapore
Same as [O-12].

**[P-4]** Optic Perineuritis as An Initial Finding of Optic Neuritis
Joonwon Lee, Kyong Jin Shin
Department of Neurology, Haeundae-paik Hospital, Inje University, Busan, Korea
Optic perineuritis (OPN) is a rare form of orbital inflammatory disease of optic nerve sheath. The clinical presentation and treatment response of OPN are known as distinct from demyelinating optic neuritis (ON). OPN exhibited a central vision sparing and dramatic steroid response in a literature. Recently, we have experienced a bilateral idiopathic ON case who was diagnosed at first OPN on brain MRI and funduscopy examination. A 50-year-old woman presented with rapidly developing blindness including central vision. The treatment response with IV steroid and plasma exchange was poor. Serial MRI and funduscopy examination exhibited optic nerve swelling, signal change, and enhancement and optic disc edema suggesting ON. Serial MRI and funduscopy examination are needed in OPN to differentiate to the temporal change of ON.

**[P-5]** Clinical Prognosis and Risk Factors of Idiopathic Optic Neuritis in China
Peng Jinjing, Cong Hengri, Yan Rong, Kong Xiyun, Li Yuxuan, Jiang Hanqiu, Wang Jiawei, Wenbini, Zhang Xiaojun
1Department of Neurology, Beijing Tongren Hospital, Capital Medical University, Beijing, China
2Eye Center, Beijing Tongren Hospital, Capital Medical University, Beijing, China
Background: The clinical prognosis of idiopathic optic neuritis (ION) in China is largely unknown.
Objective: To identify the clinical prognosis and the risk factors of ION in China.
Methods: Medical record review and supplementary follow-up of ION patients between 2003 and 2007 were performed.
Results: Totally 107 ION cases with an average follow-up duration of 8.0 years were included. (1)Visual acuity in the affected eyes was ≥ 20/40 in 79.9%, ≤ 20/200 in 7.8% at the end of follow-up. Adult, binocular involvement in first attack, severe visual loss, and MS/NMO conversion were independently associated with poor recovery. (2)The estimated 10-year recurrence rate was 48.8%. MS/NMO conversion was proved to be the independently risk factor for higher recurrence rate. (3)21 of the 107 (19.6%) cases developed either CMS or NMOSD. The estimated 5 and 10-year combined conversion rate was 15.6% and 22.8%. Female sex, recurrent ON, poor visual recovery and brain MRI lesions were independently associated with higher risk of MS/NMO. Moreover, worse visual loss, poor visual recovery and normal brain MRI were statistically more common in NMOSD converters compared to CMS converters.
Conclusions: More severe visual loss, poor visual recovery and lower combined conversion rate to MS/NMO for ION in Chinese population were found compared to Western countries. White matter lesions on brain MRI and good visual recovery were found to be good predictors for Chinese ION converting into MS, whereas worse visual loss and poor visual recovery with normal brain MRI suggested higher likelihood of the ION converting into NMOSD.
[P-6] Clinical Features in Chinese Patients with Acute Disseminated Encephalomyelitis
Xiaoan Zhong, Bingjun Zhang, Yuge Wang, Yanlu Huang, Zhengqi Lu, Xue-qiang Hu, Wei Qiu.
Department of Neurology, the Third Affiliated Hospital of Sun yat-sen University
No.600 Tianhe Road, Guangzhou 510630, Guangdong Province, China

Background: Clinical manifestations of acute disseminated encephalomyelitis (ADEM) are heterogeneous in Chinese patients.
Object: To study the clinical features of Chinese patients with ADEM.
Methods: Data of 44 ADEM patients based on the 2012 criteria were reviewed and analyzed.
Results: There were 23 monophasic ADEM and 21 multiphasic ADEM patients. Among them, 14 patients had definite incentive within 2 weeks preceded the onset of neurological symptoms. The common presenting symptoms were fever, disturbance of consciousness, mental disorder, headache, vomiting, epilepsy, paralysis, sensory disturbance and ataxia. Autoimmune antibody abnormalities were observed in 14 patients. ADEM with small lesions was diagnosed in 18 of 44 patients; ADEM with large confluent white matter lesions was observed in 10 patients; ADEM with additional symmetric bithalamic involvement was observed in 12 patients; one patient showed some degree of hemorrhage into the large demyelinating lesions; ADEM lesion with numerous T2 hyperintense and ring-enhancing lesions without diffusion restriction, that is called “babysbreath” like lesion was found in 3 patients.
Conclusions: ADEM is a heterogeneous entity and is best viewed as a ‘syndrome’ rather than a specific disorder in China.

Poster Session 2
MS Clinical Epidemiology

[P-7] The Association between Sodium Intake and Multiple Sclerosis in Isfahan Population
Ghorbani Sara, Raesi Sina, Mahmoodzade Amirhosssien
Isfahan University of Medical Sciences, Hezar Jairb Avenue, Isfahan, Iran

Background: The number of patients with Multiple Sclerosis (MS) is increasing in Iran, which has encouraged researchers to search factors affecting MS. Studies show that high-salt diets worsen MS and are considered as an environmental trigger. In presence of additional salt, developed Th17 cells are more pathogenic and are considered as an environm ental trigger. In presence of high-salt diets, developed Th17 cells are more pathogenic and are considered as an environm ental trigger.
Objective: Because of the role of salt in Th17, we hypothesized that sodium chloride would be higher in MS patients than healthy controls. Therefore, we investigated the association between salt and incidence of MS in Isfahan population.
Methods: A case-control study containing 23 patients and 23 healthy controls was performed in Isfahan, Iran. Na level was measured in 24-hour urine. Laboratory values of the patients were compared with healthy controls, using the Chi-square test. The level of significance was set at p<0.050 in all analysis. All calculations were done using SPSS.
Results: In this study, the OR obtained was 0.988 (95% CI: 0.215–1.618) with a p-value of 0.027. These results show a relationship between urine-Na and the incidence of MS in Isfahan population. In other words, 1 (mEq/day) increase in urine-Na can increase the chance of MS development 0.988 times.
Conclusion: Based on this study, salt consumption can be considered as a MS trigger factor in genetically susceptible people.

[P-8] Association between Body Mass Index and Multiple Sclerosis’ Features in Indonesia
Situmeang RF1,2, Yoesdyanto K1, Siahaan YMT1,2
1Department of Neurology Siloam Hospitals Lippo Village
2Faculty of Medicine Pelita Harapan University, Banten, Indonesia

Background: Body mass index (BMI) has been linked with multiple sclerosis (MS). Individuals with genetically determined obesity are more likely to develop MS, and the progression of MS will be worse in subjects who have higher BMI.
Objectives: To find out the BMI profile in Indonesian MS patients and its association with the onset and severity.
Methods: During a year period, 45 subjects from MS Clinic in Tangerang – Indonesia were observed through age, gender, onset, MS type, disease duration, Expanded Disability Status Scale (EDSS) and BMI. We classified BMI based on Asian Pacific range. Any changes of BMI retrospectively were reported. Association between BMI, MS onset and severity (EDSS) were calculated using logistic regression analysis.
Results: The mean age was 35.62 years old (13 to 56, SD 11.65). There were 39 females and 6 males. The onset mean was 33.40 years (11 to 53, SD 11.77). Among the subjects, 66.7% had relapsing remitting MS (RRMS), 24.3% had primary progressive MS (PPMS), and 8.9% had secondary progressive MS (SPMS). Mean (SD) MS duration was 4.27 years (4.802). Most subjects suffered mild disability; 55.6% had EDSS 0-3. Mean (SD) BMI was 22.11 kg/m2 (5.27), being classified as underweight (17.8%), normoweight (46.7%), overweight (13.3%), and obese (22.3%). Elevations of BMI prior to MS manifestations were shown in 17% subjects. We found no significant correlation between BMI, MS onset, and EDSS.
Conclusions: Differ from studies in Western countries, we found no association between BMI and MS features in Indonesia.

[P-9] Risk Factors of Multiple Sclerosis and Neuromyelitis Optica
Sharareh Eskandarieh1, Ibrahim Abdollahpour 2, Abdoreza Naser Moghadasi 1, Amir Reza Azimi 1, Mohammad Ali Sahraian 1*
1MS Research Center, Neuroscience Institute, Tehran University of Medical Sciences, Tehran, Iran
2Department of Epidemiology and Biostatistics, School of Public Health, Arak University of Medical Sciences, Arak, Iran

Background: Autoimmune syndromes such as multiple sclerosis (MS) and neuromyelitis optica (NMO) are chronic, public health menace and life time threat.
Method: A population based case- control study design was performed based on a study for patients with a diagnosis of MS from Iranian MS Society registry center and NMO patients at the Sina hospital in Tehran in 2015. We design a questionnaire to cover the main epidemiological variables such as demographic data for
estimation of adjusted odds ratio. The results of this study examined some important potential risk factors for MS and NMO. **Result:** A total of 1513 Patients with MS, 83 patients with NMO and 400 healthy controls participated in the survey. MS and NMO patients were predominantly female. There were decreased MS odds among males (OR=0.644). Among younger subject with MS (18-27 years old), the (OR)=1.542; 95% confidence interval (CI)= 1.174-2.025 comparing to NMO patients with older age (48 years and older), (OR)=3.496; 95% confidence interval (CI)= 1.599-7.644. MS The point estimates were greater than eight-fold increased risk associated with a history of MS (OR)=8.806; 95% confidence interval (CI)= 4.101-18.909. **Conclusion:** MS and NMO is more prevalent among female. Mean age at disease onset among Iranian patients with NMO is low. We indicated that the risk of MS is lower in males and older age than 27 years. The risk of NMO is lower in age less than 48 years. Having positive family history of MS among relatives, can increase the risk of MS substantially.

**[P-10]** Possible Relationship between Cytomegalovirus Infection and Neuromyelitis Optica and Multiple Sclerosis
Omidi Mirmosayyebi,2, Yahid Shaygonnejad1, Sayyed Hamid Zarkesh-Esfahani1, Navid Manouchehri1,2
1Department of Neurology, Isfahan Neuroscience Research Center (INRC), Isfahan University of Medical Sciences, Isfahan, Iran
2Medical Student Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

**Introduction:** Neuromyelitis Optica (NMO) is a demyelinating disease of the central nervous system that autoantibodies react against aquaporin-4(AQP4) expressed on astrocytes. NMO has clinical manifestations resembling those of Multiple Sclerosis (MS). The presence of AQP4 antibody in NMO patients is a hallmark factor that differentiates the NMO from MS. Viruses can cause inflammation in white and grey matter of the brain. Inflammatory alterations facilitate transfer of autoantibody from blood-brain barrier. The aim of this study was to evaluate the possible association between Cytomegalovirus (CMV) infection and induction of NMO and MS.

**Materials and methods:** In order to assess the presence of CMV, Real Time PCR was performed on serum samples from 25 NMO patients, 30 MS patients and 30 healthy individuals as control.

**Results:** Despite validity of Real Time PCR assay which was confirmed using internal controls and housekeeping genes, none of the sample was positive for CMV in any of the patients or the controls.

**Conclusion:** Despite high incidence of CMV infection and high sensitivity of Real Time PCR for detection of CMV virus, we could not detect any CMV contamination in any of the samples. Therefore, we suggest that the study will be performed in bigger sample size. It can be concluded that the studied NMO and MS patients were negative for active CMV infection.

**[P-11]** Depression in Multiple Sclerosis, Prevalence and Contributing Risk Factors
Alireza Nikseresht, Maryam Sharifian Dorche

Clinical Neurology Research Center, Department of Neurology, Shiraz University of Medical Sciences, Shiraz, Iran

**Introduction:** Multiple sclerosis (MS) is a chronic autoimmune demyelinating disease of the central nervous system (CNS) which is affect young adult especially young females. In this study we tried to investigate the prevalence of depression among female patients with MS and most important contributing risk factors.

**Methods:** During a cross-sectional study 1750 patients with MS from our outpatient’s clinic in Shiraz Southern Iran were involved. Depression was assessed using the Beck Depression Inventory-II (BDI-II). Descriptive analysis and multiple logistic regressions were performed to examine the association between depression and disability, education, employment, marriage status, course and income.

**Results:** Overall, 647 patients (37 %) had moderate to severe depression. The mean age of participants was 38.2 years (SD = 9.57). The results obtained from logistic regression analysis showed that expanded disability status scale (EDSS), Progressive course and unemployment (P < 0.01) were significantly related to the severity of depression. Marriage and higher education had related to lower depression scales.

**Conclusion:** These findings suggest that depression in patients with MS has multiple contributing factors and patients with higher social supports and lesser disability have lower rates of depression. Physiotherapy, regular employment and family supports may help to reduce depression.

**[P-12]** Factors that Affect EDSS Score in Indonesia Multiple Sclerosis Patients
Situmeang RF1,2, Yoesdyanto K’, Hendrik TC1, Siahaan YMT1,2
1Departement of Neurology Siloam Hospitals Lippo Village
2Faculty of Medicine Pelta Harapan University, Banten, Indonesia

**Background:** Multiple sclerosis (MS) is a debilitating disease that affects people in their productive age. The Expanded Disability Status Scale (EDSS) is a method of quantifying disability in MS and monitoring its progressivity overtime. Several factors give impact to EDSS would help physicians improve their quality of care.

**Objectives:** To evaluate the factors that affect EDSS in Indonesian MS patients.

**Methods:** During five-year period in our MS Clinic, we observed 85 MS patients regarding their age, gender, onset and duration, clinical symptoms, oligoclonal band, use of disease modifying treatment (DMT), MS type, and EDSS.

**Results:** The mean age was 34.66 (14 to 59, SD 11.9), female to male ratio was 8.3:1. The mean of onset and duration were 30.62 (11 to 54, SD 11.6) and 4.02 years (SD 3.9). Clinical presentations were mostly motor, sensory, and cerebellar symptoms. Oligoclonal band in CSF was detected in 30%. Around 43.5% were either on medication or was treated by DMTs. MS types were mostly motor, sensory, and cerebellar symptoms. Oligoclonal band in CSF was detected in 30%. Around 43.5% were either on medication or was treated by DMTs. MS types were predominantly female. There were decreased MS odds among males (OR=0.644). Among younger subject with MS (18-27 years old), the (OR)=1.542; 95% confidence interval (CI)= 1.174-2.025 comparing to NMO patients with older age (48 years and older), (OR)=3.496; 95% confidence interval (CI)= 1.599-7.644. MS The point estimates were greater than eight-fold increased risk associated with a history of MS (OR)=8.806; 95% confidence interval (CI)= 4.101-18.909.**
Conclusion: Age, onset, duration, type of MS, and several clinical symptoms including spasticity, motor weakness, and autonomic symptoms had significant correlation with EDSS.

**[P-13]** Socioeconomic Status and Disability in Multiple Sclerosis

K.E. Harding1,2, O.H. Williams1,2, M.D. Willis1,2, M Wardle1, T.P. Pickersgill1, N.P. Robertson1,2

1Institute of Psychological Medicine and Clinical Neuroscience, Cardiff University, United Kingdom
2Department of Neurology, University Hospital of Wales, Cardiff, United Kingdom

Background: The association of between MS prevalence and socioeconomic status (SES) is well established. However, little is known of the effects of SES on progression of disability.

Objective: To investigate the association between SES and disability within a population-based MS cohort from northern Europe.

Methods: 2277 patients were assigned SES quartile, based on their address using the Welsh Index of Mass Deprivation (WIMD). Association with demographic characteristics was tested using chi-squared and Student's t-test. Time to and age at EDSS disability milestones were tested using Kaplan-Meier survival analysis and Cox proportional hazards regression, adjusted for relevant clinical co-variates.

Results: More patients were of higher SES (p<0.0001), with no difference in SES distribution by gender (p=0.33) or disease course (p=0.36). Annualised relapse rate in the first five years of disease was inversely proportional to SES (p=0.018). Mean followup was 18.9 years. There was a significant difference in time to and age at all disability milestones, with those of lowest SES reaching EDSS milestones 7-10 years earlier than those of highest SES. This effect persisted even after adjustment for age at onset, sex, disease course, and annualised relapse rate.

Conclusions: Although patients of higher SES are more likely to develop MS, they have fewer relapses and are slower to acquire fixed disability across the trajectory of disease. SES should be taken into account when designing studies investigating accumulation of disability in MS. Further research is required to understand why SES affects long-term outcomes in MS and whether this effect is seen globally.

**[P-14]** Systematic Literature Review of the Economic and Disease Burden of Relapse Remitting Multiple Sclerosis and Its Management in Australia, South Korea, Taiwan, Brazil, and Russia

Y. Wu1, M. Casamayor2, P. Aran Terol2, R. Gani2, A. van Engen1

1Teva Pharmaceuticals, Frazer, PA, USA
2Quintiles Advisory Service, Reading, UK

Background: Data on healthcare burden and cost of relapse remitting multiple sclerosis (RRMS) are lacking for certain countries.

Objective: To review published literature on epidemiology, treatment guidelines, and economic costs for relapse remitting multiple sclerosis patients in Australia, South Korea (SK), Taiwan, Brazil, and Russia.

Methods: A systematic literature review was undertaken to analyse articles published between 2006 and 2016 identified from several databases (e.g. PubMed and Cochrane) and relevant national websites.

Results: Incidence of RRMS varied considerably across countries (from ~0.13 in SK to 3.7 in Australia per 100,000) as did prevalence (from 2.96 in Taiwan to 125 in Australia per 100,000). Prevalence was found to be increasing in all countries except Russia. Total economic costs were correlated with incidence and prevalence. Average annual cost per patient was highest in Australia at US$38,353 (Brazil: US$19,629; Russia: US$13,259; SK: US$1,847; Taiwan: US$5,105). In countries for which disaggregated data were available, the main drivers of the total costs were treatment cost and loss of productivity. All 5 countries had published treatment guidelines which were similar across countries with glatiramer acetate and beta-interferon as the preferred first-line treatments for RRMS. Guidelines recommend restricting oral therapies to aggressive forms of RRMS or second- and subsequent treatment lines. Testing for neutralizing antibodies against beta-interferons was not recommended.

Conclusions: The burden of RRMS and its associated costs are high in many Asia-Pacific countries and in other geographic areas. RRMS continues to be a disease area of high unmet need and causes high health-related costs in these countries.

**Poster Session 3**

MS Clinical Features

**[P-15]** Clinical Profile of Patients with Multiple Sclerosis (MS): A North Indian Perspective

P. Banerjee, D. Khurana, V. Lai

Department of Neurology, Post Graduate Institute of Medical Education and Research, Chandigarth, India

Background: The landscape of Multiple Sclerosis in India has been changing in the last few decades. However, data and studies on MS from India are limited.

Objectives: To study the clinical scenario of the disease in North Indian population and obtain detailed demographic and disease characteristics.

Methods: Data was retrospectively collected from the MS registry database of the department of Neurology, PGIMER from 2013 till present. The parameters taken into account were patient demographics, EDSS at last visit, MS course, Annual Relapse rate and current treatment.

Results: 118 patients were recruited in the study. Median age of onsetwas 28+10.87 (Range-10-70 years), females were 57.63% and males 42.37%. Median duration of MS was 13 years and an IQR (inter quartile range) of 49.5. Mean EDSS at last visit was 3.65. The number of patients with EDSS 0-3.3-6, above 6 were 24.44%,27.5% and 0.08%, respectively. The MS course at the time of admission were 71.91% Relapse Remitting type,2.54 % Secondary Progressive type, 4.24% Progressive Relapsing and 11.86% Clinically isolated syndrome. Mean Relapse rates during entire period of follow up were 0.37+0.71.75% had no relapse, 16.26% had 1 and 5.76% showed >2 relapses.28.72% were on Interferon(IFN) Beta 1a,0.85% on IFN Beta 1b,10.17% on Glatiramer,6.78% on Azathioprine, and 4.24% on...
Natalizumab, 4.24% on Methotrexate, 0.85% were administered Mitoxantrone.

**Conclusion:** Our results displayed similar trends to the Western MS with a few exceptions. North Indian MS has higherrmale proportion and younger age of disease onset (<20years) as compared to western MS. This data reflects a difference in MS patient characteristics in India.

**[P-16] Clinical Feature of Multiple Sclerosis in RSUPN Cipto Mangunkusumo (RSCM) Jakarta Indonesia From Januari 2014 Until July 2016**

Al Rusmana, P Heptayana, RA Arpandy, R Estiasari

**Department of Neurology Faculty of medicine University of Indonesia-RSUPN Cipto Mangunkusumo, Jakarta, Indonesia**

**Background:** Based on data from WHO (2013), the incidences of Multiple Sclerosis (MS) in Indonesia still rare (0-5/100,000 people with MS), but number on MS cases in Indonesia especially in RSUPN Cipto Mangunkusumo (RSCM) increase, and nowadays publication about MS in Indonesia still rare.

**Objective:** To descript the feature and spectrum of MS in RSCM

**Methods:** A retrospective analysis from medical record of patients with MS in RSCM from January 2014 until july 2016.

**Results:** Twenty-three patients were diagnosed as MS. Male to female ratio is 1:3.6. Malay Mongoloid race were the predominant racial group (91,3%) followed by Arabic (4,5%) and Mongoloid (4,3%), with mean age at onset 29,1+11,5. Relapsing remitting MS is the most common subtype of MS (87%) followed by Primary progressive MS (8,7%) and Tumefactive MS (4,3%). Early clinical manifestations is dominated by motor symptoms (43,5%) followed by sensory (34,8%), visual (17,3%) and cerebellar (4,3%). The initial EDSS score was 4.0 in 43,5% patients. MRI showed hiperintense multiple brain lesions on T2 (95,7%) and hiperintense multiple cervical lesions on T2 (52,2%). More than half of patients have positive oligoclonalband (60,9%), but more than quarter can't be checked because of funding constrain. DMT (interferon β-1a) was given to 34,8% patient, azathrioprine (21,7%) and methylprednisolon (43,5%).

**Conclusions:** Within two years, the number of patients with MS in RSCM increase. But in it′s management, there are some limitation either in diagnostic examination and treatment because of funding constraints and DMT currently isn′t covered by national health insurance.

**[P-17] Multiple Sclerosis in Children and Adolescents**

Authors: Talab R, Talabova M, Kizlo L

1 Department of Neurology, Charles University in Prague, Faculty of Medicine in Pilsen, Czech Republic

2 MS Center, Department of Neurology, University Hospital in Hradec Kralove, Czech Republic

3 Department of Radiodiagnostics, University Hospital in Hradec Kralove, Czech Republic

**Background:** In recent years there have been numerous reports about multiple sclerosis (MS) occurring in chilhood and adolescence. Pediatric multiple sclerosis constitutes about 2-5 % of all MS cases. The purpose of this poster is to document Czech experience of this population based on clinical observations.

**Objective:** To study the frequency of MS in children and adolescents, to describe the clinical and radiological feature, and to document the treatment in these population.

**Methods:** Children and adolescent diagnosed with MS at the MS center, University Hospital in Hradec Kralove, Czech Republic, between 1997 and 2011 were included. Gender, previous disease, age, risk factors, time to second attack, EDSS, predictors of activity MS, cerebral magnetic rezonance (MR) findings and treatment were recorded.

**Results:** The study included 41 patients (10 boys and 31 girls) who received MS diagnosis. Median age at onset was 16,7 years. Infantine MS (IMS) was 6 patients, median at onset was 10,5 years. Juvenile MS (JMS) was 35 patients, median at onset was 17 years. The most important risk factor was infection in 51,2%. Median EDSS at IMS was 1,75 and at JMS 1,5. The second attack has developed a total of 35 children, 9 boys and 26 girls. The median time to the other attacks was 19 months for boys, for girls 9,5 months. Almost all patients were treated with steroids in the acute phase and later with glatiramer acetat (22) and interferon-beta (12). Seven patients were escalated into natalizumab.

**Conclusion:** The time to other attacks is important predictor activity and prognosis of MS in children and adolescent. The patients were treated with same medical drugs as adults with MS and tolerated it well.

**[P-18] Progressive Multiple Sclerosis in Malaysia: A Retrospective Single Center Study**

Viswanathan S

Department of Neurology, Kuala Lumpur Hospital, Kuala Lumpur, Malaysia.

**Background:** Prior studies in Malaysia have shown that progressive Multiple sclerosis is rare.

**Objective:** To look at the the proportion of patients with progressive MS at a single tertiary referral center

**Method:** Longitudinal time series looking at data from the demyelinating diseases database accessed by a single neurologist.

**Diagnosis of MS was through the 2010 Mac Donalds criteria.**

**Results:** Over an 11-year period beginning from 2005 to 2016, out of 169 patients with MS, 9.5% (16) had progressive MS of which 3 had primary progressive MS and the rest had secondary progressive MS. The majority were young, females with most of Malay followed by Chinese and Indian origin. Of the secondary progressive MS patients, most had failed either interferons or mitoxantrone and were not on any disease modifying therapy at the current time.

**[P-19] Correlation Between Fatigue in Multiple Sclerosis Patients and Sleep Disorders**

Koseoglu M, Ilbay V, Polat D, Soylemez E, Ozturk O, Ozerden M, Atakli D, Soysal A.

Bakirkoy Research and Training Hospital for Psychiatry, Neurology, Neurosurgery; Department of Neurology; Istanbul, TURKEY

**Introduction:** Fatigue is highly frequent in multiple sclerosis (MS). It appears to be multifactorial, with primary or disease-related factors involved, as well as secondary factors, including comorbidities. Patients with MS are at increased risk for comorbid sleep disturbances, which can profoundly contribute to quality of life and fatigue.
Purpose: To evaluate the sleep disorders seen in fatigued MS patients.

Materials & Methods: Fatigue was assessed via the Fatigue Severity Scale (FSS). Tests performed to show sleep disorders were as follows; Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), Insomnia Severity Index (ISI), RLS severity rating scale (RLSSG), Berlin and Stop-bang questionnaire. Quality of life was evaluated by Short-Form-36 (SF-36). Disease severity quantified by Expanded Disability Status Scale (EDSS) and Beck Depression Inventory (BDI) was performed in order to exclude effects of depression.

Results: A total of 100 patients with MS (65 females, 35 males, mean age 35.31±9.15 y) were enrolled. The median MS duration was 5.83±4.51 (1-18) year, the median EDSS score was 1.48±1.33. It was determined that fatigue was present in 53% of MS patients. When comparing fatigued (N=53) and non-fatigued (N=47) patients, no statistically difference obtained in respect to disease duration but EDSS and BDI scores of the fatigued MS patients were detected higher. Significantly higher PSQI, ESS, RLSSG values were observed in fatigued MS patients (p= 0.001; p= 0.001, p= 0.01 respectively).

Conclusions: The findings of our study revealed that in MS patients suffering from fatigue sleep disorders should be considered in the etiology.

[P-20] Epilepsy in MS Patients
Faraji F1, Talaie A2*
1Associate professor of Neurology, Medicine Faculty, Arak University Of Medical Sciences, Arak, Iran
2MSC of Nutrition, Health Department, Islamic Azad university, Arak Branch, Iran

Background: A review of 29 published clinical series of adult patients who had epileptic seizures and multiple sclerosis (MS) yielded a prevalence of 2.3%, about three to six times that in the general adult population. The probable anatomic basis for the seizures is areas of inflammation, edema, and/or demyelination in the cerebral cortex and the juxtacortical white matter. Epilepsy usually appears late in the course of disease, although a single episode or a cluster of seizures can represent the onset symptom or a relapse of MS. Prognosis of epilepsy during the course of MS is usually good but the choice of AEDs remains a matter of debate. Seizures may take several forms: Generalized tonic-clonic seizures, simple or complex Partial seizures. Paroxysmal symptoms in many appear similar to an epileptic seizure but are of different origin. Examples of paroxysmal symptoms include: paroxysmal pain (e.g., trigeminal neuralgia), tonic spasms, Lhermitte’s sign, Uhthoff’s symptoms. Seizures are usually diagnosed by the clinical history and an electroencephalogram (EEG). The findings indicate that RRMS/Epilepsy patients have more extensive cortical inflammation than RRMS patients with no history of epilepsy. In most of the patient’s plaques are localized in the frontal region, associated with severe disability status. MRI shows numerous subcortical plaques. However, pure intracortical lesions are unlikely to be demonstrated with conventional MR, in contrast to double inversion recovery sequence. Interferons, Glatiramer acetate, Dalfampridine and Intrathecal baclofen can increase the occurrence of seizures.

Conclusion: In respect to MS patients with epilepsy, we must consider the form of epilepsy, MRI findings and appropriate choice of drug.

Tayebeh Sabokbar1,2, Abbas Shakoori2, Ehsan sharifipour1, Seyed Amir Hejazi1
1Neurology & Neurosciences Research Center, Qom University of Medical Sciences, Qom, Islamic Republic of Iran
2Tehran University of Medical Sciences, Department of Medical Genetics, Cancer Institute, Tehran, Islamic Republic of Iran

Introduction: Familial autoimmunity was investigated in major autoimmune diseases, i.e. rheumatoid arthritis, systemic lupus erythematous, autoimmune thyroid disease and type 1 diabetes mellitus. Also numerous studies support the adverse autoimmune reaction in multiple sclerosis (MS). We report a family suffered from definite MS and autoimmune hyperthyroidism with their family pedigree.

Report: Five family-relative patients suffered from MS to our hospital between 2008 and 2015. Their clinical states and brain & spinal cord MRI were compatible with definite MS disease. There were newly growing and tumefactive lesions in the back ground of demyelinating lesions in all patients. Autoimmune hyperthyroidism was found in two of the girls which were the first-generation family members. Pedigrees were drawn with pedigree software for family-based clinical data and demonstrated not recessive and not X-linked but more likely dominant pattern of penetrance with some degree (60-70%).

Conclusions: This family report with pedigrees emphasized on the autoimmune origin of MS and inheriting adverse reactions leading to these diseases.

[P-22] A Longitudinal 11-Year Follow-Up Study On Mortality in Patients with Multiple Sclerosis at A Single Tertiary Referral Center in Malaysia
Viswanathan S
Department of Neurology, Kuala Lumpur Hospital, Kuala Lumpur, Malaysia

Background: Patients with Multiple Sclerosis (MS) have an increase in mortality compared with the general population.

Objectives: At our tertiary referral center, the Department of Neurology, Kuala Lumpur Hospital we longitudinally followed up patients with MS over a 10 year period and looked for the number of patients who had died over that time period, causes of death, types of MS and mean duration of death from the onset of diagnosis.

Methods: This was a retrospective study with time series with longitudinal follow-up, extracting longitudinal real world data from the demyelinating diseases database at Kuala Lumpur Hospital, Malaysia.

Results: Out of 168 patients with MS, mortality was seen in 3.5% of patients, all females involving all three races; Malays, Indians and Chinese. All patients had progressive disease either secondary or primary progressive disease. Mean duration of disease was 5.83 years with mean age at death of 24.1 years. The
main cause of death was all cause sepsis. Compared to previous studies in the 1980’s in Malaysia where in mortality was > than 30%, these results are much better and may reflect earlier diagnosis and access to treatment.

Conclusions: Mortality due to indirect causes unrelated to MS has improved over the last few decades in Malaysia.

Poster Session 4
MS MRI

[P-23]
The Effects of the HLA-DRB1*04:05 Allele on Intracortical Lesions Detected by 3-Dimensional Double Inversion Recovery Imaging in Japanese Patients with Multiple Sclerosis

K Shinoda1, T Matsushita1, Y Nakamura1, K Masaki1, R Yamashita1, O Togao2, A Hiwatashi2 and J-I Kira1
1Department of Neurology, Neurological Institute, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan
2Department of Clinical Radiology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

Same as [O-3]

[P-24]
Deep Learning of Joint Myelin-T1w MRI Features on Normal-ApPEARING Brain Tissues Distinguishes Multiple Sclerosis from Healthy Controls

Y. Yoo, T. W. Tang, T. Brosch, D.K.B. Li, S. Kolind, I. Vavasour, A. Rauscher, A. Traboulsee, R. Tam
University of British Columbia, Vancouver, BC, Canada

Same as [O-9]

[P-25]
Investigation of Microscopic Tissue Changes in Multiple Sclerosis: A Sodium (23Na) MRI Study

Philipp Eisele, MD1; Simon Konstandin, PhD1; Martin Griebe, MD1; Kristina Szabo, MD1; Marc E. Wolf, MD1; Angelika Alonso, MD1; Christopher J. Schwarzbach, MD1; Anne Ebert, PhD1; Christina Togao1; Christel Weiß, PhD4; Melissa Ong, MD5; Stefan O. Schoenberg, MD5; Lothar R. Schad, PhD1; Achim Gass, MD1
1Department of Neurology, Universitätshypertension Mannheim, University of Heidelberg, Theodor-Kutzer-Ufer 1 – 3, 68167 Mannheim, Germany
2MR-Imaging and Spectroscopy, Faculty 01 (Physics/Electrical Engineering), University of Bremen, NW 1 Otto-Hahn-Allee 1, 28359 Bremen, Germany
3Computer Assisted Clinical Medicine, Universitätshypertension Mannheim, University of Heidelberg, Theodor-Kutzer-Ufer 1 – 3, 68167 Mannheim, Germany
4Department for Statistical Analysis, Universitätshypertension Mannheim, University of Heidelberg, Ludwig-Krehl-Straße 13 – 17, 68167 Mannheim, Germany
5Institute of Clinical Radiology and Nuclear Medicine, Universitätshypertension Mannheim, University of Heidelberg, Theodor-Kutzer-Ufer 1 – 3, 68167 Mannheim, Germany

Same as [O-22]

[P-26]
The Consistency of Myelin-Specific Magnetic Resonance Imaging Across Sites and Scanner Manufacturers in vivo

Lee, LE1, Ljungberg, EA2, Mackay AL3, Rauscher A1, Li DKB1, Traboulsee AL1, Figley CR1, Kolind SK1
1Department of Medicine (Neurology), University of British Columbia, Vancouver, British Columbia, Canada
2Department of Physics and Astronomy, University of British Columbia, Vancouver, British Columbia, Canada
3Department of Radiology, University of British Columbia, Vancouver, British Columbia, Canada

Background: Myelin water imaging provides quantitative measure of myelin by measuring the signal from water trapped between the myelin bilayers. Myelin water fraction (MWF), the ratio of myelin water to the total water content, can be used as an in-vivo marker of demyelination and remyelination in multiple sclerosis.

Objective: To determine the consistency of MWF measurements in white matter (WM) and grey matter (GM) regions of interest (ROIs) in healthy human brains across sites and scanner manufacturers.

Methods: MWF maps were generated using a whole-brain 3D Gradient and Spin Echo (GRASE) sequence data, which were acquired for three healthy subjects using a Philips Achieva 3T MRI scanner in Vancouver, Canada and Siemens Verio 3T MRI scanner in Winnipeg, Canada. Eight WM and GM ROIs were compared across the scans from the two sites.

Results: There was a strong correlation between the MWF estimates from Philips 3T and Siemens 3T (slope=0.98, r=0.91, p<0.001). Individually, subject 1 (r=0.89, p<0.001), subject 2 (r=0.93, p<0.001), and subject 3 (r=0.94, p<0.001), also showed high correlation. The correlation remained significant when only WM was included (r=0.88, p<0.001).

Conclusion: Dual-site acquisition and analysis of MWF estimates were in good agreement. This is the first time a clinically feasible protocol for multi-echo T2 relaxation has been demonstrated across sites and scanner manufacturers. This result opens the door for multicenter studies and clinical trials, as it can provide valuable information on pathological changes resulting from underlying disease or abnormality in MS.

[P-27]
INSPIRATION-MRI: Standardized Acquisition and Centralized Quantitative Reading of MRI Scans of RRMS Patients in German Daily Clinical Practice

A. Gass1, J. Gregori2, S. Hoffmann3, A. Fuchs4, C. Cornelissen1
1Neurological Clinic, Medizinische Universität Mannheim, Germany
2Medini GmbH, Heidelberg, Germany
3Novartis Pharma GmbH, Nuremberg, Germany

Background: INSPIRATION is a non-interventional study, conducted in Germany, to validate the feasibility and potential benefit of standardized MRI-acquisition and central-quantitative MRI-reading in clinical practice for RRMS-patients.

Objective: MRI has become an integral part of MS-patient management. However, quantitative analysis of lesion-load is not trivial and has mainly been realized in clinical trials. We investigate whether additional quantitative information and visualization of
lesion-load is regarded useful in the daily management of RRMS-patients.

Methods: INSPIRATION included 253 patients in 15 centers. Sites underwent expert training and standardized sequence implementation. A centralized quantitative MRI-data analysis is performed (volume of T2-lesions, T1-hypointense and contrast-enhancing lesions. Brain volume changes are also assessed.

Results: 392/394 (99.5%) data sets passed the quality analysis. 34.7% of the patients were treated with fingolimod upon study inclusion (21.5%-interferons, 17.9%-dimethylfumarate, 7.6%-copaxone, 6.8%-natalizumab, 10.8%-no/other). The mean number (±SD)/ml volume (±SD)/OT2 lesions at baseline was 30.1 (±2.8)/11033.1 (±1578.9), of black holes 4.0 (±0.9)/4903.3 (±135.5), Gd+ lesions 0.4 (±0.2)/31.1 (±20.3). 103 patients with a 12-months follow-up MRI: T2 lesions 32.5 (±4.7)/11634.4 (±2297.4), black holes 4.3 (±1.4)/547.4 (±210.0), Gd+ lesions 0.2 (±0.1)/180.0 (±14.1).

Conclusions: More sophisticated, additional quantitative MRI-analysis is provided in a real world situation and revealed differences between the estimation of lesion numbers by the centers and the quantitative approach. A centralized approach might improve the comparability of MRI scans. The quantitation of lesion load and volumes and visualization of MRI-abnormalities may facilitate MRI-data use by the responsible neurologist to support patient management.

[P-28]

Persistent MRI Lesion Activity and Brain Volume Loss as Predictors of Long Term Disability Progression under Treatment in Relapsing–Remitting Multiple Sclerosis

M.P. Sormani1, L. Kappos1, D. Plani-Meier1, D. Häring1, D. Tomic1, N. de Stefano1

1University of Genoa, Biostatistics Unit, Department of Health Sciences, Genoa/Italy
2Neurological Clinic and Polyclinic, Departments of Medicine, Clinical Research, Biomedicine and Biomedical Engineering, University Hospital Basel, Basel, Switzerland
3Novartis Pharma AG, Basel/Switzerland
4University of Siena, Siena, Italy

Background: Relapsing-remitting multiple sclerosis (RRMS) patients free from relapses can still have magnetic resonance imaging (MRI) lesion activity and brain volume loss (BVL).

Objective: We investigated MRI activity parameters, measured early during treatment with fingolimod, as potential predictors of long-term disability progression in RRMS patients with no clinical signs.

Methods: FREEDOMS/FREEDOMS-2 study patients treated with fingolimod who were relapse-free during first year of therapy were included (n=1066). The impact of 1-year MRI markers on 4-year disability progression was evaluated using multivariate Cox models. Candidate predictors included: number of new T2 lesions over Year 1, persistent lesion activity (defined as presence of new T2 lesions in both the first and second 6 months), and the Year 1 percentage brain volume change (PBVC; cut-off 0.4% or 0.8%).

Results: Amongst tested markers, PBVC>0.8% (hazard ratio [HR]=1.67; p=0.002) and persistent T2 lesion activity (HR=1.70; p=0.007) were independent predictors of long-term disability progression in patients under therapy. Risk of 4-year disability progression for patients with both PBVC >0.8% and persistent T2 lesion activity (4.9% of total population) was 28% compared with 14% for patients with PBVC ≤0.8% and no persistent lesion activity (64.9% of total population, HR=2.63; p=0.001).

Conclusions: In patients without relapse during first year of fingolimod treatment, persistent lesion activity was a better predictor than number of new T2 lesions in identifying patients with a higher risk of future disability. A combination of 1-year persistent MRI lesion activity and a high rate of 1-year PBVC was associated with the highest disability progression risk.

[P-29]

Brain Volume Loss Correlates with Long-term Disability Worsening in Patients with MS: SIENA Analysis of TEMSO MRI Data

E-W Radue1, J Wuerefel1, K Thangavelu2, S Cavalleri2, T Sprenger1, 4

1Medical Image Analysis Center (MIAC), Basel, Switzerland
2Sanofi Genzyme, Cambridge, MA, USA
3University Hospital Basel, Basel, Switzerland
4DKD Helios Klinik, Wiesbaden, Germany

Background: In TEMSO (NCT00134563), SIENA (structural image evaluation using normalisation of atrophy) analysis determined that teriflunomide significantly reduced brain volume loss (BVL) vs placebo, which was strongly correlated with disability worsening. Subgroup analyses showed that teriflunomide significantly slowed BVL, independently of disability worsening, over 2 years.

Objective: To explore BVL and long-term disability worsening in an analysis of TEMSO and its extension (NCT00803049).

Methods: Blinded SIENA analysis of patient scans (n=969) determined BVL in Year 1 and Year 2. Percentage brain volume changes (PBVC) from baseline to Year 2 were categorised into quartiles (Q1–Q4) to evaluate probability of 12- and 24-week confirmed disability worsening (CDW) over 5 years in the extension. Probability of worsening was derived from Kaplan-Meier estimates. Quartiles were compared using a Cox proportional hazards model (covariates: PBVC categories, Expanded Disability Status Scale strata at baseline, and region).

Results: The group with the greatest BVL from baseline to Year 2 (Q1; n=177) had a significantly higher probability of both 12- and 24-week CDW after 5 years than those in the quartile with the lowest BVL (Q4; n=178): Q1 vs Q4 hazard ratios, 0.611 (95% confidence interval [CI] 0.432, 0.865; P=0.0055) and 0.566 (95% CI 0.386, 0.830; P=0.0036) for 12- and 24-week CDW after 5 years, respectively.

Conclusions: These analyses support the association between BVL and later disability worsening. Greater rates of BVL over 2 years are predictive of longer-term disability worsening at 5 years in the TEMSO extension.

Poster Session 5

MS/NMO OCT

[P-30]

The Maculo-Papillary Bundle and Inner Ganglion Cell Layer Are Affected More Prominently in Radiologically Isolated Syndrome

Rana Karabudak, Atay Vural, Nazire Pınar Acar, Meryem Aslı Tuncer, Güliz Sayat, Sibel Kadayifclar
Longitudinal Follow Up of Retinal Nerve Fibre Layer (RNFL) Thickness in Multiple Sclerosis (MS) and Its Significance
Suvekshumkar R, Chinaranjeevi K, M. Dhar
1Department of Neurology, Amrita Institute of Medical Sciences and Research Centre, Kochi, Kerala, India
2Department of Ophthalmology, Amrita Institute of Medical Sciences and Research Centre, Kochi, Kerala, India

Background: RNFL is increasingly being used as an additional noninvasive investigative tool in MS.

Objectives: 1. To study RNFL thickness values in patients affected with Relapsing and Remitting Multiple Sclerosis (RRMS). 2. To look for progressive decrease in RNFL thickness over time.

Methods: 14 RRMS patients diagnosed by the modified McDonald 2010 criteria were included in the study. The RNFL thickness at baseline was documented. The value was compared with 12 age matched normal controls. The non-optic neuritic (NON) eye of these patients were then followed up over six months and a repeat OCT was done. MRI Brain T2 lesions and Contrast enhancing new lesions were also noted at base line and after 6 months.

Results: The study included 14 patients (28 eyes) with mean age of 34.78 ± 8.91 years and a male: female ratio of 1.9:1. The mean RNFL thickness of MS patients at baseline was 93.16 ± 16.86 compared to age matched normal control 99.02 ± 10.79, p value significant. The mean RNFL thickness of only the NON eye when compared with controls were not statistically significant. The mean RNLF of NON eye at baseline in right eye (RE) was 91.6 ± 19.61 which reduced to 84.90 ± 16.4 after six months. Similarly, the RNFL baseline values of left eye (LE) was 98.64 ± 14.72 and was reduced to 89.419 ± 14.15 both p value were significant.

Conclusions: OCT has a role as a noninvasive tool to document axonal loss and its progression over time in patients with MS.

Comparison of Optical Coherence Tomography with Corpus Callosum Index in Assessing Cognitive Dysfunction Among The Multiple Sclerosis Patients
Behnaz Sedighi1, Amir-Khosrou Ghaseminejad2, Zohreh Abna3, Amir Sharafat4

1Associate Professor of Neurology - Neurology Research Center, Kerman University of Medical Sciences, Kerman, Iran
2Assistant Professor of Ophthalmology - Ophthalmology Research Center – Kerman University of Medical Sciences, Kerman, Iran
3Neurologist, Private Practice, Kerman, Iran
4Resident of Neurology – Kerman University of Medical Sciences, Kerman, Iran

Background: Multiple sclerosis is a neurodegenerative disease of the central nervous system. Retinal nerve fiber layer (RNFL) is an unmyelinated cluster of nerves and could its thickness could be an indicator of axonal loss and brain atrophy in multiple sclerosis (MS) patients. We compared the thickness of RNFL in a group of patients with relapsing remitting MS who received regular treatments in a span of three years.

Method: Patients with confirmed relapsing remitting MS were enrolled in the study. Baseline demographic and disease data were recorded from all patients. RNFL thickness was measured in all patients at baseline using an optical coherence tomography (OCT) method. The patients were followed up for three years while they received routine treatments. At the three years mark OCT measurements were repeated.

Results: In a sample of 12 patients (11 females) the mean ± SD of age and duration of disease was 35.6 ± 6.1 and 5.3 ± 5.8 years respectively. The mean ± SD of EDSS score was 1.7 ± 1 among patients at baseline. The mean ± SD of total RNFL thickness values at baseline and after three years was (left: 101.2 ± 9.1 and 92 ± 7.9 micrometers; P value: 0.0001) and (right: 99.7 ± 86.3 and 86.3 ± 20.3 micrometers; P value: 0.01) respectively.

Conclusion: The measurements of RNFL thickness using OCT provides significant evidence of axonal atrophy after a short time span among RRMS patients despite receiving treatments. Patients can benefit from similar measurement as a tool for evaluation of treatment efficacy.
Background: Multiple sclerosis is a neurodegenerative disease of central nervous system. Previous studies have demonstrated that optical coherence tomography (OCT) is an inexpensive and accessible tool to evaluate the progress of Multiple sclerosis (MS).

Objective: In the current study, OCT and corpus callosum index (CCI) have compared for early evaluation of axonal damages such as cognitive dysfunction in MS patients.

Methods: Corpus callosum index of thirty MS patients and 30 age- and sex-matched healthy controls were assessed by MRI. In addition, cognitive function of MS patients was evaluated by Brief International Cognitive Assessment for MS (BICAMS) test and retinal nerve fiber layer thickness measured by OCT.

Results: The findings of our study demonstrated that CCI among the patients with impaired cognition had lower than the control groups and there was no significant correlation between cognitive status and CCI (P value=0.804). Among impaired cognition group, 81.8% of patients had abnormal OCT, while only two patients had normal OCT, furthermore our data showed significant difference between OCT and cognition (P value=0.026).

Conclusion: According to this study, OCT is as useful method in evaluation of axonal loss and to predict cognitive dysfunction in MS patients comparing with CCI or other measures.

Correlation among Visual Function, Thickness of Circumpapillary Retinal Nerve Fiber, and Macular Ganglion Cell-Inner Plexiform Layers in Previous Neuromyelitis Optica

Objective: To investigate association among visual acuity (VA), mean deviation of visual field (MD), and circumpapillary retinal nerve fiber layer (RNFL) and macular ganglion cell-inner plexiform layer (GCIPL) thicknesses in previous optic neuritis (ON) eyes of AQP4-positive neuromyelitis optica spectrum disorder (NMOSD) patients

Materials and Methods: Thirty-three previous ON eyes underwent complete ophthalmic examination and SD-OCT imaging to analyze RNFL and GCIPL thicknesses after at least 6 months of the last episode of acute optic neuritis.

Results: Visual field examination could not be performed in 5 eyes that had severe visual impairment (VA: hand motion in 3 eyes, light perception in 1 eye, and no light perception in 1 eye). Twenty-eight eyes were included and analyzed, as follows: mean VA: 0.48±0.61; mean MD: -9.61±9.16; mean average RNFL thickness: 66.21±11.16 μm; and, mean average GCIPL thickness: 57.68±6.917 μm. LogMAR VA and MD were significantly correlated with the average, superior, nasal, and inferior quadrants of RNFL, but not with the temporal quadrant. All eyes (12/12) with an average RNFL thickness greater than 70 μm had an MD of at least -5.5. All eyes (9/9) with an average RNFL thickness less than 60 μm had an MD less than -10. Neither VA nor MD can indicate levels of GCIPL loss.

Conclusion: In previous optic neuritis eyes of AQP4-positive NMOSD patients, average circumpapillary RNFL thickness can predict mean deviation of visual field by using cut point thicknesses of 60 and 70 μm, which are compatible with mean deviations of -10 and -5.5, respectively.

Correlation among Visual Function, Thickness of Circumpapillary Retinal Nerve Fiber, and Macular Ganglion Cell-Inner Plexiform Layer Thicknesses in Neuromyelitis Optica Spectrum Disorder and Multiple Sclerosis Eyes without Clinically Attacked Optic Neuritis

Objective: To investigate association among visual acuity (VA), mean deviation of visual field (MD), and circumpapillary retinal nerve fiber layer (RNFL) and macular ganglion cell-inner plexiform layer (GCIPL) thicknesses in previous optic neuritis (ON) eyes of AQP4-positive neuromyelitis optica spectrum disorder (NMOSD) patients

Materials and Methods: Thirty-three previous ON eyes underwent complete ophthalmic examination and SD-OCT imaging to analyze RNFL and GCIPL thicknesses after at least 6 months of the last episode of acute optic neuritis.

Results: Visual field examination could not be performed in 5 eyes that had severe visual impairment (VA: hand motion in 3 eyes, light perception in 1 eye, and no light perception in 1 eye). Twenty-eight eyes were included and analyzed, as follows: mean VA: 0.48±0.61; mean MD: -9.61±9.16; mean average RNFL thickness: 66.21±11.16 μm; and, mean average GCIPL thickness: 57.68±6.917 μm. LogMAR VA and MD were significantly correlated with the average, superior, nasal, and inferior quadrants of RNFL, but not with the temporal quadrant. All eyes (12/12) with an average RNFL thickness greater than 70 μm had an MD of at least -5.5. All eyes (9/9) with an average RNFL thickness less than 60 μm had an MD less than -10. Neither VA nor MD can indicate levels of GCIPL loss.

Conclusion: In previous optic neuritis eyes of AQP4-positive NMOSD patients, average circumpapillary RNFL thickness can predict mean deviation of visual field by using cut point thicknesses of 60 and 70 μm, which are compatible with mean deviations of -10 and -5.5, respectively.


**Materials and Methods:** Spectral-domain OCT data were obtained in non-optic neuritis eyes of 13 seropositive NMOSD patients, 8 RRMS patients, and 21 eyes of age-matched healthy controls.

**Results:** In seropositive NMOSD group, non-optic neuritis eyes show statistically significant difference neither in any circumpapillary RNFL thickness nor macular GCIPL thickness compared to control group ($p=0.37$, respectively). In RRMS group, the eyes with well documentation of no prior clinical optic neuritis attack show significantly thinner of RNFL and GCIPL thinning in non-optic neuritis eyes of AQP4-IgG positive neuromyelitis optica spectrum disorder (NMOSD), an entity of which clinical presentation often overlap to MS.

**Conclusions:** As none of significant subclinical retinal ganglion cell damage was evidenced by either circumpapillary RNFL or macular GCIPL parameters thinning in non-optic neuritis eyes of seropositive NMOSD. The presence of OCT parameters thinning in non-optic neuritis eyes especially circumpapillary RNFL at temporal quadrant and any of macular GCIPL may suggest subclinical optic neuritis attack or insidious deterioration frequently found in RRMS eyes.

**Poster Session 6**

**MS Genetical and Immunological Studies**

**[P-37] The Role of Genetic Susceptibility Variants in Predicting Clinical Course in Multiple Sclerosis: A Cohort Study**

Gongbu Pan,1 Steve Simpson, Jr,1 Ingrid van der Mei,1 Jac C. Charlesworth,1 Robyn Lucas,1 Anne-Louise Ponsonby,1 Yuan Zhou,1 Feitong Wu,1 AusLong/Ausimmune Investigator Group,1 Bruce V. Taylor1

1Menzies Institute for Medical Research, University of Tasmania, Hobart, Australia

2National Centre for Epidemiology and Population Health, Research School of Population Health, The Australian National University, Canberra, Australia

3Murdock Children’s Research Institute, University of Melbourne, Melbourne, Australia

A full list of members of the AusLong/Ausimmune Investigator Group is provided in the Acknowledgments.

**Same as [O-4]**

**[P-39] Distinct Repertoires of CD4 and CD8 T Cells in Multiple Sclerosis Patients with and without Deletion-type Copy Number Variations**

Guzailiayi Maimaitijiang1, Koji Shinoda1, Yuri Nakamura1, Katsuhisa Masaki1, Takuya Matsushita1, Ryo Yamasaki1, Yasunobu Yoshikai1, Jun-ichi Kira1

1Department of Neurology, Neurological Institute, Kyushu University, Fukuoka, Japan

2Division of Host Defense, Medical Institute of Bioregulation, Kyushu University, Fukuoka, Japan

**Same as [O-8]**
those in the presence of other control antigens, whereas no significant differences were found between these two groups.

Conclusions: With this method, adequate MBP-reactive CD4+CD25+ Tregs derived from autologous naive CD4+ T cells of MS patients were obtained and returned to normal without immune defects, and even upregulated their immunosuppressive function mostly through the elevated release of IL-10 and TGF-β1.

[P-40] The Higher the Total Number of Relapses, the Lower the Number of Circulating Follicular Helper T Cells from the Patients with Multiple Sclerosis


Neurology of Saitama Medical Center, Saitama Medical University, Kawagoe-shi, Saitama, Japan

Background: Follicular helper T (Tfh) cells are distinct subset of CD4+ helper T cells that are essential for germinal center formation, affinity maturation, and the development of most high-affinity antibodies and memory B cells.

Objective: To find out the pathogenic role of Tfh cells in the course of multiple sclerosis (MS).

Methods: Twenty-five MS patients, age 22 - 68, 7 men, 19 women, (10 patients at relapse, and 16 patients at remission) participated in this study. We have defined circulating human Tfh cells as a subset of CXCR5+ CD4+ T cells. Peripheral heparinized blood samples (2 ml) were obtained from each patient. FACS analysis was carried out using a FACS Canto II cytometer (BD Biosciences).

Results: The frequency of circulating Tfh cells was 6.02±3.07 % (mean ± SD) and at relapse was 4.21±3.28 %, at remission was 7.16±2.39 %. There was a correlation between accumulated number of relapses and the frequency of Tfh cells (p=0.01).

Conclusions: Our findings indicated that circulating Tfh cells, CXCR5+ CD4+ T cells, may decrease as the number of relapses accumulate.

[P-41] DDIT4 and Its Associated LncRNA DDIT4 Modulate TH17 Cell Differentiation Through DDIT4/TSC/mTOR Pathway

Fang Zhang, MD; Guiyou Liu, MS; Changjuan Wei, MD, PhD; Junwei Hao, MD, PhD

1Department of Neurology, Tianjin Neurological Institute, Tianjin Medical University General Hospital, Tianjin 300052, China
2School of Life Science and Technology, Harbin Institute of Technology, Harbin, China

Background: Inflammation in several autoimmune diseases, including MS, has been linked to abnormal differentiation of IL-17-producing Th (Th17) cells. However, the factors that promote Th17-driven autoimmunity are unclear.

Objective: Here, we present evidence that DDIT4 and its associated lncRNA DDIT4 inhibit Th17 cell differentiation.

Methods: We knockdown and overexpression of IncDDIT4, and then observed the changes of Th17 cells.

Results: Isolation of naive CD4+T cells from peripheral blood mononuclear cells of multiple sclerosis patients revealed increased levels of IncDDIT4 and DDIT4 following stimulation with Th17-inducing cytokines but not following Treg, Th1, or Th2 induction. Over expression of IncDDIT4 in CD4+T cells from patients with multiple sclerosis reduced IL17 transcription through decreased activation of DDIT4 and reduced activation of the DDIT4/mTOR pathway, which is known to inhibit Th17 differentiation. Importantly, silencing IncDDIT4 in CD4+T cells from patients with multiple sclerosis enhanced Th17 differentiation through increased activation of DDIT4/mTOR pathway.

Conclusions: Our results suggest that IncDDIT4 and DDIT4 inhibition has potential as a therapeutic strategy for multiple sclerosis and other Th17-driven autoimmune diseases.

[P-42] Linc-MAF-4 Increase Annual Relapse Rate of Multiple Sclerosis Patients Through Regulation of CD4+ T Cell Differentiation

Fang Zhang, MD; Guiyou Liu, MS; Changjuan Wei, MD, PhD; Chao Gao, MD; Junwei Hao, MD, PhD

1Department of Neurology, Tianjin Neurological Institute, Tianjin Medical University General Hospital, Tianjin 300052, China
2School of Life Science and Technology, Harbin Institute of Technology, Harbin, China

Background: In the current study, we noted that the linc-MAF-4 is predominant in Th1 cells and can regulate Th1/Th2 differentiation. Since multiple sclerosis is a CD4+ T related autoimmune disease, whether linc-MAF-4 that regulate the pathogenesis of multiple sclerosis still need further elucidation.

Methods: For this study, we recruited 26 multiple sclerosis patients according to the revised McDonald Criteria. Then we chose 6 patients for microarray analysis. Microarray assays identified outstanding differences in linc-MAF-4 and MAF-4 expression, which were verified through real-time PCR. We knockdown and overexpression linc-MAF-4, and then observed the changes of CD4+ T cell subsets and the function of CD4+ T cells.

Results: The expression of linc-MAF-4 was significantly increased in the peripheral blood mononuclear cells of patients with multiple sclerosis, and this linc RNA regulate encephalitogenic T helper type 1 (Th1) cell differentiation. Transfection of synthetic linc-MAF-4 in naive CD4+ T cells facilitated Th1 differentiation and inhibited Th2 differentiation through inhibiting MAF directly, which is a Th2 transcription factor. Linc-MAF-4 also promote the activation of CD4+ T cells of multiple sclerosis patients. The expression level of linc-MAF-4 was correlated with annual relapse rate and number of lesions.

Conclusion: Our results suggested that linc-MAF-4 is probably involved in the regulation of encephalitogenic T cells in the pathogenesis of MS.

[P-43] E3 Ubiquitin-protein Ligases CUL2 and UBR2 are Downregulated in Peripheral Blood Lymphocytes Isolated from Multiple Sclerosis Patients

X. Ma; C. Wei; Y. Wang; L. Zhang; J. Hao

1Department of Neurology and Tianjin Neurological Institute, Tianjin Medical University General Hospital, Tianjin 300052, China
2State Key Laboratory of Medicinal Chemistry Biology, College of Pharmacy, Collaborative Innovation Center for Biotherapy, and
Objective: Ubiquitination has a tightly connection with the regulation of immune system, and ubiquitin related enzymes may have regulatory effects on immune responses. However, the possible involvement of ubiquitin related enzymes of ubiquitin-proteasome system in multiple sclerosis (MS), an autoimmune disease mediated by CD4+ T cells, is still unclear. We sought to identify novel ubiquitin related enzymes, which may contribute to the pathogenesis of MS.

Design and Methods: In this study, 27 patients with relapse-remitting multiple sclerosis (RRMS) and 18 healthy controls were enrolled. Blood samples were collected from both of MS patients and controls and periphery blood mononuclear cells (PBMCs) were isolated. The transcriptional differentiations of 84 key genes of ubiquitin related enzymes between MS and healthy controls were examined by using RT2 ProfilerTM PCR Array. The result was validated by quantitative real-time PCR (qRT-PCR) and western blot.

Results: We found that 30 genes of ubiquitin related enzyme are expressed differently from healthy control. Especially, E3 ubiquitin ligases CUL2 and UBR2 were downregulated both in mRNA and protein level in MS patients.

Conclusions: Ubiquitin-proteasome system is skewed in the patients with MS, and E3 ubiquitin ligases CUL2 and UBR2 is associated with the etiology of MS.

The Possible Role of Fractalkine (CX3CL1) in Immunopathogenesis of Primary Progressive Multiple Sclerosis
Ceyla İrkeç1, Tuba Kuz2, Işıl Fidan2
Gazi University Faculty of Medicine, Neurology1 and Microbiology2 Departments, Ankara, Turkey

Background: Primary progressive multiple sclerosis (PPMS) differs from relapsing remitting multiple sclerosis (RRMS) in its immunological, pathological, radiological and genetic characteristics. Immunologically chemokine mediated inflammation one of the part of this neuroinflammatory and neurodegenerative process. Fractalkine (CX3CL1) is one of the chemokine, that implicate inflammatory cell migration to central nervous system.

Objective: A minority of patients suffer from a progressive clinical course without remissions PPMS and there is not enough information about this progressive process so we aim in our study that assessing the role of fractalkine (CX3CL1) in patients between PPMS, RRMS and controls.

Method: Patients in the group of PPMS and RRMS had this diagnosis via the McDonald Criteria which was recommended by the International Panel on MS Diagnosis. Serum fractalkine concentrations in the groups of PPMS, RRMS and controls were measured by Enzyme Linked Immunosorbent Assay (ELISA) method.

Results: Fractalkine serum levels markedly increase in inflammatory neurological disease. The most important result in our study was, serum fractalkine levels in PPMS patients was significantly lower than RRMS patients and control groups.

Conclusion: In accordance with our results, the significant decreased serum fractalkine levels in patients with PPMS suggested that fractalkine might has a role in immunopathogenesis of PPMS. Our data support the hypothesis that PPMS is immunologically different from RRMS and fractalkine will be a therapeutic target.

Usefulness of CSF Examination in Diagnosis of CNS Demyelinating Disease and CNS Lymphoma
Ikeguchi R (MD), Shimizu Y (MD), Shimizu S (MD), Kitagawa K (MD)1
1Department of Neurology, Tokyo Women’s Medical University School of Medicine, Tokyo, Japan

Background: The diagnosis of central nervous system (CNS) demyelinating disease by radiographical examination is often difficult because of its similarity to CNS tumour.

Objective: To elucidate whether cerebrospinal fluid (CSF) findings are useful in diagnosis of CNS demyelinating disease and CNS tumour.
Methods: We measured CSF cell count, level of protein, glucose, interleukin (IL)-6, IL-10, soluble IL-2 receptor (sIL-2R), myelin basic protein (MBP), and IgG index. Sixty-six multiple sclerosis (MS) patients, 42 neuromyelitis optica spectrum disorder (NMOSD) patients, 20 tumefactive demyelinating lesion (TDL) patients, 13 CNS lymphoma patients, and 10 glioma patients were included. Logistic regression analysis and receiver operating characteristic (ROC) curve analysis were done to detect diagnostic marker of each disease.

Results: The CSF level of protein, sIL-2R, and IL-10 were significantly higher in CNS lymphoma than that in MS, NMOSD, and TDL. In addition, onset age of MS, NMOSD, and TDL was significantly younger than that of CNS lymphoma. In multiple logistic regression analysis, CSF level of sIL-2R and onset age were identified as predictor of CNS lymphoma. Analysis of ROC curve showed that CSF sIL-2R and onset age were useful for differentiating patients with CNS lymphoma from those with CNS demyelinating diseases (area under curve [AUC] 0.929).

Conclusions: CSF sIL-2R was useful in differentiating CNS demyelinating diseases and CNS lymphoma. Combination of CSF findings and clinical data such as onset age may be also helpful to diagnose correctly these diseases.

[P-47]
The Possible Role of Apelin and Adiponectin in Multiple Sclerosis Pathogenesis
C. Irkeç1, F. Yekeler Ozdemir2, T. Altıparmak1, R. Tural3, N. Altan2
Gazi University Faculty of Medicine, Departments of Neurology1 and Biochemistry2, Ankara, Turkey
Objective: In this study we determine that whether there is a difference between apelin and adiponectin levels at age and stage of the disease in relapsing-remitting multiple sclerosis (RRMS) patients. Apelin hasn’t been investigated yet and adiponectin has been a small amount. We thought that these proteins has a possible role in multiple sclerosis (MS) pathogenesis and a candidate biomarkers for diagnosis and modulation of the therapy.

Methods: We include 34 RRMS patients and 20 healthy controls in this study who examined in our medical center. Patients serum samples were obtained; apelin and adiponectin levels were evaluated with enzyme–linked immunosorbent assay (ELISA) method.

Results: There isn’t any significant statistically difference between in attack and remission groups of serum apelin and adiponectin levels. In remission groups apelin shows a positive correlation, adiponectin has a negative correlation with age. However in healthy control group there is no significant difference between them. Moreover in remission groups there is a statistically significant high levels of apelin and adiponectin in females than males.

Conclusion: Many studies have been conducted about the effects of adipocytokines in MS previously. Apelin hasn’t been investigated yet and adiponectin has been a small amount. Further investigations require for contribute MS pathogenesis with larger series and more detailed methods.

[P-48]
Reduced Semaphorin 3A Level in Multiple Sclerosis
Mazdak Ganjilkhani-hakemi1*, Mahsa rezaeepoor1, Shima Shapouri1, Fereshte Aleshehbofsooli1, Nahid Eskandari1, Masoud Etemadifar2
1Department of Immunology, Faculty of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran.
2Multiple Sclerosis and Neuroimmunology Research Center, Isfahan University of Medical Sciences, Isfahan, Iran.
Purpose: Semaphorin-3A (Sema-3A) and its particular receptor neuropilin-1 (NP-1) appear on some immune cells and act as a suppressor of immune cell over-activation. Sema3A as an immune modulator could participate in pathogenesis of autoimmune diseases. In the current study, we aimed to investigate Sema3A gene expression in peripheral blood mononuclear cells (PBMCs) and its serum level in relapsing-remitting multiple sclerosis (RRMS) patients.

Materials and Methods: In the current study, we aimed to investigate Sema3A expression in peripheral blood mononuclear cells (PBMCs) and its serum level in relapsing-remitting multiple sclerosis (RRMS) patients. Fifteen newly determined and untreated RRMS patients were chosen and assessed in relapsing and remitting phases, then compared with fifteen healthy individuals.

Results: Our results revealed that serum level of Sema3A and its gene expression in PBMCs of RRMS patients were significantly lower than in normal subjects. We also showed that this down regulation has a high predictive value based on ROC analysis data.

Conclusion: These results may lighten an unknown aspect of Sema-3A role in some autoimmune disorders like multiple sclerosis (MS) and also propose a probable therapeutic approach for the future. Moreover, we suggest that Sema3A could be considered as a diagnostic biomarker for MS disease.

[P-49]
Serum Retinol Levels are Associated with Brain Volume Loss in Patients with Multiple Sclerosis
H. Yokota1,3, T. Shuta1, T. Kamata2, N. Sanjo1, T. Yokota1
1Department of Neurology, Nitobe Memorial Nakano General Hospital
2Department of Neurology, Musashino Red Cross Hospital
3Department of Neurology and Neurological Sciences, Tokyo Medical and Dental University
Background: Brain atrophy has been recognised as an endpoint of irreversible tissue loss that is closely associated with disability in patient with multiple sclerosis (MS). Although predicting future brain volume loss is important, studies have been shown only few biomarkers that can predict brain volume loss (BVL).

Objective: The aim of this study is to elucidate the association between longitudinal BVL and serum biomarker candidates.

Methods: This single-centered retrospective observational study intended to cover MS patients during January, 2008 to March, 2016. Inclusion criteria were: 1) patients who have brain MRI two times with intervals of more than 24 months; 2) patients who have blood test at the time or within 3 months of MRI scan. Evaluation of brain volume was done using SIENAX and SIENA in the FMRIB software library (FSL). Three serum biomarker candidates, uric acid (UA), 25-hydroxyvitamin D (25(OH)D) levels and retinol binding protein (RBP) levels were measured.

Results: Twenty-three patients with MS were included in this study. We found that serum RBP levels were significantly correlated with percentage brain volume change (PBVC) (p = 0.044).
0.0079). Furthermore, best subset selection of multiple linear regression models identified baseline normalised brain volume (NBV) and serum RBP as the best predictors of PBVC ($R^2 = 0.23$, $p = 0.027$).

**Conclusions:** Our study shows that lower serum retinol levels are associated with greater longitudinal brain volume loss and that serum RBP and can be a predictor of brain volume loss.

**[P-50]**

**N-3 Polyunsaturated Fatty Acids and Multiple Sclerosis; A Systematic Review of Clinical Trials**

Iman Namjoo, Narges Ghorbani, Mohammad Borzu Esfahani, Behnood Abbasi

Food Security Research Center and Department of Community Nutrition, Isfahan University of Medical Sciences, Isfahan, Iran

**Background:** Multiple sclerosis (MS) is a chronic, inflammatory and neurodegenerative disease. Remarkable interest has been shown in the potential anti-inflammatory and immunomodulatory effects of omega-3 fatty acids in MS and other autoimmune inflammatory disorders.

**Objective:** To evaluate the effect of omega-3 fatty acids supplementation on clinical outcomes and immunity aspects in MS patients.

**Methods:** According to the inclusion and exclusion criteria, we searched PubMed, ISI, Science Direct and Google scholar by these terms: Omega-3 Fatty Acid, n-3 Polyunsaturated Fatty Acid, Fish Oils, Multiple Sclerosis and other related terms. We also searched reference lists and citations of primary articles and relevant reviews to identify any other eligible studies. Two authors assessed eligibility and extracted data.

**Results:** Of the 493 studies identified, 6 clinical trials met the defined inclusion criteria. There was no significant difference in Expanded Disability Status Scale (EDSS), quality of life (QOL), fatigue, rate and severity of relapse between intervention and control groups. Of the three studies, only one study showed improvement in QOL. No differences seen in cytokines, chemokines and adhesion molecules levels between the two groups, although one study showed decreased levels of inflammatory cytokines (TNF$\alpha$, IL-1$\beta$, IL-6) and nitric oxide metabolites in intervention group compared with placebo group.

**Conclusion:** There are no beneficial effects of omega-3 fatty acids supplementation on clinical outcomes and immunity aspects in MS patients. We found that evidence for the efficacy of omega-3 fatty acids supplementation is still lacking in MS, and more randomized controlled trials are needed to confirm the results.

**Poster Session 7**

**MS Treatment**

**[P-51]**

**Disease Modifying Treatments in MS: Clinical Outcomes of Induction and Escalation Strategies**

OH Williams$^{1,2}$, KE Harding$^{1,2}$, A Rimmer$^3$, MD Willis$^{1,2}$, TP Pickersgill$^2$, F Joseph$^1$, M Wardle$^2$, NP Robertson$^{1,2}$

$^1$Institute of Psychological Medicine and Clinical Neuroscience, Cardiff University, UHW, Cardiff, UK
$^2$Department of Neurology, Helen Durham Centre for Neuroinflammatory Disease, UHW, Cardiff, UK
$^3$Department of Neurology, Royal Gwent Hospital, Newport, UK

**Same as [O-11]**

**[P-52]**

**Clinico-Radiological Phenotype and Number of Lesions on MRI Influences Medication Choice in Multiple Sclerosis**

P Aouad$^{1,2}$, A Fontes-Villaba$^{1,2}$, Y Lee$^{1,2}$, A Kirby$^2$ and J Parratt$^{1,2}$

$^1$University of Sydney, Sydney, NSW, Australia
$^2$Royal North Shore Hospital, Sydney, NSW Australia

**[P-53]**

**Time Matters in Multiple Sclerosis – International Consensus Recommendations on Diagnosis, Management and Treatment Access**

William Carroll$^1$, Helmut Butzkueven$^2$, Suhayl Dhib-Jalbut$^3$, Jeremy Hobart$^4$, Gisela Kobelt$^5$, George Pepper$^6$, Maria Pia Sormani$^7$, Christoph Thalheim$^8$, Anthony Traboulsee$^9$, Timothy Vollmer$^{10}$, Gavin Giovannoni$^{11}$

Centre for Neuromuscular and Neurological Disorders, Western Australian Neuroscience Research Institute, University of Western Australia, Perth, WA, Australia

$^2$Melbourne Brain Centre, Royal Melbourne Hospital, University of Melbourne, Parkville, Australia

$^3$Department of Neurology, RUTGERS-Robert Wood Johnson Medical School, New Brunswick, NJ, USA

Plymouth University Peninsula Schools of Medicine and Dentistry, Plymouth, UK

$^4$European Health Economics, Mulhouse, France

$^5$Shift.ms, Leeds, UK

$^6$Biostatistics Unit, University of Genoa, Genoa, Italy

$^7$Patient Advocate in Multiple Sclerosis, Brussels, Belgium

$^8$Department of Medicine, University of British Columbia, Vancouver, BC, Canada

$^9$Department of Neurology, University of Colorado Denver, Aurora, CO, USA

$^{10}$Queen Mary University London, Blizard Institute, Barts and The London School of Medicine and Dentistry, London, UK

**Background:** Disease understanding, diagnostic criteria, treatment options and monitoring procedures in multiple sclerosis (MS) are evolving.

**Objective:** We present international consensus recommendations for improving diagnosis, management and treatment access in MS.

**Methods:** Structured discussions and literature searches conducted in 2015 examined the personal and economic impact of MS, current practice in diagnosis, treatment and management, definitions of disease activity and barriers to accessing disease-modifying therapies (DMTs).

**Results:** We recommend a clear treatment goal: to maximize neurological reserve, cognitive function and physical function by reducing disease activity. Campaigns to raise awareness of MS and improved access to MS specialists and services are needed to reduce delays in diagnosis. Treatment should start early, with an appropriate DMT and lifestyle measures. All parameters that predict relapses and disability progression should be included in the definition of disease activity and monitored regularly. When disease control is suboptimal, switching to a DMT with a different
mechanism of action should be considered. Treatment decisions should be shared and consider all appropriate DMTs. Monitoring data should be recorded in registries to generate real-world evidence.

Access to DMTs varies; in 14 countries examined, 13–69% of people with MS received a DMT in 2013. To improve access, all costs to all parties should be considered in economic evaluations. We encourage the continuing investigation, development and use of cost-effective therapeutic strategies and alternative financing models.

Conclusions: We recommend a therapeutic strategy in MS based on proactive monitoring and shared decision-making. Early diagnosis and improved treatment access are also key.

[P-54]

Disease Modifying Treatments in Multiple Sclerosis: Utilisation in Clinical Practice

OH Williams, KE Harding, A Rimmer, TP Pickersgill, F Joseph, M Wardle, NP Robertson.

1. Institute of Psychological Medicine and Clinical Neuroscience, Cardiff University, UHW, Cardiff, UK.
2. Department of Neurology, Helen Durham Centre for Neuroinflammatory Disease, UHW, Cardiff, UK.
3. Department of Neurology, Royal Gwent Hospital, Newport, UK.

Background: The number of disease modifying treatments (DMT) for MS continues to expand, although there is limited data concerning their long term use and utilisation in clinical practice.

Objective: Descriptive analysis of historic and current DMT utilisation in relation to treatment pathways, course length, indications and discontinuation reasons in real practice.

Methods: A subset of a population-based cohort of MS identified 515 patients with prospective data on DMT utilisation, indication and reasons for discontinuation were classified. Descriptive and survival analysis were conducted.

Results: 893 drug initiation events were identified in 515 patients. 2nd line treatment was initiated in 45%, 3rd line=15%, 4th line=5%, 5th line=1%, 6th line=0.4%. The commonest DMT initiated was interferon (61%) followed by alemtuzumab, with proportional increase in prescription with each line of treatment escalation (1st=13%, 2nd=16%, 3rd=22%). Persistence on DMT was a median of 1.7 (1.5-2.0) years for interferon and 1.5 (1.2-2.4) years for copaxone. Discontinuation occurred on 619 occasions, with the commonest reason being intolerance of side effects in 58%.

Conclusion: This analysis provides data on the translation of trial data and guidelines into real clinical practice, and highlights the impact of treatment access constraints on prescription patterns.

The relatively short time spent on individual therapies contrasts with experience in highly controlled clinical trials and suggests that the greatest limitation to drug efficacy in routine clinical practice may be drug adherence. A greater understanding of drug utilisation, indication and discontinuation will be of benefit in informing practical strategies and treatment decisions in clinical practice.

[P-55]

Sex Differences in Outcomes of Disease Modifying Treatments for Multiple Sclerosis: A Systematic Review

Rui Li, Xiaobo Sun, Yaqing Shu, Zhifeng Mao, Wei Qiu, Zhengqi Lu, Xueqiang Hu

Department of neurology, the third affiliated hospital of Sun Yat-sen University, Guangzhou, China

Background: Multiple sclerosis (MS) is a chronic autoimmune demyelinating disease of the central nervous system, with sexual dimorphism. This paper performed comprehensive analysis on previous literatures about sex differences of disease modifying treatments (DMTs) effects in MS.

Methods: We searched PubMed, MEDLINE, Web of science databases. Studies were included if they investigated sex differences in DMTs outcomes in MS patients.

Results: Fourteen studies with 11425 participants were included. Some clinical trials showed women may get more benefit from interferon-beta treatment in RMRMS and SPMS patients.

Conclusion: Sex differences of DMTs effects were observed in MS patients in some clinical trials or cohort studies, which may due to the sexual dimorphism in immunologic status and many other aspects.

[P-56]

Multiple Sclerosis Injection in The Form of Use Disease Modifying Drugs, Why is The End?

Murat Terzi, Sedat Şen

Ondokuz Mayıs University, Faculty of Medicine, Department of Neurology

Objective: Multiple sclerosis (MS) is an autoimmune inflammatory disease of central nervous system. In this article real-life data of immunomodulatory therapy used in injection form is submitted.

Results: We evaluated a total of 956 multiple sclerosis patients. 468 patients treatment were cut for any reason. The distribution of treated patients were as; interferon beta (IFN-B) 1A subcutaneous 247 patient, IFN-B 1B 1A intramuscular 292 patient, glatiramer acetate 220 patient. Table 1. Duration of treatment was similar in all drug, minimum 1 year, maximum 19 years, with a mean of 5 years. Table 2.

Ratio to be the drug of first choice of treatment, interferon beta (IFN-B) 1A subcutaneous %83 patient, IFN-B 1B intramuscular %86 patient, IFN-B 1A intramuscular %93 patient, glatiramer acetate %64. Glatiramer acetate is frequently used two and third treatment option than others drugs. Table 3.

The most common reason for drug withdrawal frequent attacks and the progression of the disease. IFN-B 1A intramuscular is the highest rate (%657) of drug withdrawal. Table 4.

Of drugs are given EDSS scores and annual attack ratio, before treatment and after 5 years. Figure 1.

Conclusion: The most common reason for drug withdrawal frequent attacks and the progression of the disease. Interferon beta (IFN-B) 1A subcutaneous of the withdrawal rate is higher due to the side effects of other treatments. IFN-B 1B intramuscular is the highest rate (%657) of drug withdrawal. IFN-B 1A intramuscular is least effective on the annual attack. All treatment effectiveness decreases the years went on.

[P-57]

Is Severity of Adverse Events Affected by the Dose and Frequency of Glatiramer Acetate Treatment of Relapsing-Remitting Multiple Sclerosis (RRMS)?

Y. Wu, S. Gandhi, A. Grinspan, S. Kolodny, F. J. Zagmutt

OH Williams, KE Harding, A Rimmer, TP Pickersgill, F Joseph, M Wardle, NP Robertson.

1. Institute of Psychological Medicine and Clinical Neuroscience, Cardiff University, UHW, Cardiff, UK.
2. Department of Neurology, Helen Durham Centre for Neuroinflammatory Disease, UHW, Cardiff, UK.
3. Department of Neurology, Royal Gwent Hospital, Newport, UK.
Background: Glatiramer acetate at 40 mg/mL three-times weekly (GA40) has a lower administration frequency (AF) than once-daily (GA20). Differences in the severity of injection-related adverse events (IRAEs) and injection-site reactions (ISRs) between dose/frequency regimens may be clinically relevant.

Objective: To compare severity of IRAEs/ISRs in published randomized controlled trials of GA20 and GA40 in RRMS patients.

Methods: IRAEs include ISRs and immediate post-injection reactions. IRAE/ISR counts per patient-year from the GLACIER and GALA trials were grouped by patient-reported severity (mild: allows normal daily activity; moderate: interferes with normal activity; severe: prevents normal activity). A Bayesian network meta-analysis was used to compare the incidence rate ratio (IRR) by severity of IRAE/ISR between GA20, GA40, and placebo, using GA40 as common comparator. Differences were considered statistically significant when the confidence in IRR≥1 (PrIRR) was >95%.

Results: The 1,613 patients included reported 7,881 (7,719) mild, 1,378 (1,111) moderate, and 53 (45) severe IRAEs (ISRs). The incidence of mild IRAEs [IRR=2.17, CI: (1.02–4.05), PrIRR=97.9%] and ISRs [2.21 (1.03–4.11), 97.9%] was over twice as high with GA20 than with GA40. Patients receiving GA20 experienced 5.74 (2.70–10.82), 99.7% and 4.43 (2.02–8.31), 99.5% times more moderate IRAEs and ISRs, respectively, than those treated with GA40. Mild and moderate IRAEs/ISRs were lowest for placebo. Severe IRAEs/ISRs incidences were not significantly different across all comparisons.

Conclusions: GA40-treated patients experienced significantly lower incidence of mild and moderate IRAEs/ISRs than patients treated with GA20. Moderate IRAEs/ISRs were more than double what would be expected from the higher AF of GA20; but proportional to AF differences for mild IRAEs/ISRs.

Methods: 7342 pregnancies from Teva’s database of patients treated with GA during the peri-conception period were compared with the rates of abnormal pregnancy outcomes reported in two large registries.

Results: 4447 out of 7342 pregnancies (60.5%) were reported prospectively. Duration of exposure to GA was not reported. 2235 of these prospective cases had a known outcome. Analysis of prospective cases with known outcome revealed 42 live births with congenital malformation, 16 cases of elective termination due to an anomaly, 10 stillbirths, and six intrauterine deaths. The rate of congenital anomalies in the prospective cases with known outcome was compared to rates from the EUROCAT and MACDP databases. Overall, pregnancies during exposure to branded GA were not at higher risk for congenital anomalies than is expected in the general population.

Conclusions: These data provide evidence that GA exposure during pregnancy appears safe and without teratogenic effect.

Comparison of Pregnancy Outcomes in Glatiramer Acetate Pregnancy Database to EUROCAT and MACDP Registries

1Teva Pharmaceutical Industries, Frazer, Pennsylvania, USA
2Teva Pharmaceutical Industries, Petach Tikva, Israel
3Department of Neurology, University Hospital, Lund, Sweden
4Stony Brook University Medical Center, Stony Brook, New York, USA
5SUNY University at Buffalo, Buffalo, New York, USA
6Loyola University Chicago, Chicago, Illinois, USA

Background: Appropriate counseling and treatment for women with multiple sclerosis who may become pregnant requires an understanding of the effects of exposure to disease modifying therapies (DMTs) during pregnancy. Current reports/studies are limited in their usefulness mostly by small sample size. Branded glatiramer acetate (GA) is a DMT approved for the treatment of relapsing forms of multiple sclerosis that has been shown to be efficacious, with a favorable safety profile and more than two decades of clinical use.

Objective: To compare pregnancy outcomes from Teva’s global pharmacovigilance database to EUROCAT and MACDP two population-based registries for the surveillance of congenital anomalies.

Methods: Time Course of Glatiramer Acetate Efficacy in Patients with Relapsing-Remitting Multiple Sclerosis (RRMS) in the Glatiramer Acetate Low-Frequency Administration (GALA) Study

S. Kolodny1, M. D. Davis2, N. Ashtamker3, J. R. Steineman4, V. Knappertz2,4
1Teva Pharmaceutical Industries, Cleveland, Ohio, USA
2Teva Pharmaceutical Industries, Frazer, Pennsylvania, USA
3Teva Pharmaceutical Industries, Netanya, Israel
4Heinrich-Heine Universität Düsseldorf, Düsseldorf, Germany

Background: In the GALA study, glatiramer acetate 40 mg/mL three-times weekly (GA40) significantly reduced annualised relapse rate (ARR), time to first relapse, and cumulative number of enhancing T1 and new/enlarging T2 lesions in GA-naïve RRMS patients.

Objective: To analyse the timing of efficacy onset of GA40 during the 1-year placebo-controlled phase.

Methods: Baseline-adjusted percent reduction in ARR and percent of relapse-free patients were calculated to examine treatment effect over time. Reductions in the numbers of enhancing T1 and new/enlarging T2 lesions were analysed separately at Months 6 and 12.

Results: Baseline demographics showed no significant differences between groups. GA40-treated patients exhibited >30% ARR reduction 47 days after treatment initiation. Compared with patients given placebo, GA40-treated patients exhibited consistent, low ARR, with reductions of 33.4% at 2 months, 28.7% at 6 months and 33.4% at 12 months. Proportions of relapse-free patients also differed between groups; 94.3% of GA40-treated patients versus 91.5% of patients given placebo were relapse-free at 2 months, 83.5% versus 77.5% at 6 months, and 76.0% versus 65.2% at 12 months. GA40-treated patients demonstrated reductions of 38.0% in enhancing T1 (P=0.001) and 24.2% in new/enlarging T2 (P=0.005) lesions compared with placebo at 6 months.

Conclusions: GA40 demonstrated efficacy in reducing relapses within 2 months of treatment initiation and sustained this effect throughout the trial. GA40-treated patients exhibited significant reductions in enhancing T1 and new/enlarging T2 lesions as early as early as
[P-60] Magnetic Resonance Imaging (MRI) Indicators of Brain Tissue Loss: 3-Year Results of the Glatiramer Acetate Low-Frequency Administration (GALA) Open-Label Extension Study in Relapsing-Remitting Multiple Sclerosis

S. Kolodyny1, R. Zivadinov2, M. G. Dwyer1, N. P. Bergsland2, D. P. Ramasamy2, E. M. Carl3, M. D. Davis4, O. Khan4
1Teva Pharmaceutical Industries, Cleveland, Ohio, USA
2Buffalo Neuroimaging Analysis Center, Department of Neurology, School of Medicine and Biomedical Sciences, State University of New York at Buffalo, Buffalo, New York, USA
3Teva Pharmaceutical Industries, Frazer, Pennsylvania, USA
4Department of Neurology, Wayne State University School of Medicine, Detroit, Michigan, USA

Background: The 12-month, placebo-controlled GALA study showed that glatiramer acetate 40 mg/ml three-times weekly (GA40) significantly reduced annualized relapse rate and MS lesion formation. Patients completing the placebo-controlled phase were eligible for the open-label extension.

Objective: To evaluate early start (ES) versus delayed start (DS) of GA40 on changes in brain volume over 36 months in the GALA study.

Methods: ES patients (n=834) received GA40 for 36 months. DS patients (n=419) switched from placebo to GA40 at Month 12. MRI outcomes included percent brain volume change (PBVC) using the SIENAX method, and percent change in gray matter (GM) and white matter (WM) volumes using the SIENAX multi-time point method from baseline to Month 36 and from Month 12 to 36.

Results: 85.9% of ES and 77.6% of DS patients completed 36 months of follow-up. ES patients showed less GM volume loss (Δ –2.01 vs –2.33, P=.073 [baseline to Month 36]; –1.16 vs –1.53, P=.116 [Month 12 to 36]). There was a trend toward less volume loss in ES patients (adjusted mean PBVC: –1.81 vs –1.98, P=.16 [baseline to Month 36]; –1.13 vs –1.27, P=.080 [Month 12 to 36]). No significant differences were observed in WM, thalamic, or deep GM volume change.

Conclusions: Over 36 months, patients randomised to early initiation of GA40 showed less GM atrophy than those initiating GA40 after Month 12. Since deep GM structures showed no differences between groups, the benefit of early initiation of GA40 is inferred to be preservation of cortical GM volume.

[P-61] Long-Term Efficacy of Fingolimod Treatment in Relapsing-Remitting Patients Who Did Not Respond to Interferon Treatment

Ludwig Kappos1, Nadia Tenenbaum2, Alit Bhatt2, Yu Chen2, Jeffrey Cohen3
1Neurological Clinic and Policlinic, Departments of Medicine, Clinical Research, Biomedical and Biomedical Engineering, University Hospital Basel, Basel, Switzerland
2Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA
3Novartis Healthcare Pvt. Ltd., Hyderabad, India
4Neurological Institute, Cleveland Clinic, Cleveland, OH, United States

Background: Fingolimod reduces clinical and MRI activity in patients switching from interferon (IFN). Assessing long-term efficacy in this population is important clinically.

Objective: To evaluate the long-term efficacy of fingolimod in MS patients who had evidence of disease activity (NEDA-negative) on IFNβ-1a treatment during the 12-month TRANSFORMS trial.

Methods: 341/435 patients who were randomized to IFNβ-1a in the TRANSFORMS study, switched to either 0.5/1.25mg (TRANSFORMS extension) or 0.5mg fingolimod (LONGTERMS) after Month 12 and were classified as responders (NEDA), none of following by Month 12: confirmed relapses, new/enlarging T2 (NET2) lesions, gadolinium-enhancing T1 lesions, or 3-month confirmed disability worsening; n=101) and non-responders if activity in any of these outcomes had occurred (NEDA-negative, n=240). Efficacy was estimated using a negative binomial regression model for annualized relapse rate (ARR) up to 96 months and annualized rate of NET2 lesions up to 36 months post fingolimod-switch.

Results: Median exposures to IFNβ-1a and fingolimod were comparable for NEDA-negative vs. NEDA: 364 vs. 365d and 2064 vs. 2223d. Patients in the NEDA-negative group were younger (35.6y vs. 37.3y); more NEDA-negative patients had 2-3 relapses in the year before TRANSFORMS (36% vs. 24%). Post fingolimod-switch, both ARR (0.74 on IFN treatment, 0.24 during fingolimodM0-M36) and annualized rate of NET2 lesions decreased (3.3 on IFN treatment, 0.81 during fingolimodM0-M36) in the NEDA-negative group; corresponding estimates post-switch in the NEDA group: ARR, 0.15; NET2 lesions, 0.33.

Conclusions: Patients not achieving NEDA on IFNβ-1a in the TRANSFORMS core study had improved long-term efficacy outcomes after switching to fingolimod.

[P-62] Critical Appraisal of Effectiveness of Oral Fingolimod in Relapsing Multiple Sclerosis

Rizalyy Pinzon
Duta Wacana Christian University School of Medicine, Bethesda Hospital Yogyakarta

Background: Oral fingolimod has been accepted in Indonesian food drug administration recently. We performed critical appraisal analysis for the effectiveness of oral fingolimod in relapsing multiple sclerosis.

Method: We searched in Pubmed database using keywords: fingolimod and multiple sclerosis and clinical trial. We limit our searches only for articles that can be obtained in full text, published in 10 years, and published in English. We used Jadad scale to measure the quality of the evidences.

Result: We found 18 trials that measure the effectiveness of oral fingolimod in relapsing multiple sclerosis. We only find 3 trials with design randomized and double blind fashion. The three trials are: FREEDOMS I study, FREEDOMS 2 study, and TRANSFORMS study. The FREEDOMS study compared with placebo, and the TRANSFORMS study compared with injectable interferon. All of the studies have good quality in methodology (Jadad scale > 3). The result of the three study showed the benefit of oral fingolimod in reducing the relapse compared with placebo with relative risk reduction range from 48%-54%, and also reduce the new lesion in T2 brain MRI with relative risk reduction range from...
(35% to 74%). The oral fingolimod effective in reducing the brain volume loss with relative risk reduction range from (31%-35%).

Conclusion: Our systematic review found that oral fingolimod improved clinical outcomes. The availability of oral fingolimod in Indonesia makes it one of the good choices in treatment of multiple sclerosis in Indonesia.

[P-63]
Randomised Placebo-controlled Phase 3 Study of Delayed-release Dimethyl Fumarate in Patients with Relapsing Multiple Sclerosis from Asia-Pacific and Other Countries

T. Saida,1 T. Yamamura,2 T. Kondo,3 J. Yun,4 M. Yang,5 J. Li,6 L. Mahadavani,7 B. Zhu,8 S.I. Sheikh9
1Kansai Multiple Sclerosis Centre, Kyoto Min-iren Central Hospital, Kyoto, Japan
2National Center Hospital, NCNP, Tokyo, Japan
3Kyoto University Graduate School of Medicine, Kyoto, Japan
4Biogen, Cambridge, MA, USA

Background: The Phase 3 DEFINE/CONFIRM studies demonstrated a favourable benefit-risk profile of delayed-release dimethyl fumarate (DMF), mainly in white MS patients.

Objective: To report results of a Phase 3 study in MS patients from Asia-Pacific and other countries.

Methods: In this 24-week, randomised, placebo-controlled study, 225 patients from Japan (n=114), South Korea, Taiwan, Czech Republic, and Poland were randomized 1:1 to DMF 240 mg twice daily or placebo. The primary endpoint is the total number of new gadolinium-enhancing (Gd+) lesions over brain MRI scans at Week 12, 16, 20, and 24. Secondary endpoints are the total number of new Gd+ lesions and the number of new/newly enlarging T2 lesions from Baseline to Week 24.

Results: A total of 213 patients completed the study. Compared with placebo, DMF reduced the mean number of new Gd+ lesions during Weeks 12–24 by 84% (P<0.0001), mean number of new Gd+ lesions from Baseline to Week 24 by 75% (P<0.0001), and mean number of new/newly enlarging T2 lesions at Week 24 by 63% (P<0.0001). Commonly reported adverse events in DMF-treated patients were flushing and related symptoms (30% [DMF] vs 9% [placebo]) and gastrointestinal tolerability events (33% [DMF] vs 16% [placebo]). Mean absolute lymphocyte counts decreased by ~16% from Baseline to Week 24 in DMF-treated patients, remaining within normal limits. Efficacy and safety in Japanese and Asian subgroups were consistent with the overall population.

Conclusions: These results indicate that the beneficial effects of DMF demonstrated in white patients extend to Asian (including Japanese) MS patients.

[P-64]
Laquinimod Disability Progression Effects are Maintained with Increasingly Rigorous Confirmation Time Intervals

S. Kolodny,1 G. Giovannoni,2 A. Grinspan,3 H.-P. Hartung,4 B. A. C. Cree,5 F. Barkhof,6 A. Uccelli,7 M. P. Sormani,8 S. Krieger,9 B. M. J. Uitdehaag,10 X. Montalban,11 J. R. Steinerman,12 V. Knappertz,13
1Teva Pharmaceutical Industries, Netanya, Israel
2Teva Pharmaceutical Industries, Frayer, Pennsylvania, USA
3Heinrich-Heine Universität Düsseldorf, Düsseldorf, Germany
4Biogen, Cambridge, MA, USA
5Teva Pharmaceutical Industries, Frazer, Pennsylvania, USA
6Vrije Universiteit University Medical Centre, Amsterdam, The Netherlands
7University of California San Francisco, San Francisco, California, USA
8Vrije Universiteit University Medical Centre, Amsterdam, The Netherlands
9University of Genoa, Genoa, Italy
10Icahn School of Medicine at Mount Sinai, New York, New York, USA
11Hospital Universitari Vall d’Hebron, Barcelona, Spain

Background: Oral laquinimod 0.6 mg once-daily (QD) demonstrated consistent reductions of 3-month confirmed disability progression (CDP) in the Phase III ALLEGRO and BRAVO trials.

Objective: To explore the durability of laquinimod’s effect on CDP, additional analyses utilised increasingly rigorous durations for disability confirmation.

Methods: Using pooled data from the ALLEGRO and BRAVO trials, laquinimod effects on 6-, 9-, and 12-month CDP were analysed. CDP was defined as an increase in EDSS of >1 point from baseline for patients with baseline EDSS ≤5.0, or an increase in EDSS of >0.5 point from baseline for patients with baseline EDSS of 5.5. For confirmation of disease progression, the increased EDSS value compared with the reference value had to be increased at all time points. Therefore, all initial progressions for patients with 12-month CDP events had to occur in the first study year.

Results: The treatment effect of laquinimod on CDP was maintained over all tested confirmation intervals. The treatment-effect hazard ratios were 0.66, 0.54, 0.53, and 0.55 for 3, 6, 9, and 12-month CDP, respectively; P<0.005, all comparisons. As expected, there was a reduction in the incidence of CDP over time demonstrated for the placebo group: proportions of placebo patients with CDP at 3, 6, 9, and 12 months were 15%, 12%, 9%, and 7%, respectively. No baseline demographic, clinical, or magnetic resonance imaging factors were predictive of CDP at the different time points.

Conclusions: Despite increasingly demanding criteria for CDP, a profound effect of laquinimod for reducing disability progression was consistently demonstrated.

[P-65]
ARPEGGIO: Design of a Randomized, Placebo-Controlled Study to Evaluate Oral Laquinimod in Patients with Primary Progressive Multiple Sclerosis (PPMS)

S. Kolodny,1 G. Giovannoni,2 A. Grinspan,3 H.-P. Hartung,4 B. A. C. Cree,5 F. Barkhof,6 A. Uccelli,7 M. P. Sormani,8 S. Krieger,9 B. M. J. Uitdehaag,10 X. Montalban,11 J. R. Steinerman,12 V. Knappertz,13
1Teva Pharmaceuticals, Cleveland, Ohio, USA
2Barth and The London School of Medicine and Dentistry, London, UK
3Teva Pharmaceutical Industries, Frazer, Pennsylvania, USA
4Heinrich-Heine Universität Düsseldorf, Düsseldorf, Germany
5University of California San Francisco, San Francisco, California, USA
6Vrije Universiteit University Medical Centre, Amsterdam, The Netherlands
7University of Genoa, Genoa, Italy
8Icahn School of Medicine at Mount Sinai, New York, New York, USA
9Hospital Universitari Vall d’Hebron, Barcelona, Spain

Background: There are no approved disease-modifying treatments (DMTs) for PPMS. In studies of laquinimod in relapsing-remitting multiple sclerosis (RRMS), the effect size on confirmed disability progression (CDP) was more pronounced than expected based on the observed relapse rate reduction. This suggests a different mechanism of action, involving central mitigation of neurodegenerative processes for laquinimod in contrast to other DMTs with predominantly peripherally mediated anti-inflammatory effects. Given several failures of peripheral
immunomodulation in PPMS, a centrally acting agent warrants clinical study.

**Objective:** The Phase II ARPEGGIO (A Randomized Placebo-controlled trial Evaluating laquinimod in PPMS, Gauging Gradients In MRI and clinical Outcomes) trial assesses efficacy, safety, and tolerability of a once-daily oral dose of laquinimod versus placebo in PPMS patients.

**Methods:** Approximately 375 patients with PPMS were to be randomized to laquinimod 0.6 mg or 1.5 mg daily or placebo. The primary endpoint is percent brain volume change on magnetic resonance imaging (MRI) from baseline to Week 48. Secondary endpoints include CDP defined by Expanded Disability Status Scale or Timed 25-foot Walk worsening, as well as MRI assessments.

**Results:** ARPEGGIO recruitment began in January 2015 and is now fully enrolled. As of January 2016, the laquinimod 1.5 mg daily arm was discontinued after the occurrence of cardiovascular events.

**Conclusions:** Based on results of preclinical and RRMS studies, this proof-of-concept trial will assess laquinimod mitigation of brain parenchymal loss in patients with PPMS, a disease state for which there are no approved DMTs.

**[P-66]**

**Teriflunomide is Effective in Reducing Brain Volume Loss in Previously Treated Patients: A Subgroup Analysis of TEMSO SIENA Data**

**Background:** In TEMSO (NCT00134563), teriflunomide 14 mg was associated with significant reductions in brain volume loss (BVL), as determined by SIENA (structural image evaluation using normalisation of atrophy) analysis, and demonstrated positive effects on annualised relapse rate and disability worsening in both treatment-naïve patients and those previously exposed to disease-modifying therapy (DMT).

**Objective:** To report effects of teriflunomide on BVL according to prior DMT exposure in a subgroup analysis of TEMSO.

**Methods:** Blinded SIENA analysis of patient scans (n=969) determined BVL in Year 1 (n=808) and Year 2 (n=709). Analyses were performed according to DMT status in the 2 years before study entry. Between-group comparisons were made using rank ANCOVA.

**Results:** At baseline, normalised brain volume was lower in prior-treated vs treatment-naïve patients. Teriflunomide 14 mg significantly reduced median percentage BVL vs placebo in treatment-naïve patients from baseline to Year 1 (30% reduction, \( P=0.0025 \)) and baseline to Year 2 (17% reduction, \( P=0.0109 \)). In prior-treated patients, teriflunomide 14 mg had a greater effect on median percentage BVL from baseline to Year 1 (53% reduction, \( P=0.0119 \)) and baseline to Year 2 (51% reduction, \( P=0.0019 \)). Effect sizes were maintained upon stratification of the prior-treated group by number of DMTs received.

**Conclusions:** These data support the beneficial effects of teriflunomide on slowing BVL in both prior-treated and treatment-naïve patients, vs placebo. Teriflunomide 14 mg was associated with a more profound effect on slowing BVL in prior-treated patients, consistent with previously reported positive outcomes.

**[P-67]**

**Reversibility of Natalizumab Effects on Peripheral Immune Cell Dynamics in Patients with Multiple Sclerosis**

**Background:** Although the effects of natalizumab, an anti-α4-integrin monoclonal antibody, on immune cell composition were described previously, the time-course of reversibility of these effects is not well characterized.

**Objective:** To characterize the reversibility of natalizumab-mediated changes in pharmacodynamic markers in multiple sclerosis patients following therapy interruption.

**Methods:** Pharmacokinetic, pharmacodynamic, and peripheral immune cell data were available from AFFIRM (2-year natalizumab phase 3 study) and RESTORE (treatment-interruption study). Serum natalizumab concentrations were measured using ELISA. α4-integrin expression and saturation, lymphocyte subsets, and VCAM-1 binding were assessed using flow cytometry. Pharmacokinetic/pharmacodynamic changes over time were estimated using repeated-measure models.

**Results:** Natalizumab treatment resulted in increased blood lymphocytes (cells/L) from 2.1x10^9 to 3.5x10^9. Starting 8 weeks after the last natalizumab dose, total lymphocyte counts decreased significantly in patients interrupting treatment versus those continuing natalizumab (3.1x10^9 vs 3.5x10^9, \( P=0.031 \)), plateauing at pre-natalizumab levels from week 16 onward (1.8x10^9-1.9x10^9). Lymphocyte counts remained within the normal range at all timepoints. All measured cell subpopulations, α4-integrin expression/saturation, and sVCAM demonstrated this reversibility. Ex vivo VCAM-1 binding to lymphocytes increased until approximately 16 weeks after the last natalizumab dose, then plateaued, suggesting reversibility of immune cell functionality of α4-integrin-VCAM-1 adhesion.

**Conclusions:** The effects of natalizumab on peripheral immune cells and other pharmacodynamic markers were reversible, with changes starting at week 8; levels returned to those observed or expected in non-natalizumab patients approximately 16 weeks after the last natalizumab dose. Accurate characterization of the
Population Pharmacokinetic Modeling of Natalizumab Efficacy Using Body Weight as a Classification Factor for Extended Interval Dosing

D Amarante, KK Muralidharan, M Subramanyam, K Evans, D Steiner, P R Ho, H Koendgen, J Elkins, I Nestorov

Biogen, Cambridge, MA, USA

Background: Body weight has been associated with natalizumab concentration and alpha-4 integrin receptor saturation. Since high receptor saturation (>90%) has been suggested to increase progressive multifocal leukoencephalopathy risk, some clinicians have attempted to reduce steady-state trough receptor saturation to ~80% by employing extended-interval dosing (EID)—eg, 300 mg q6wk rather than 300 mg q4wk—based on several factors, including body weight.

Objectives: To investigate the impact of using body weight as a stratification variable in selecting relapsing-remitting multiple sclerosis patients for a natalizumab EID regimen.

Methods: A clinical trial simulation analysis was conducted using 2 virtual natalizumab-naive populations generated from Biogen’s clinical database. Group A, which comprised the entire range of body weights from the database, received 300 mg intravenous q4wk dosing; group B, which comprised those in the lowest body-weight quintile, received 300 mg intravenous q6wk dosing. Natalizumab concentration, gadolinium-enhancing (Gd+) lesions, and annualized relapse rate (ARR) were simulated monthly using previously developed models. ARR and the proportion of subjects with Gd+ lesions were compared between treatment groups after 1 year of treatment.

Results: Efficacy measured by Gd+ lesions did not differ between groups stratified by body weight, but ARR was 25% higher in group B (q6wk dosing) than group A (q4wk dosing).

Conclusions: Based on the simulation, using body weight as an EID stratification variable may have minimal impact on MRI but confer a loss of clinical efficacy as measured by ARR. A limitation...
of this simulation analysis is that variables other than body weight were not explored.

[P-71] TRUST-Study: Methods of an Optional MRI-Safety Surveillance for Progressive Multifocal Leukenencephalopathy (PML) in Relapsing-Remitting Multiple Sclerosis Patients Treated with Natalizumab


1Department of Neurology, University Medicine Mannheim UMM, University of Heidelberg, Mannheim, Germany, 2Medical Image Analysis Center (MIAC AG), Basel, Switzerland, 3Tisinn GmbH, Heidelberg, 4MS Center Dresden, Center for Clinical Neuroscience, University Hospital Carl Gustav Carus, Dresden University of Technology, Dresden, 5Department of Neurology, Cologne General Hospitals, University of Cologne, Cologne, 6Department of Neurology, Hospital Augsburg, Augsburg, 7Department of Neurology, Jewish Hospital Berlin, Berlin, 8Department of Neurology, University Hospital Erlangen, Friedrich-Alexander University Erlangen, Erlangen, 9Department of Neurology, Cantas-Hospital Bad Mergentheim, Bad Mergentheim, 10Clinical Neuroimmunology and Neurochemistry, Department of Neurology, Hannover Medical School, Hannover, 11Department of Neurology, Philipps-University and University Clinics Giessen and Marburg, Marburg, Germany, 12Biogen, Zug, Switzerland, 13Biogen, Ismaning, 14Department of Neurology and Center for Neuropsychiatry, Medical Faculty, Heinrich-Heine University Düsseldorf, Düsseldorf, Germany.

Background: MRI signs of PML may precede clinical manifestations, making early detection crucial; however, identification requires extensive experience. Clinically, MRI-utilization and -reading experience are heterogeneous and expert-second-opinion (ESO) reading by neuroradiologists is uncommon.

Objectives: To investigate consequences of integrated patient-management and optional MRI ESO in natalizumab-treated patients to detect PML and improve collaboration among neurologists, (neuro-)radiologists, and MS experts.

Methods: This non-interventional study will include ≥1260 patients (≥12 months on natalizumab before study start; 3-year follow-up). Outcomes include MRI procedures and patient-related data, with optional pseudonymized MRI ESO read focusing on pharmacovigilance measures.

Results: Until 6-December-2015, 844 patients were included by 143 centres (821 MRI datasets, 67 radiologists (representing 417/844 patients) consulted for optional MRI ESO). Recommended MRI protocol was followed in 43.6% of cases, 98% of scans were of sufficient quality, and earlier reference scans were provided in 14% of cases. Scans were evaluated for PML signs and reports sent to sites within 3.3 working days of scan receipt. Of 6 suspected-PML cases identified, 4 received PML diagnosis. Upon MRI ESO read for all 4 patients, PML was detected in 2 patients and subsequently confirmed in the other 2. One patient was nonsymptomatic to the PML lesion.

Conclusions: MS MRI-safety surveillance is relatively new, and optional patient care processes are still developing. Upon PML suspicion, extended diagnostic work-up can be initiated via optional MRI-central reading. These initial results emphasize the value of close interdisciplinary collaboration for patient surveillance but need to be proven in larger settings.

[P-72] Efficacy of Alemtuzumab Is Durable Over 6 Years in Patients with Active Relapsing-Remitting Multiple Sclerosis and an Inadequate Response to Prior Therapy in the Absence of Continuous Treatment (CARE-MS II)

S Broadley, R Alroughani, D Brassat, H-P Hartung, C Oreja-Guevara, KW Selma, B Singer, P Vemmers, S Whay, DH Marginol, K Thangavelu, M Chirieac, E Havrdova, on behalf of the CARE-MS II and CAMMS03409 Investigators

1School of Medicine, Gold Coast Campus, Griffith University, Australia, 2Amini Hospital, Sharq, Kuwait, 3Parpan Hospital and Mixed Unit of Research 1043, University of Toulouse, Toulouse, France, 4Heinrich-Heine University, Düsseldorf, Germany, 5University Hospital San Carlos, Madrid, Spain, 6Medical University of Łódź, Łódź, Poland, 7MS Center for Innovations in Care, Missouri Baptist Medical Center, St Louis, MO, USA, 8University of Lille, CHU Lille, LIRIC – INSERM U995, FHU Imminent, Lille, France, 9Hope Neurology, Knoxville, TN, USA, 10Sanofi Genzyme, Cambridge, MA, USA, 11First Medical Faculty, Charles University in Prague, Prague, Czech Republic.

Background: In CARE-MS II (NCT00548405), alemtuzumab showed superior efficacy versus SC IFN-β-1a over 2 years in patients with active RMS and inadequate response to prior therapy (≥1 relapse).

Objective: Evaluate 6-year clinical efficacy/safety in CARE-MS II alemtuzumab-treated patients.

Methods: Patients received 2 annual courses of alemtuzumab (12 mg) in CARE-MS II, and as-needed alemtuzumab retreatment or other disease-modifying therapy (DMT) in an extension (NCT00930553). Endpoints: annualised relapse rate (ARR), 6-month confirmed disability worsening (CDW; ≥1-point EDSS increase [≥1.5-point if baseline EDSS=0]), 6-month confirmed disability improvement (CDI; ≥1-point EDSS decrease [baseline score ≥2.0]), no evidence of disease activity (NEDA), adverse events (AEs).

Results: Through 6 years, 344/393 (88%) of patients who enrolled in the extension remained on study. Low ARR was maintained (Year 6: 0.15). Through Year 6, 72% of patients were free from 6-month CDW; 43% achieved 6-month CDI. Mean EDSS score increased from baseline to Year 6 by 0.10; 77% of patients had improved/stable EDSS scores at Year 6. In each individual year, most patients achieved NEDA (60% in Year 6). 50% of patients received no additional alemtuzumab after the initial 2 courses and no other DMT. Infusion-associated reactions and infections decreased over time. Thyroid AEs peaked at Year 3, declining thereafter. Serious AE rate was low.

Conclusions: Alemtuzumab efficacy was maintained over 6 years despite 50% of patients receiving no additional treatment since Month 12. Based on these findings, alemtuzumab may provide a unique treatment approach for RMS patients with durable efficacy in the absence of continuous treatment.
**[P-73] Durable Suppression of Disease Activity by Alemtuzumab in the Absence of Continuous Treatment Over 6 Years in Patients with Active Relapsing-Remitting Multiple Sclerosis and an Inadequate Response to Prior Therapy (CARE-MS II)**

Richard AL Macdonell,1 Christopher LaGanke,2 Jérôme De Sèze,3 Mark S Freedman,4 Mario Habek,5 Raymond MM Hupperts,6 Volker Limroth,7 Krzysztof W Selmań,8 David H Margolin,9 Karthinathan Thangavelu,2 Eva Havrdova10; on behalf of the CARE-MS II and CAMMS03409 Investigators

1Brain Research Institute, Florey Institute of Neuroscience and Mental Health, Melbourne, Victoria, Australia
2North Central Neurology Associates, Cullman, AL, USA
3Hôpital Hautepierre, Strasbourg, France
4University of Ottawa and the Ottawa Hospital Research Institute, Ottawa, Ontario, Canada
5Department of Neurology, University of Zagreb, School of Medicine, Zagreb, Croatia
6Orbs Medisch Centrum, Maastricht University Medical Center, Sittard, The Netherlands
7Klinik für Neurologie und Palliativmedizin, Köln, Germany
8Medical University of Łódź, Łódź, Poland
9Sanofi Genzyme, Cambridge, MA, USA
10First Medical Faculty, Charles University in Prague, Prague, Czech Republic

**Background:** In patients with active relapsing-remitting multiple sclerosis (RRMS) and an inadequate response (≥1 relapse) to prior therapy, alemtuzumab significantly increased the proportion of patients with no evidence of disease activity (NEDA) versus subcutaneous interferon beta-1a over 2 years (CARE-MS II; NCT00548405).

**Objective:** Evaluate disease activity over 6 years in alemtuzumab-treated patients from CARE-MS II.

**Methods:** Patients received 2 treatment courses of alemtuzumab 12 mg in CARE-MS II (5 consecutive days at Month 0; 3 consecutive days at Month 12), and as-needed alemtuzumab retreatment or another disease-modifying therapy in an extension study (NCT00930553). NEDA was defined as absence of clinical disease activity (CDA: relapse or 6-month confirmed disability worsening), and MRI disease activity (gadolinium-enhancing TI hypointense or new/enlarging TI hyperintense lesions).

**Results:** Through 6 years, 344/393 (88%) of patients who enrolled in the extension remained on study. In each year of the extension, the proportions of patients free of relapse (Year 3: 81%; Year 4: 80%; Year 5: 84%; Year 6: 88%), CDA (76%, 75%, 80%, 85%) and MRI disease activity (68%, 70%, 68%, 69%) remained high. The majority of patients achieved NEDA annually (53%, 54%, 58%, 60%). 50% of patients received no additional treatment after their initial 2 courses of alemtuzumab.

**Conclusions:** Alemtuzumab durably suppressed disease activity over 6 years, despite 50% receiving no additional treatment since Month 12. Based on these findings, alemtuzumab may provide a unique treatment approach for RRMS patients with durable efficacy in the absence of continuous treatment.

**[P-74] Adverse Drug Reactions Induced by Multiple Sclerosis Medications**

Abolfazli R.1- Gholami Kh.2 - Salehbayat M.3 - Mohebbi N.4 - Javadi MR.5 - Heidari K.6 - Shalviri G.5 - Samadzadeh S.1

1Tehran University of Medical Sciences, Department of Neurology, Amiralam hospital, Tehran, Iran
2Tehran University of Medical Sciences, Faculty of Pharmacy, Department of Clinical Pharmacy, Tehran, Iran
3Tehran University of Medical Sciences, International Campus, Tehran, Iran
4Ministry of Health, Iranian ADR Monitoring Center, Tehran, Iran

**Objective:** To assess nature and frequency of adverse drug reactions (ADRs) induced by MS medications.

**Method:** In an observational cross-sectional study, ADRs of all outpatients referred to a neurologist who have been received at least one drug modifying therapy (DMT), for a duration of at least 3 months, were evaluated.

**Results:** Out of 250 patients, were enrolled in the study, 191 (76.4%) including 42 males and 149 females developed at least one ADR. The total number 484 ADRs were detected in these patients that 0.61% was recognized as serious, and 5.9% as preventable ADRs. ADR occurrence was higher in females than males. The highest number of ADRs occurred with IFN β1a (72%) and Rebif® was the most frequent cause of ADRs (85.5 %). Flu-like symptoms 38.4%, headache 26.4%, hair loss 20.4%, and injection site pain (ISP) 20% of patients, had the highest rate of detected ADRs. The causality assessment of ADRs revealed that 65.2% of ADRs were detected as possible, followed by 22.9% as certain, 11.5% as unlikely, and 0.2 %as probable. There was one case of hepatitis induced by Rebif® and one seizure induced by CinnoVex® that lead to medication withdrawal.

**Conclusion:** All DMTs are associated with ADRs, as noted in present study. The high frequency of ADRs detected shows that there is a need for planning a strong program including patient education and encourage health professionals to report MS medications ADRs over a prolonged period of time to reduce these ADRs and to increase the adherence of patients to DMTs.

**[P-75] The Antioxidative Effect of Melissa Officinalis on the Patients with Multiple Sclerosis**

Fardin Farají1, Ali Akbar Malekirad2, Afsoon Talaie3, Atefeh Poooyandeh4, Mohammad Abdollahi1

1Associate professor of Neurology, Arak University of Medical Sciences, Arak, Iran
2Department of Biology, Payame Noor University, Tehran, Iran
3Msc of Nutrition, Faculty of Health, Islamic Azad University, Arak branch, Iran
4Medicine Student, Arak University of Medical Sciences, Arak, Iran

**Introduction:** Multiple sclerosis (MS) is a chronic inflammatory and neurodegenerative disease of the central nervous system (CNS). There are evidences which suggest inflammation, invading inflammatory cells, oxidative stress, release of reactive oxygen and nitrogen species cause demyelination and axonal destruction within CNS, the pathological hallmarks of MS. The aim of this study was to determine the effect of Melissa officinalis (Lemon balm) infusion, a great source of antioxidants, on oxidative stress status in patients with MS.
**Methods:** The study was a before-after clinical trial carried out on 45 MS patients. They were treated by Lemon balm infusion in form of tea bag twice per day (1.5 g/100 mL) for one month. DNA damage, lipid peroxidation (LPO), MPO and Beta-glucuronidases were measured in the plasma before and after using Lemon balm infusion.

**Results:** The results showed that there was a significant difference in lipid peroxidation (LPO) in MS patients before and after intervention (p=0.005). Also there was significant difference in DNA damage, MPO and Beta-glucuronidases in MS patients after using lemon balm (p=0.014, 0.018 and 0.230 respectively).

**Conclusion:** It is concluded that infusion of Lemon balm markedly improves oxidative stress condition and DNA damage in MS patients and also propose, it can be used as a dietary supplement.

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**Poster Session 8  
NMO Clinical Features and Epidemiology**

**[P-76] The Effect of Body Mass Index on Disease Outcomes in Neuromyelitis Optica Spectrum Disorder with Aquaporin4-Igg: Preliminary Results of Multicenter Study in Korea**

Sung-Min Kim1, Byung-Jo Kim2, Yoo-Whan Kim2, Ohyun Kwon3, Jung-Hwan Oh4, Sa-Yoon Kang4, Kee-Hong Park5, Sung-Rae Cho6, Kyung Seok Park6.

1 Department of Neurology, Seoul National University Hospital, Seoul, 2 Neuroimmunology, Institute of Psychiatry, Psychology & Neuroscience, King’s College London, London, UK, 3 Department of Neurology, Gyeongsang National University School of Medicine, 4 Department of Radiology, Gyeongsang National University School of Medicine, 5 Department of Neurology, Seoul National University Bundang Hospital, Seongnam

Same as [O-14]

**[P-77] Processing Speed, Cognitive Flexibility and Mood Disturbances in Neuromyelitis Optica Spectrum Disorder**

A. Combes1,2, K. McMullen1, S. Kolind1,3, R. Carruthers1, A. Trabousee1

1Neurology, Medicine, University of British Columbia, Vancouver, Canada, 2Neuroimaging, Institute of Psychiatry, Psychology & Neuroscience, King’s College London, London, UK, 3Radiology, Medicine, University of British Columbia, Vancouver, Canada

Same as [O-15]

**[P-78] The Prevalence, Incidence and Baseline Characteristic of Neuromyelitis Optica in Tehran**

Sharareh Eskandanieh, Mohammad Ali Sahraian*, Amir Reza Azimi, Abdorreza Naser Moghadasi, Narges Sistany Allahabadi, MS Research Center, Neuroscience Institute, Tehran University of Medical Sciences, Tehran, Iran.

**Background:** Neuromyelitis Optica (NMO) is a severe inflammatory demyelinating disease of the central nervous system.

**Objective:** In this study we aimed to estimate prevalence, incidence and epidemiological aspects, of NMO in Tehran, Iran.

**Methods:** A population-based prospective study was conducted on patients registered with diagnosis of NMO who met the Wingerchuk 2006 diagnostic criteria in clinic registry of Sina Hospital (as the only referral center for NMO patients in Tehran province), during the time period between 23 July 2015 to August 22 2016. Crude prevalence and incidence was calculated in living residents of the defined study region. We design a questionnaire to cover the main epidemiological variables which is associated with individual level for NMO.

**Result:** Totally of 96 patients fulfilled the NMO diagnostic criteria with mean age of 36.59. The overall crude prevalence of NMO among the population living in Tehran province was 0.812 per 100,000 (1.364 in female and 0.268 in male respectively) and crude incidence was 0.152.

Female to male ratio was 5:1 and the mean age of disease onset was 29.31 years old (minimum=8, maximum=68) and the disease affected patients in younger ages group 18-27. Out of 96 patients whose titer of NMO-IgG was measured, 50.6% were seropositive (37.5% in males and 52.1% in female).

**Conclusions:** Based on results of our largest population based study from Western Asia, the prevalence and incidence of NMO in Tehran is similar to other Caucasian population. The mean age of disease onset among our subject is lower than other region.

**[P-79] Gender Effect on Neuromyelitis Optica Spectrum Disorder with Aquaporin4-Immunoglobulin G**

Sung-Min Kim, M.D. Ph.D.1, Patrick Waters. PhD.2, Mark Woodhall, Ph.D.2, Ohyun Kwon1, Yoo-Jin Kim, B.A.1, Jin-Ah Kim,1 So Young Cheon1, Sehoon Lee, MD, Seong Seo Ro Joo, MD,4 Dong Gun Kim, M.D.,4 Kyeong Cheon Jung, M.D. Ph.D.1, Kwang-Woo Lee, M.D.,Ph.D.1, Jung-Joon Sung, M.D., Ph.D.1, Kyung Seok Park. MD, PhD.1,4

1Dept. of Neurology, Seoul National University, College of Medicine, Seoul, Korea, 2Dept. Pathology, Seoul National University, College of Medicine, Seoul, Korea, 4Dept. of Neurology, Seoul National University, Bundang Hospital, Gyeonggi, Korea

**Background:** Neuromyelitis optica spectrum disorder with aquaporin4-immunoglobulin G (NMO-AQP4) is an inflammatory demyelinating disease characterised by a high female predominance. However, the effect of gender in patients with NMOsd-AQP4 has not been fully evaluated.

**Objective:** To determine the effect of gender in clinical manifestations and prognosis of patients with NMOsd-AQP4 among Asians.

**Methods:** The demographics, clinical and radiological characteristics, pattern reversal visual evoked potential (VEP) test results, and prognosis of 102 patients (18 male) with NMOsd-AQP4 were assessed.
Objective: To investigate clinical presentations of seropositive NMO spectrum disorders (NMOSD) in a tertiary-care hospital in Thailand

Methods: We conducted a case series study of 33 consecutive patients diagnosed with seropositive NMOSD at our tertiary-care hospital (Maharaj Nakorn Chiang Mai Hospital) from 2010 to 2013.

Results: All thirty-three patients were diagnosed with NMOSD according to Wingerchuk criteria 2007. Thirty-two patients were women. Mean age of onset was 39 years (range, 20 to 59 years). Fifteen patients (45%) could not ambulate without aid (EDSS > 4.5). These patients had longer duration of symptoms before the correct diagnosis was made (67 months vs 22 months, P = 0.026). Fifteen patients (44%) did not fulfill revised diagnostic criteria 2006. Brain MRI from three patients met the diagnostic criteria of multiple sclerosis and one patient had bilateral T2 hyperintense of amygdala and hippocampi. CSF samples were available in 15 patients and 13 samples showed abnormal results. Six patients had positive ANA results. One patient had concurrent Hashimoto’s thyroiditis and one patient had discoid lupus erythematosus.

Conclusion: Seropositive NMOSD has variable clinical presentations. Delay in the diagnosis can lead to severe disability. Brain MRI in NMOSD may be indistinguishable from those seen in multiple sclerosis. Some patients with NMO spectrum disorder have concurrent other autoantibodies or systemic autoimmune diseases.

[80] Seropositive NMO Spectrum Disorders in a Tertiary-Care Hospital in Thailand

Atiwat Soontornpun1, Surat Tanprawate1, Pakamas Pasogpakdee2
1. Division of Neurology, Department of Internal medicine, Faculty of Medicine, Chiang Mai University
2. Siriphat Medical Center, Faculty of Medicine, Chiang Mai University

Background: Previous studies suggested that the prevalence of neuromyelitis optica (NMO) is higher among nonwhites whom conventional multiple sclerosis is less common. Limited studies have been published regarding presentations of this disease in Thailand.

Objective: To determine the prevalence of NMO spectrum disorders (NMOSD) in a tertiary-care hospital in Thailand.

Methods: We conducted a case series study of 33 consecutive patients diagnosed with seropositive NMOSD at our tertiary-care hospital (Maharaj Nakorn Chiang Mai Hospital) from 2010 to 2013.

Results: All thirty-three patients were diagnosed with NMOSD according to Wingerchuk criteria 2007. Thirty-two patients were women. Mean age of onset was 39 years (range, 20 to 59 years). Fifteen patients (45%) could not ambulate without aid (EDSS > 4.5). These patients had longer duration of symptoms before the correct diagnosis was made (67 months vs 22 months, P = 0.026). Fifteen patients (44%) did not fulfill revised diagnostic criteria 2006. Brain MRI from three patients met the diagnostic criteria of multiple sclerosis and one patient had bilateral T2 hyperintense of amygdala and hippocampi. CSF samples were available in 15 patients and 13 samples showed abnormal results. Six patients had positive ANA results. One patient had concurrent Hashimoto’s thyroiditis and one patient had discoid lupus erythematosus.

Conclusion: Seropositive NMOSD has variable clinical presentations. Delay in the diagnosis can lead to severe disability. Brain MRI in NMOSD may be indistinguishable from those seen in multiple sclerosis. Some patients with NMO spectrum disorder have concurrent other autoantibodies or systemic autoimmune diseases.

[81] Prevalence of Neuromyelitis Optica Spectrum Disorder in Multi-Ethnic Penang Island, Malaysia

Jyh Yung Hor1, Thien Thien Lim1, Yuen Kang Chia1, Chun Fai Cheah1, Kenny Tan1, Han Bing Chow1, Yee Ming Ching1, Masita Arip3, P E Samuel Easaw4, Gaik Bee Eow4
1Department of Neurology, Penang General Hospital, Penang, Malaysia;
2Island Hospital, Penang, Malaysia;
3Autoimmune Unit, Allergy and Immunology Research Centre, Institute for Medical Research, Kuala Lumpur, Malaysia;
4Department of Medicine, Penang Medical College, Penang, Malaysia.

Background: Epidemiological studies (mostly hospital-based) suggest that neuromyelitis optica spectrum disorder (NMOSD) could be more common among non-White populations. There is a lack of data about the prevalence of NMOSD in the tropical Asian populations.

Objective: A population-based study was carried out to estimate the prevalence of NMOSD in multi-ethnic Penang Island, Malaysia.

Methods: Medical records of NMOSD patients followed up at Penang General Hospital (the sole public neurology referral centre in Penang Island) were reviewed. Neurologists in private practice and paediatric neurologists were contacted for further cases.

Results: There was a total of 13 NMOSD patients who resided in Penang Island (all females; all aquaporin 4 seropositive; 11 Chinese, 2 Malays). Another 12 NMOSD patients (11 females; 9 Chinese, 2 Malays, 1 Indian; including 1 child) residing in neighbouring regions were excluded from the prevalence calculation. The crude prevalence of NMOSD in Penang Island was 1.85/100,000 population (Penang Island population: 703,300; 55.6% Chinese, 33.7% Malay, 9.8% Indian). For breakdown among different ethnicities, the prevalence was 2.82/100,000 among Chinese, 0.84/100,000 among Malays, and none among Indians.

Conclusion: There may be some differences in NMOSD prevalence among different ethnic groups in Asia. It appears that the prevalence among Asians is comparable to the Whites, but lower than the Blacks. The relatively higher NMOSD-to-multiple sclerosis ratio in tropical Asia (approximately 2:1) has made NMOSD to be more easily recognisable. More population-based studies worldwide in different geographical regions and among different ethnic groups, coupled with genetic studies, are useful to clarify this issue.

[82] Clinical Characteristics of Neuromyelitis Optica in Cipto Mangunkusumo National Hospital Jakarta Indonesia

PH Nainggolan, Al Rusmana, R Estiasari, D Imran
Department of Neurology, Faculty of Medicine University of Indonesia, Cipto Mangunkusumo National Hospital

Background: Neuromyelitis optica (NMO) is severe demyelinating disease of central nervous system. Clinical cases of NMO in Cipto Mangunkusumo National Hospital (RSCM) have been reported but not been characteristically analyzed.

Objective: To evaluate the clinical characteristic of NMO in RSCM, Jakarta, Indonesia.

Methods: The study was conducted on patients registered with the diagnosis of NMO/NMOSD at the RSCM, Jakarta, Indonesia in period of January 2014 – July 2016.

Results: There were 21 patients with NMO. All were women with mean of age at onset was 30.3±16.9. Nine (45%) patients presented with optic neuritis and 12 (55%) with myelitis at the time of onset. AQP4 antibody only performed in 3 cases since the cost is very high. AQP4 antibody was found in 2 patients and oligoclonal band in 1 case. Cytomegalovirus and Herpes simplex virus DNA was detected in CSF each in 1 case. Three patients had MRI brain lesions and 16 had long extended transverse myelitis (LETM), located in cervical (8), thoracic (1), and cervico-thoracic (7).
Intravenous methylprednisolone was used in all patients and plasmapheresis in 5 patients for relapse. Eighteen patients got Azathioprine for long term therapy. Median of the Expanded Disability Status Scale (EDSS) was 7.00.

**Conclusion:** In RSCM, NMO found all in women and cervical segment was the most common site of lesion. Intravenous methylprednisolone was the first line treatment for relapse and Azathioprine for long term. AQP4 antibody still a high cost test in Indonesia. CMV and HSV DNA was found in CSF and need further evaluation.

**Background:** Neuromyelitis optica spectrum disorders (NMOSD) is a group of the demyelinating and inflammatory disease that preferentially involve the optic nerve and spinal cord. Mounting evidence indicates that brain abnormalities are being recognized more frequently in NMOSD, especially, have accompanied pre-existing NMOSD. However, Clinical studies related to NMOSD manifesting brainstem involvement as initial symptoms are still scarce.

**Methods:** We retrospectively analyzed 78 NMOSD patients manifesting brainstem involvement as initial symptoms. Data were collected regarding clinical characteristics, laboratory tests, and magnetic resonance imaging findings.

**Results:** 85.9% of patients were female. Median age at onset was 25 years (21-53 years), mean duration was 13.2 months. The frequently initial symptoms were headache (36.9%), nystagmus (15.4%), diplopia (32.1%), bowel or bladder dysfunction (44.9%), movement disorders (64.1%), sensory disturbances (71.8%), neuropathic pain (41.1%), nausea and vomiting (80.8%), hiccup (39.7%), choking cough or dysphagia (21.8%), vertigo and dizziness (32.1%), pruritus (16.7%). Brainstem lesions were involved in midbrain (11.5%), pons (26.9%), medulla (85.9%), in dorsal part (92.3%), the medulla lesions extending to upper cervical (34.6%), hypothalamus (30.8%), periaqueductal regions (28.2%). Anti-AQP4 antibody was positive in 34.7%.

**Conclusions:** The NMOSD could initially present with different brainstem symptoms, nausea and vomiting, hiccup were the first most frequent brainstem symptoms, the medulla lesions, including the medulla lesions extending to upper cervical, especially in dorsal part, and periaqueductal regions were unique to NMOSD. All of these would be helpful to the early diagnose and treatment of the NMOSD.

**P-84**

**How to Differentiate Longitudinally Extensive Transverse Myelitis of Neuro-Behcet Syndrome from Neuromyelitis Optica Spectrum Disorders?**

Aksel Siva1, Ugur Uygunoqlu1, Burcu Zeydan2, Melih Tutuncu1, Yesim Ozguler1, Emire Seyahi1, Serdal Ugurlu1, Orhun Kantarci2, Ayse Altintas1, Sabahattin Saim1
1Department of Neurology, Istanbul University Cerrahpasa School of Medicine, Istanbul, Turkey
2Department of Neurology, Mayo Clinic, Rochester, MN, USA
3Department of Internal Medicine, Division of Rheumatology, Istanbul University Cerrahpasa School of Medicine, Istanbul, Turkey

**Background:** Longitudinally extensive transverse myelitis (LETM) is one of the main characteristic features of Neuromyelitis Optica Spectrum Disorders (NMOSD). Spinal cord involvement although not common in Neuro-Behcet’s syndrome (NBS), but may be seen and usually presents with as LETM.

**Objective:** To compare and differentiate of LETM seen in NBS and NMOSD.

**Methods:** All patients were seen in Istanbul University Cerrahpasa Neuroimmunology Unit. All myelitis cases of NBS and NMOSD consistent with LETM (3-or-more vertebral segments) were included. Demographic, clinical, imaging and laboratory features were studied.

**Results:** There were 26 cases of myelitis of NBS of whom 16 were consistent with LETM and 27 cases with NMOSD-LETM. The mean age of myelitis onset was 25.6 (17-36) in NBS-LETM and 34.2 (range:12-62) in NMOSD-LETM. Female to male ratio was 4/12 (25%) in NBS-LETM, and 25/2 (92%) in NMOSD-LETM. Recurrence was observed in 4 of 16 (25%) patients in NBS myelitis and 15 of 27 (55%) patients in NMOSD. Six of 18 NMOSD patients (33%) and 1 of 7 NBS patients (14.2%) had an oligoclonal band positivity. All NBS-LETM patients (7/16) who was studied for anti-aquaporin-4 antibody were negative, whereas 48% of NMOSD patients who were studied were positive. The imaging features of LETM weren’t discriminative.

**Conclusions:** NBS-LETM occurs predominantly in men and younger age at disease onset than NMOSD. All NBS-LETM patients had systemic findings of Behcet’s Disease whereas none of the NMOSD-LETM patients had such findings. Anti-aquaporin-4 antibody is negative in NBS-LETM, however imaging findings are not discriminative.
median duration of treatment 8 months (2-20 months). Two patient (11%) still have relapse after treatment with azathioprine, with one of them has positive PCR CMV in CSF and has no relapse after treated with ganciclovir. One patient had bad compliance and got relapses one month after stop the treatment. Two patient 1mos to follow up. All patient got high dose intravenous methylprednisolone for relapse, and five (23%) patient underwent plasmapheresis.

**Conclusion:** Relevance initial treatment with immunosuppressant significantly reduces relapse rates in NMO. Evaluation of infection in CSF need to be considered in relapse that occurs during adequate treatment.

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**[P-86]**

**Comparison of Olfactory Function between Patients with Neuromyelitis Optica and Multiple Sclerosis**

Li-Min Li1 MD, Lin-Jie Zhang1 MD, Jingchun Liu2 MD, Fu-Dong Shi1 MD, PhD, Li Yang1 MD, PhD

1Department of Neurology and Tianjin Neurological Institute, Tianjin Medical University General Hospital, Tianjin, 300052, P. R. China

2Department of Radiology and Tianjin Key Laboratory of Functional Imaging, Tianjin Medical University General Hospital, Tianjin, 300052, P. R. China

**Objective:** To compare the features of olfactory function and olfactory-related gray matter (GM) between patients with neuromyelitis optica (NMO) and multiple sclerosis (MS).

**Methods:** Thirty-seven patients with NMO and 37 patients with MS were enrolled. Olfactory function was evaluated with Japanese T&T olfactometer test kit and morphological features of olfactory-related GM were assessed by using magnetic resonance imaging (MRI).

**Results:** 51.4% of patients with NMO suffered olfactory impairment, while in patients with MS with a rate of 40.5%. NMO patients with ODF had higher EDSS scores than patients with MS with ODF (p = 0.041). While the EDSS did not demonstrate to be the independent risk factors for olfactory dysfunction in NMO or MS analyzed by multivariate logistic regression. MR imaging results shown that NMO with ODF had smaller OB than MS with ODF (p = 0.031). Olfactory-related gray matter (GM) atrophy was found in patients with NMO in several regions of right orbitofrontal cortex (OFC) and right superior frontal gyrus, while in patients with MS, reduced GM volume was found in right parahippocampal gyrus (PCG) and piriform cortex (PC). Compared with MS with ODF, patients with NMO with ODF had significant GM loss in right OFC.

**Conclusion:** The incidence of olfactory deficit in patients with NMO seemed to be higher than MS. Morphological features of the olfactory-related GM vary between patients with NMO and MS, and may be helpful in explaining the reasons of olfactory impairment in these diseases.

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**[P-87]**

**Sleep Problems in Thai Neuromyelitis Optica Spectrum Disorder and Multiple Sclerosis: A Pilot Study**

Patama Gomutbutra, Pakamas Pasokpakdee

Division of Neurology, Faculty of Medicine Chiang Mai University, Thailand

**Background:** A recent polysomnographic study in Asian found neuromyelitis optica spectrum disorder (NMOSD) patients had less sleep efficacy and more periodic limb movement (PLM) than healthy controls. However, there is a paucity of information about sleep problems in Thai patients.

**Objective:** To study the type of sleep problems, quality of sleep, and the potential association between site of lesion in MRI and types of sleep problems.

**Methods:** A crosssectional study enrolled 30 patients, including 27 NMOSD and 3 MS patients. Types of sleep problems and sleep quality were evaluated by the Thai Modified Mayo Sleep Questionnaire (TMSQ) and Thai Pittsburgh Sleep Quality Index (TPSQ), consequently.

**Results:** According to TMSQ, 78% of subjects had at least one type of sleep problems. The top three sleep problems were nocturnal leg cramp, snoring, and PLM, respectively. Among those who had a leg cramp, 74% also had either snoring or sleep apnea. Based on TPSQ, 60% of subjects had ‘poor’ sleep quality. As detected by MRI, the lesion site included spinal cord (90%), optic nerve (39%), infratentorial lesion (25%). However, there were no significant association between lesion sites and sleep problems.

**Conclusions:** Sleep disturbance in NMOSD and MS patients are very common. The most common sleep problems was nocturnal leg cramp. It should be noted that most of the leg cramp patients also had features suggestive OSA. Since lesion sites may not predict sleep problem, therefore, sleep problems should be evaluated in every NMOSD and MS patient.

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**[P-88]**

**Risk Factors for Pneumonia Complication in Neuromyelitis Optica Spectrum Disorders**

Bingjun Zhang1, Yi Zhong2, Zhengqi Lu1

1Department of Neurology, the Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China

2Department of Rheumatology and Immunology, the Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China

**Background:** Although pneumonia complication is inevitable in many patients with a progressive clinical course of idiopathic demyelinating diseases, few studies have focused on the incidence and risk factors of pneumonia complication in neuromyelitis optica spectrum disorders (NMOSD).

**Objective:** The aim of this study was to investigate the incidence and risk factors of pneumonia complication in NMOSD.

**Methods:** One hundred and fifty-two NMOSD patients with pneumonia (n = 20) and without pneumonia (n = 132) were enrolled. The clinical, laboratory and magnetic resonance imaging features between two groups were assessed. The correlation between pneumonia and the severity of NMOSD was determined by using spearman correlation analysis. Logistic regression analysis was used to determine independent risk predictors for pneumonia complication in NMOSD.

**Results:** 13.2% NMOSD patients had pneumonia complication. Pneumonia was positively correlated with the severity of NMOSD (r=0.390, p<0.001). Pneumonia complication occurred more frequently in NMOSD patients with Expanded Disability Status Scale (EDSS) >3 than in NMOSD patients with EDSS ≤ 3 (40.5% vs 4.3%, p<0.001). Smoking history (odds ratio [OR] 44.34, 95% confidence interval [CI] 2.67-736.65), midbrain lesion (OR 76.70, 95% CI 2.46-2390.37), and high EDSS (OR 1.45, 95% CI 1.02-2.07) were independently risk factors of pneumonia complication in NMOSD.
Conclusions: Pneumonia is not rare in NMOSD patients. Pneumonia is associated with the severity of NMOSD. Smoking history, midbrain lesion, and high EDSS are independently risk factors of pneumonia complication in NMOSD.

[C-P-89]

What is The Relationship of Anti-Mog Antibodies with Optic Neuritis of Multiple Sclerosis and Neuromyelitis Optica?

Fethi Idiman, Egemen Idiman, Derya Kaya, Omercan Hasanköyglü, Betül Tercan, Pınar Özçelik, Zekyie Altun
Dokuz Eylül University, Cumhuriyet Blv No:144, 35210 Alsancak/Izmir, Turkey

Background: Optic neuritis(ON) is a presenting symptom of neuromyelitis optica(NMO) and multiple sclerosis(MS). Their ON has some different features. The differences may originate from different immunological mechanisms. In this context anti-aquaporin-4 antibody(NMO-Ab) for NMO and Oligoclonal band(OCB) pattern of cerebrospinal fluid(CSF) for MS is of great importance. However, these markers are negative in some patients. On the other hand, myelin oligodendrocyte glycoprotein(MOG) is well known as the causative protein of MS.

Objectives: To determine the relationship between immunological parameters (NMO-IgG, OCB pattern and antiMOG-Ab) and clinical features and visual functions in NMO-ON and MS patients.

Material and Method: 14 NMO-ON(28 eyes/24 ONH+) and 24 MSON(48 eyes/33 ONH+) were evaluated. AntiMOG-Ab and Anti-AQP4Ab were tested in sera of patients with a cell based assay at the Euroimmune laboratory in Germany.

Results: The number of affected eyes and severe visual loss in NMO-ON group were more than MSON group. AntiMOG-Ab were negative in MSON group. Anti-MOG-Ab positivity only was in 2 patients with NMO-ON.Both patients had NMO-Ab(-) and OCB(-). Visual loss was bilateral and severe, and one of them had recurrent ON.

Conclusions: Anti-MOG-Ab positivity was only established in 20 % of NMO-ON patients. The findings could not directly contribute to an understanding of differential diagnosis and pathogenesis of both diseases. However, AntiMOG-Ab titration can be used in some NMO-IgG(-) cases for diagnosis. On the other hand, visual loss of our antiMOG(+) patients was heavier in contrast to the literature. Therefore, to determine the relationship between immunological parameters and visual functions and pathogenesis should be investigated AntiMOG-Ab in the larger and different disaggregated groups.

Poster Session 9

NMO MRI

Evaluation of NMOSD2015 Imaging Guideline for Differential Diagnosis of CDMS and NMOSD in Thai Patients

Orasa Chawalparit1, Siri-on Triragam1, Siriwan Piyapittayanan1, Smatorn Thakolwiboon1, Jiraporn Jitprapaiakulsan1, Chanon Ngamsombut1, Naraporn Prayoonwiwat1, Siriraj Neuroimmunology Research Group1
1Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Same as [O-5]

[C-P-91]

q-Space Myelin Map Analysis of Brain Lesions in Neuromyelitis Optica-Spectrum Disorders: A Preliminary Study

J. Nakahara1, M. Tanikawa1, S. Suzuki1, J. Hata2,5, K. Fujiyoshi1,6, H. Fujiwara1, S. Momoshima4, M. Jinzaki4, M. Nakamura1, H. Okano1,5, S. Takahashi1 and N. Suzuki1
1Departments of Neurology1, Physiology2, Orthopedic Surgery3 and Radiology4, Keio University School of Medicine, Tokyo, Japan; 2Laboratory for Marmoset Neural Architecture, RIKEN Brain Science Institute, Saitama, Japan; 3National Hospital Organization Murayama Medical Center, Tokyo, Japan.

Same as [O-16]

[C-P-92]

The Characteristics of Spinal Imaging in Thai Patients with Demyelinating Diseases

Chaisak Dumrikarnlert1, 2, Sasarorn Siritho1, 3, Pinwalai Chulapimphun1, Chanon Ngamsombat4, Naraporn Prayoonwiwat1
1Division of Neurology, Department of Medicine, Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand
2Bangkok Hospital Headquarters, BOMS, Bangkok 10310, Thailand
3Bumrungrad International Hospital, Bangkok, 10110, Thailand
4Department of Radiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand

Background: Transverse myelitis is the common presentation in demyelinating conditions.

Objective: To determine the characteristic findings of spinal cord lesions among Thai patients with demyelinating diseases.

Methods: Medical records and spinal magnetic resonance imaging (MRI) of patients who were attending the Multiple Sclerosis (MS) and Related Disorders Clinic, Siriraj Hospital, Bangkok, Thailand between 2005 and 2015 were reviewed. The inclusion criteria were (1) patients older than 15 years with (2) at least one attack of transverse myelitis (TM), (3) available data of spinal MRI in the hospital imaging archive system, and (4) at least one anti-aquaporin-4 antibody (AQP4-Ab) test.

Results: One hundred and fifty-eight patients were eligible (27 clinically isolated syndrome [CIS], 38 MS, 55 seropositive neuromyelitis optica spectrum disorders [NMOSD], 9 seronegative NMOSD, and 29 idiopathic transverse myelitis [IDD-TM]). All groups showed female preponderance and no difference of age at onset. In each patient group, no significant difference in the mean number of spinal lesions was found. The most common levels of involvement were thoracic in IDD-TM, cervical in CIS and MS, as well as cervico-thoracic in both NMOSD groups. Long extensive TM was the most common finding in both the seropositive and seronegative NMOSD groups compared to the other groups. Peripheral location and less than 30% of spinal cord area involvement were the characteristic findings in CIS and MS. Central location and intermediate involvement were the determinants for the seropositive and seronegative NMOSD groups, respectively.

Conclusion: Based on only clinical presentations, differentiating patients with demyelinating diseases who present with TM is difficult.
**[P-93] Optic Radiation Analysis in Normal Appearing White Matter of Neuromyelitis Optica Patients as Compared with Healthy Controls Demonstrated by Using Probabilistic Tractography**

Chanon Ngamsombat, Surasee Srihasan, Butsayarin Supakomolnun, Siri-on Tritragarn, Siriwon Piyapittayan, Panida Charochaowanish, Jiraporn Jitpraipakulsan, Sasitorn Siritho, Narapon Prayoonwiwat, Orsa Chawalparit, Siriraj Neuroimmunology Research Group. Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand.

**Background:** Diffusion tensor imaging (DTI) is advanced imaging study that can early demonstrated pathological processes affecting water diffusion as a result of brain microstructural damage such as of demyelination and axonal loss. Neuromyelitis optica (NMO) is a severe autoimmmune disorder of the central nervous system characterized by severe attacks of optic neuritis, myelitis and involvement of the optic pathways are described.

**Objective:** To evaluate brain microstructural change of optic radiation in normal appearing white matter of neuromyelitis optica patients as compared with healthy controls demonstrated by using probabilistic tractography.

**Methods:** Nine NMO patients with normal appearing white matter of the optic radiation from conventional magnetic resonance imaging (MRI) and 9 healthy controls were included in this study. Probabilistic diffusion tractography of the optic radiation were performed and diffusion tensor parameters were compared between groups.

**Results:** The fractional anisotropy (FA) of the optic radiation in normal appearing white matter of NMO were statistically significant decreased (p value = 0.009) whereas mean diffusivity (MD) and radial diffusivity (RD) were statistically significant increased (p value = 0.017 and 0.008, respectively) as compared with healthy controls.

**Conclusion:** Brain microstructural damage of optic radiation in normal appearing white matter of NMO can be demonstrated by using DTI. Early myelin damage or demyelination are probably cause of abnormal decreased FA as correlate with prominent abnormal increased RD component. Further study with clinical correlation will be helpful.

**[P-94] Probabilistic Tractography of Normal Appearing White Matter Corticospinal Tract, Analysis in Neuromyelitis Optica Patients Compared with Healthy Controls**

Chanon Ngamsombat, Butsayarin Supakomolnun, Surasee Srihasan, Siri-on Tritragarn, Siriwon Piyapittayan, Panida Charochaowanish, Jiraporn Jitpraipakulsan, Chanjira Satukjchai, Narapon Prayoonwiwat, Orsa Chawalparit, Siriraj Neuroimmunology Research Group. Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand.

**Correspondence:** Chanon Ngamsombat, Department of Radiology, Siriraj Hospital, 2 Wanglang Road, Bangkokk noi, Bangkok 10700, Thailand.

**Background:** Neuromyelitis optica (NMO) is a severe autoimmmune disorder of the central nervous system including optic neuritis and transverse myelitis. NMO can have inflammation and damage to myelin and axons and involvement to corticospinal tract have been described. Diffusion Tensor imaging (DTI) can demonstrate microstructure change in the white matter fiber.

**Objective:** To evaluate any different abnormality of normal appearing white matter of the corticospinal tract demonstrated by using DTI in NMO patients as compared with healthy controls.

**Methods:** Eight NMO patients with normal appearing white matter of the corticospinal tract and 8 healthy controls were included in this study. Probabilistic diffusion tractography of the corticospinal tract were performed and diffusion tensor parameters were evaluated and compared between groups.

**Results:** The mean fractional anisotropy (FA) and mean axial diffusivity (AD) of corticospinal tracts of NMO patients were statistically significant decreased (p value = 0.004) whereas the radial diffusivity (RD) were statistically significant increased as compared with healthy controls (p value = 0.016).

**Conclusion:** DTI can demonstrate early stage involvement of corticospinal tract of NMO patients that could be myelin or axonal damage of normal appearing white matter. These findings may be used to evaluate motor impairment in NMO. Further study with clinical correlation will be benefit.

**[P-95] Brain Lesions as A Predictor of Relapsing Course of Neuromyelitis Optica Spectrum Disorder (NMOSD)**

Chayasak Wantaneeyawong MD1, Atiwat Soontornpan MD1, Surat Tanprawate MD1, Pakamas pasokpadee MD2, Siwaporn Chankrachang MD1, Angkana Nudsasarn MD1, Adisak Kittisares MD2

1Division of neurology, Faculty of Medicine, Chiang Mai university, Thailand

2Sripat Medical Center, Faculty of Medicine, Chiang Mai university, Thailand

3The northern neuroscience center, Faculty of Medicine, Chiang Mai university, Thailand

**Background:** NMOSD is a demyelinating disorder characterised by optic neuritis and spinal cord involvement. However, previous studies described that brain lesions can be found in NMOSD similar to MS. The aim of this study is to evaluate the association between brain lesions and risk of acute relapse of NMOSD.

**Objective:** To study that whether brain lesions in NMOSD patients can be used as a predictor of relapse of disease.

**Methods:** We conducted a Retrospective chart review from MS/NMOSD clinic, Chiang Mai University. NMOSD have been divided into 2 groups including monophasic and relapsing group. Data of location of brain lesions in both group were collected and analyzed by logistic regression analysis to find out odd ratios.

**Results:** 51 NMOSD (42 relapsing group, 9 monophasic group) were included in our study. Female gender was predominant in both group. Mean age at onset was 40.7 and 38.8-year-old respectively (p = 0.654). There were no significant difference in using immunosuppressive agents between both groups. Brain lesions show no significance in predicting relapsing course of NMOSD. Predictors of relapsing course were visual impairment (OR = 13.56; p=0.029) and abnormal body sensation (OR =21.72; p=0.012).

**Conclusions:** Our study showed brain lesions in NMOSD patients was not predictive factor for relapse of the disease. However visual impairment and abnormal body sensation were associated with...
Poster Session 10

NMO Immunoglobulica Studeis

[P-97]
Elevated Cerebrospinal Fluid —CRMP5 As A Biomarker of Damage to Astrocyte Foot Process and Growth Corn in AQP4-Igg-Seropositive NMO
Shuhei Nishiyama, Tatsuro Misu, Ichiro Nakashima, Toshiyuki Takahashi, Kazuo Fujihara, Masashi Aoki
Department of neurology, Tohoku University Hospital, Sendai, Japan
Same as [O-21]

[P-98]
Cytokine/Chemokine Profile in MOG-Ab+ Disorder
Kaneko K1, Sato DK1, 2, 3, Ogawa R1, Akaiishi T1, Takay Y1, Nishiyama S1, Takahashi T1, Misu T1, Kuroda H1, Tanaka S1, Nakashima I1, Nomura K1, Fujihara K1, 2, Aoki M1
1Department of Neurology, Tohoku University, Sendai, Japan
2Brain Institute and Hospital Sao Lucas Pontific Catholic University of Rio Grande do Sul (PUCRS), Porto Alegre, Brazil
3Department of Neurology, Sao Paulo University, Sao Paulo, Brazil
4Department of Neurology, NHO Yonezawa Hospital, Yonezawa, Japan
5Department of Neurology, Saitama Yonezawa Hospital, Yonezawa, Japan
6Department of Neurology, Fukushima Medical University, Fukushima, Japan

Same as [O-17]

[P-99]
Accuracy of the Fluorescence-activated Cell Sorting Assay for the Aquaporin-4 Antibody (AQP4-Ab): Comparison with the Commercial AQP4-Ab Assay Kit
Jiwan Yang1, Sung Min Kim3, 4, Yoo-Jin Kim1, So Young Cheon1, Boram Kim1, Kyeong Cheon Jung5, Kyung Seok Park1
1Department of Neurology, Gachon University, Gil Medical Center, Incheon, Korea
2Department of Neurology, Seoul National University, College of Medicine, Seoul, Korea
3Department of Pathology, Seoul National University, College of Medicine, Seoul, Korea

Same as [O-13]

[P-100]
Large Scale In-house Cell Based Assay for the Evaluation of Serostatus in Patients with Neuromyelitis Optica Spectrum Disorder Based on New Diagnostic Criteria
Yeseul Kim1, 2, Gayoung Kim1, 2, Byoung Soo Kong1, 2, Ji-Eun Lee2, Jae-Won Hyun1, 2, Su-Hyun Kim1, 2, Byoung Joon Kim1, 2, Kyungho Choi1, 2, Ho Jin Kim1, 2
1Department of Neurology, Research Institute and Hospital of National Cancer Center, Goyang, Korea
2Division of Translational and Clinical Research II, Research institute, National Cancer Center, Goyang, Korea
3Department of Neurology, Sungkyunkwan University School of Medicine, Seoul, Korea
4Department of Biochemistry and Molecular Biology, Seoul National University College of Medicine, Seoul, Korea

Background: The detection of aquaporin 4-IgG (AQP4-IgG) is now part of the diagnostic criteria for neuromyelitis optica spectrum disorder (NOMOSD).

Objective: To evaluate the serostatus of NMO patients based on the new diagnostic criteria using new in-house cell based assay (CBA).

Method: We generated a stable cell line using internal ribosome entry site (IRES)-containing bicistronic vectors, which allow the simultaneous expression of two proteins (AQP4 and GFP) separately but from the same RNA transcript. We performed in-house CBA using serum from 387 patients: 178 NMO patients diagnosed according to the new diagnostic criteria without AQP4-IgG, 65 high risk (HR) patients presenting one of the 6 core clinical characteristics of NMO, but not fulfilling dissemination in space and 144 patients with other neurological diseases including 66 multiple sclerosis patients. The serostatus of 112 NMO or HR patients were also tested by commercial CBA kit using identical serum to evaluate the correlation of two methods. All assays were performed by two independent and blinded investigators.
Results: Our in-house assay yielded 100% specificity and 80% sensitivity (142 of 178) when detecting NMOSD and 77% (50 of 65) when detecting HR patients. In comparison with commercial CBA kit, 103 of 112 patients showed correlation (89 positive and 14 negative patients), whereas 9 patients showed no correlation (7 seronegative by commercial method while seropositive by in-house method and 2 seropositive by commercial method while seronegative by in-house method).

Conclusion: These results demonstrate that our in-house CBA is a highly specific and sensitive method for detecting AQP4-IgG in NMOSD patients.

P-101
Association Between Sun Exposure, Vitamin D Intake, Serum Vitamin D Level and IgG-NMO Level in Patients with Neuromyelitis Optica Spectrum Disorder
Omrid Mirmosayyeb1,3, Vahid Shaygannejad1, Mohammad Bagher Malajie2, Navid Manouchehri3, Mohammad Reza Maracy1, Sahar Saraf Banki1, Motahar Heidarian-Beni2 and Gholamreza Askari2
1Isfahan Neuroscience Research Center and Department of Neurology, Alzahra Hospital, Isfahan University of Medical Sciences, Isfahan, Iran
2Food Security Research Center and Department of Community Nutrition, School of Nutrition and Food Sciences, Isfahan, Iran
3Department of Epidemiology and Biostatistics, Isfahan University of Medical Sciences, Isfahan, Iran

Introduction: NMOSD or Devic’s syndrome is an inflammatory disorder of the CNS that presents typically with relapses of optic neuritis or myelitis which IgG autoantibodies against aquaporin-4 water channel protein probably play a pathogenic role. Vitamin D may modulate B-cell function and dampen the synthesis of IgG and may play a role in NMO as an important factor involved in immunological pathways.

Objective: To investigate the relation between vitamin D intakes from food, vitamin D intake from sun light exposure, blood vitamin D levels and IgG-NMO level in serum.

Method: Food Frequency Questionnaires (FFQ) and Sun Exposure Questionnaire were record for assessed of vitamin D intakes from food and sun light exposure and 25(OH) vitamin D and IgG-NMO were assessed in serum in 29 patients with NMO.

Results: IgG-NMO titration in 9 patients was positive and in others was negative. Vitamin D intake, sunlight exposure scale and 25(OH) vitamin D in patients with negative IgG-NMO was more than patients with positive IgG-NMO that sunlight exposure scale and 25(OH)vitamin D were significant. Age, gender and latitude were not confounder variables.

Conclusion: Physiological variation in vitamin D may exert a major impact on IgG-NMO synthesis in patients with NMO and vitamin D may dose play role in pathogenesis of NMO.

P-102
Cerebrospinal Fluid Uric Acid Elevated in Neuromyelitis Optica Spectrum Disorders During Relapse
Yaqing Shu1*, Haiyan Li1*, Lei Zhang2*, Yuge Wang1, Youming Long1,2, Rui Li1, Yaqing Shu, Yanyu Chang, Xueqiang Hu2
1Isfahan Neuroscience Research Center and Department of Neurology, Isfahan University of Medical Sciences, Isfahan, Iran
2Department of Neurology, The Third Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China

Introduction: CSF UA levels was significantly higher in patients with BBB impaired than that in BBB intact (p<0.001), and significantly higher in longer duration than that in shorter duration of the disease (p=0.002), and significantly higher in patients with active on MRI than that in inactive on MRI (p<0.001), and significantly higher in patients with brain lesions than that without brain lesions (p=0.024). CSF UA was significantly associated with the serum UA (r=0.454, p=0.002), disease duration (r=0.383, p=0.018), BBB index (r=0.805, p<0.001), but not correlated with the age, gender, annualized relapse rate, duration and severity of the disease in NMOSDs. The multiple regression analysis demonstrated CSF UA was independent of BBB index (β=0.765, p<0.001) and serum UA (β=0.001, p=0.019) in NMOSDs.

Conclusion: CSF UA level was elevated in patients with NMOSDs during relapse, which was possibly modified by serum UA and BBB integrity.

P-103
Serum Concentration of CD40L is Elevated in Inflammatory Demyelinating Diseases
Xiaonan Zhong, Honghao Wang, Zhiwei Ye, Wei Qiu, Zhengqi Lu, Rui Li, Yaqing Shu, Yanyu Chang, Xueqiang Hu
Department of Neurology, the Third Affiliated Hospital of Sun yat-sen University No.600 Tianhe Road, Guangzhou 510630, Guangdong Province, China

Introduction: CD40L is critical for T cell–B cell collaboration. Actually, it has been demonstrated that serum CD40L is increased in multiple sclerosis (MS). However, whether level of CD40L is elevated in neuromyelitis optica (NMO) still remain unknown.

Objective: To measure the serum CD40L in NMO patients, and to determine its relationship with inflammatory demyelinating disease activity.

Methods: Serum CD40L was measured by an enzyme-linked immunosorbent assay (ELISA) in NMO (n=27), MS (n=19) patients and controls (CTLs) (n=14).

Results: Mean CD40L (pg/ml) was 3087.30±790.27 for NMO, and 2878.10±606.56 for MS, compared to 2200.60±938.53 for CTLs. CD40L levels were higher in inflammatory demyelinating disease groups compared to the CTLs (NMO, P=0.004; MS, P=0.050), and were slight higher in NMO compared with MS (P=0.255). In NMO subgroup, CD40L was almost negative correlated with C3 (P=0.147). In MS subgroup, a correlation between levels of CD40L
Comparison of Lipid Profile Between Patient with Gadolinium Enhancing Lesion on Brain MRI and Without Enhancing in Neuromyelitis Optica Spectrum Disorder

M Choi1,2, JM Seok1,2, B-O Choi1,2, BJ Kim1,2, J-H Min1,2

Background: Neuromyelitis optica spectrum disorder (NMOSD) is inflammatory, demyelinating disorder of CNS, associated with antibody against aquaporine-4 (anti AQP-4 Ab). Recent study suggest that lipids are play important role in inflammatory process, and high density lipoprotein cholesterol (HDL-C) is associated with blood brain barrier integrity. But there is no study for lipid profile difference in NMOSD patients whether brain enhancement or not. Therefore, we compared the lipid profile differences between in NMOSD patient with gadolinium enhancing lesion on brain MRI and without enhancing lesion.

Method: A total of 21 patients with NMOSD, who had antiAQP4-Ab were included. We devided patients into two groups - with gadolinium enhancing lesion on brain MRI at NMO attack and without enhancing lesion. And we compared triglycerides(TG), low density lipoprotein cholesterol(LDL-C), HDL-C and total cholesterol levels in serum between two groups at the attack period.

Result: Among 21 NMOSD patients, 7 with gadolinium enhancing lesion on MRI and 14 without enhancing lesion. In with enhancing lesion group, female was 6 and mean age was 39.57±16.15 years. And in without enhancing lesion group, female was 14 and mean age was 40.79±19.81 years. Lipid levels such as TG, LDL-C, HDL-C and total cholesterol levels were not different between the two groups (69.29±23.16 vs 111.64±68.39 mg/dL, p=0.021), 25-OHC (0.54±0.96 ng/mL vs. 0.09±0.04 ng/mL, p=0.032), and 27-OHC (2.68±3.18 ng/mL vs. 0.68±0.25 ng/mL, p=0.005) were increased in NMOSD patients. When we measured the OHCCSF index, controlling the effects of blood-brain barrier (BBB) disruption, the 27-OHC index were associated with disibility (0.723; 95% confidence interval – 0.181, 0.620; p=0.002), while the 24-OHCC index (0.51; 95% CI – 1.070, 38.121; p=0.040) and 25-OHCC index (0.677; 95% CI interval – 4.313, 18.532; p=0.004) were associated with the number of white blood cells in the CSF of NMOSD patients, respectively.

Conclusion: The OHCs could play a role in the pathogenesis of NMO.

Whole-Exome Sequencing in a Chinese Family with Neuromyelitis Optica Spectrum Disorder

Yanyu Chang1, Qiao Huang2, Yanlu Huang1 Yuge Wang1, Xiaobo Sun1, Shibai Yi3,4, Jinxing Bei3,4, Lisheng Peng1, Xueqiang Hu1, Allan Kermode5,6, Wei Qiu1

Background: Hydroxycholesterol (OHc), a metabolite of CNS cholesterol, is involved in diverse cellular responses to inflammation and demyelination, which may also be involved in the pathogenesis of NMO.

Object: To develop a method for the quantitative analysis of three major OHCs (24S-, 25-, and 27-OHCS), and to evaluate their concentration in the serum (OHCS) and cerebrospinal fluid (OHCCSF) of patients with NMO.

Method: The levels of OHCS in the serum and CSF of 26 NMO patients and 23 controls were measured by liquid chromatography-silver ion coordination ionspary tandem mass spectrometry and liquid chromatography-electrospray ionization tandem mass spectrometry with picolinyl ester derivatization, respectively. The linear range, precision, and accuracy were assessed for the validation of our assay methods.

Results: The 24S-OHC (2.35±1.60 ng/mL vs. 1.51±0.48 ng/mL, p=0.022), 25-OHC (0.54±0.96 ng/mL vs. 0.09±0.04 ng/mL, p=0.032), and 27-OHC (2.68±3.18 ng/mL vs. 0.68±0.25 ng/mL, p=0.005) were increased in NMO patients. When we measured the OHCCSF index, controlling the effects of blood-brain barrier (BBB) disruption, the 27-OHC index were associated with disibility (0.723; 95% confidence interval – 0.181, 0.620; p=0.002), while the 24-OHCC index (0.51; 95% CI – 1.070, 38.121; p=0.040) and 25-OHCC index (0.677; 95% CI interval – 4.313, 18.532; p=0.004) were associated with the number of white blood cells in the CSF of NMOSD patients, respectively.

Conclusion: The OHCs could play a role in the pathogenesis of NMO.
members from this family (two with NMO and two controls), and supplemented by HLA-DP genotyping. Data were analyzed using bioinformatics methods to identify variants associated with NMO.

**Results:** One mutation within the CNPY3 gene (chr6:42902216-G>A) was found to co-segregate with the NMODS phenotype. The CNPY3 gene encodes a protein associated with toll-like receptor function. No HLA-DP alleles co-segregated with the NMODS phenotype.

**Conclusions:** CNPY3 is implicated as a potential susceptibility gene in this Chinese NMODS family by whole-exome sequencing. It indicates that toll-like receptor function may relate to NMO. Further studies are warranted to validate these preliminary results.

**[P-107] No Association of AQP4 Polymorphisms with NMO and Multiple Sclerosis**

Ting-Ting Yang1,*, Yang He2,*, Ya-Juan Xiang2,*, Dong-Hui Ao1, Yang-Yang Wang1, Qi Zhang1, Xiang-Jun He1, Shan-Shan Zhong1,*, Jian Wu1, Guang-Zhi Liu1

1Department of Neurology, Beijing Tsinghua Chang Gung Hospital, Beijing, 102218 China
2Department of Neurology, Peking University People’s Hospital, Beijing, 100044 China

**Backgrounds:** Both multiple sclerosis (MS) and neuromyelitis optica spectrum disorder (NMO) are inflammatory demyelinating disorders of the central nervous system (CNS). Various genetic and environmental factors have been identified to contribute to etiology of MS and NMO. AQP-4, expressed in astrocytes in the brain, spinal cord, optic nerve and supportive cell in sensory organs, is the most abundantly distributed water channel in CNS. It has been observed that expression or immunoreactivity of AQP4 is abolished in NMO lesions which differs from MS. However, conflicting results have been reported regarding the association between AQP4 polymorphisms and NMO or MS. Considering the ethnic differences of genetic variations, replications in other cohorts are required.

**Methods:** In this study, we examined the associations of common AQP-4 single nucleotide polymorphisms (SNPs) with NMO/neuromyelitis optica spectrum disorders (NMO/MS) in Northern Han Chinese population. Six selected AQP-4 SNPs were genotyped by high-resolution melting (HRM) method.

**Results:** Compared with health control (HC), there is no significant difference of AQP-4 allele and genotype frequency in MS or NMO/NMOSD group.

**Conclusions:** Our study showed no significant association of common AQP4 SNPs with MS or NMO/NMOSD, strongly suggesting that polymorphisms of AQP4 gene are unlikely to confer MS or NMO/NMOSD susceptibility, at least in Northern Han Chinese population.

**Posters Session 11**

**NMO Treatment**

**[P-108] Predictors of Treatment Response to Immunosuppressive Therapy in Neuromyelitis Optica Spectrum Disorder**

Su-Hyun Kim, Jae-Won Hyun, Hyo-Jin Jo, AeRan Joung, Ho Jin Kim
Department of Neurology, Institute and Hospital of National Cancer Center, Korea

Same as [O-6]

**[P-109] Outcomes of Rituximab Therapy in Anti-Rituximab Antibody-Positive Patients with NMO**

Zhang Li1,*, MD, Li T1,*, MD, Yang CS1, MD, Zhang C1, MD, Li Y1, MD, Shi FD1,*, MD, PhD, Yang L1,*, MD, PhD

1Department of Neurology, Tianjin Neurological Institute, Tianjin Medical University General Hospital, 154 Anshan Road, Heping District, Tianjin 300052, P. R. China.

**Introduction:** Rituximab is a chimeric anti-CD20 monoclonal antibody that was found to target and proficiently reduce circulating CD20+ B cells in humans. A developing autoimmune disorder of the central nervous system (CNS) which is predisposed to the optic nerves and spinal cord. Rituximab signifies the first genetically engineered chimeric anti-CD20 monoclonal antibody that was found to target and proficiently reduce circulating CD20+ B cells in humans. A developing autoimmune disorder of the central nervous system (CNS) which is predisposed to the optic nerves and spinal cord. Rituximab signifies the first genetically engineered chimeric anti-CD20 monoclonal antibody that was found to target and proficiently reduce circulating CD20+ B cells in humans. A developing autoimmune disorder of the central nervous system (CNS) which is predisposed to the optic nerves and spinal cord.

**Result:** B cells can perform a widespread array of normal roles that, when dysregulated, may cause NMO disease activity: antigen presentation, proinflammatory and anti-inflammatory cytokine construction, and immunoglobulin production. Potential mechanisms comprise development of AQP4-specific plasmablast clones, failure to abolish autoreactive B-cell subsets, inadequate antigen-specific regulatory B cells, and the loss of anergic maintenance. Most of the investigations revealed that EDSS significantly in all patients with Rituximab treatment will be decreased at treatment. No new or enlarged lesions or pathological gadolinium-enhancement were observed in serial brain and spinal cord MRIs, after treatment.

**Conclusion:** According to all the studies about the effects of rituximab therapy in NMO, it can decrease attacks, relapses, EDSS, brain, and spinal cord lesions in NMO patients.
Acute and Maintenance Therapy for Optic Neuritis in Neuromyelitis Optica Spectrum Disorders and Multiple Sclerosis

Takai Y1, Warabi Y1, Yoshida H2, Isozaki E1
Departments of 1Neurology and 2 Neuroophthalmology, Tokyo Metropolitan Neurological Hospital, Tokyo, Japan

Background: Effective therapies have not yet been established for optic neuritis (ON) in neuromyelitis optica spectrum disorders (NMOSD) and multiple sclerosis (MS).

Objective: The aim of this study is to evaluate the efficacy of traditional therapy with steroids and immunosuppressants for ON attacks in patients with NMOSD and MS.

Methods: We retrospectively investigated the consecutive medical records of 30 Japanese NMOSD patients with anti-AQP4-IgG antibodies and 77 MS patients, and selected 9 NMOSD and 8 MS patients with ON attacks. We examined acute and maintenance therapies for each ON attack, and classified visual functions from FS0 to FS6 by the Functional system (FS) in EDSS.

Results: Acute therapy with high-dose intravenous methylprednisolone (IVMP) or plasma exchange for ON attacks in NMOSD patients significantly improved their visual functions from mean FS4.3 to FS3.4, leaving moderately severe visual disturbance. Acute therapy was followed by the tapering of oral prednisolone therapy over 399±522 days. Longer tapering terms resulted in longer intervals to the next relapse. The use of maintenance therapy with oral prednisolone or immunosuppressants (azathioprine, tacrolimus, or mizoribine) did not influence the interval to the next relapse. Acute therapy was provided for all ON attacks in MS patients, and visual dysfunction remained in one eye in 2 patients.

Conclusions: Traditional therapy with steroids and immunosuppressants for ON in patients with NMOSD and MS did not fully prevent relapses or visual impairment. We need to develop more effective therapeutics for ON in NMOSD and MS.

Clinical Efficacy of Plasmapheresis in Patients with Severe Acute Attack of CNS Inflammatory Disease and Predictors for Long Term Outcome

Aungsumart S, Apiwattanakul M.
Neuroimmunology Unit, Department of Neurology, Prasat Neurological Institute 312 Rajavithi Road Bangkok Thailand

Objectives: To evaluate the clinical efficacy of plasmapheresis in severe attack of CNS inflammatory disease and prognostic factors that associate with good outcome after plasmapheresis.

Methods: Retrospective study of 24 patients diagnosed with CNS inflammatory disease (NMOSD seropositive; 20, NMOSD seronegative; 1, idiopathic transverse myelitis; 3). Total of 27 episodes of severe acute attacks (optic neuritis; 11, myelitis; 16) were evaluated. Plasmapheresis was performed due to poor response to high-dose intravenous methylprednisolone (IVMP) therapy. The outcomes of this study are functional outcome improvements at 6 months after plasmapheresis.

Results: Plasmapheresis following IVMP therapy led to significant improvement in 81% (22 from 27 acute attacks) after 6 months of follow up. The median EDSS at acute attack in myelitis group was reduced from 8.5 (range 7.5-9.0) to 6.25 (range 1-8.5) after plasmapheresis. The median VOS in optic neuritis group was reduced from 5 (range 4.0-6.0) to 2 (range 0-4.0) after plasmapheresis. Baseline EDSS score ≤ 6 before attack was associate with significance improvement at 6 months (p= 0.02, OR 58.33 95%; CI 1.92-1770).

Conclusion: Plasmapheresis following IVMP therapy is effective in the treatment of severe attack of CNS inflammatory disease. Lower baseline of pre-existing neurological damage may be associated with better prognosis.
Anti-Inflammatory Effect of Oral-Formulated Tacrolimus in Experimental Autoimmune Encephalomyelitis Mice

Suk-Won Ahn, Myung-Jin Kim, Dae-Woong Kang, Hae-Bong Jung, Jung-Joon Sung
Department of Neurology, Chung-Ang University Hospital, Chung-Ang University College of Medicine, Seoul, Republic of Korea

Background: It is well established that multiple sclerosis (MS) is a T-lymphocyte mediated autoimmune disease characterized by CNS inflammation. Although the many DMTs are presumed to be significantly effective compared to randomized control groups, the preventive efficacy of DMTs for MS relapse is limited, and DMTs may induce serious adverse effects. Therefore, we tested the immunosuppressive anti-inflammatory effect of oral-formulated Tacrolimus (FK506) for the MS using EAE mice model.

Materials and Methods: The mice with approximately 80 days were randomly divided into 3 experimental groups: an EAE mice group without treatment, an EAE mice group with 5mg/kg Tacrolimus treatment and an EAE mice group with 10mg/kg Tacrolimus treatment. Before autoimmunization with using MOG for EAE mice, the oral form of Tacrolimus was administrated 5 mg/kg or 10 mg/kg. Clinical score of EAE mice, spinal cord staining of myelination and western blot were evaluated.

Results: After autoimmunization, EAE scores of each group are constantly increased as time goes by, however mean scores of each group shows significant difference in some days. The more weight increasing as time goes by, however mean scores of each group shows significant difference in some days. The more a group taking large dose of Tacrolimus gets a lower score. Group of control EAE mice shows demyelination in spine and inflammation in perivascular area; however, Tacrolimus groups' staining present decreased demyelination and inflammation with weak band line of all immunized biomarker.

Discussion: Our results revealed that Tacrolimus plays a therapeutic role by inhibiting the activity of autoimmunization in MS pathogenesis via inactivation of the inflammatory cells. In conclusion, the present study suggests that Tacrolimus administration could be a promising neuroprotective strategy for treating MS.

Therapeutic Effects and Expression of Erythropoietin in Experimental Autoimmune Encephalomyelitis

Sa-Yoon Kang1, Hikyung Kwen2
1Department of Neurology, Jeju National University School of Medicine, Jeju, Republic of Korea
2Department of Neurology, Hankook General Hospital, Jeju, Republic of Korea

Background: Erythropoietin (EPO) has neuroprotective effects in many models of damage and disease of the nervous system where neuroinflammation plays a substantial role, including experimental autoimmune encephalomyelitis (EAE).

Objective: The aim of this study was to assess the therapeutic effect of EPO during the course of EAE and to elucidate the EPO expression pattern in the spinal cord of Lewis rats with EAE.

Methods: We used an EAE model induced in Lewis rats by immunization with myelin basic protein and complete Freund's adjuvant (CFA). Control rats were immunized with CFA alone. Immunized rats were given recombinant human EPO (rhEPO) intraperitoneally at a dose of 5,000 U/kg for 7 consecutive days, either starting on day 3 post-immunization or on the day of clinical symptom onset. After immunization, the rats were observed daily for clinical signs of EAE. EPO expression was investigated by Western blot analysis and immunohistochemistry.

Results: Therapeutic administration of rhEPO to EAE rats once daily significantly reduced the disease severity and shortened the duration of paralysis in EAE rats, and reduced the accumulation of inflammatory cells in EAE spinal cords. The duration of paralysis was significantly reduced in early treatment group than control EAE rats treated with saline (4.6±0.4 days vs. 6.5±0.2 days). Western blot analysis showed that EPO expression was significantly elevated relative to controls in the rat spinal cord during the peak stage of EAE.

Conclusion: Our study showed that EPO expression begins to increase at the start of EAE and that rhEPO administration may be therapeutic candidate for multiple sclerosis.

The Multiple Sclerosis Patient Diagnosed Through A Taste Disorder

A 21 years old man referred to our hospital because of headache. Brain MRI revealed demyelinating lesions suggestive of MS and punched out-lesions in corpus callosum. Patient's neurological examination was normal. 9 months later, follow up MRI revealed that lesion count had raised and a gadolinium enhanced lesion appeared. But the patient had no complaints. Then we accepted the patient as radiologically isolated syndrome.
Multiple Sclerosis and Migraine; Coincidence or Co Morbidity?
Taşkın Duman1, Derya Uludüz2, Murat Güntel1, Özcan Demetgül1,须岑波

1Mustafa Kemal University, Medicine Faculty, Department of Neurological Sciences Antalya- Turkey
2Department of Neurology, Isfahan University of Medical Sciences

Isolated Cranial Neuropathies are seen rarely in MS patients. In this case report, a thirty-two years old female patient was admitted with taste disorder complaints. She had a taste disorder for nearly 20 days and had no other complaints. Hypoesthesia at the right side of her face, increased deep tendon reflexes and positive Babinski reflex at the right side. MRI showed hyperintense demyelinated plaque formations at series of T2 and FLAIR. Looking at the patient’s medical history, we found out that she had a numbness at her right leg and arm 5 years ago that she did not regard as significant, which resolved spontaneously in three days. During lumbar puncture results showed oligo clonal band type 2 formation was detected. As a result, patient received Multiple Sclerosis diagnosis on the base of a taste disorder. Isolated Cranial Neuropathy is seen rarely in MS patients. It has been detected in 6.3% of patients at all stages of the disease and 6.2 as a symptom during admission. It has been established that in 7 attacks out of 95 (7.4) the third nerve, in 12 (12.6) the sixth nerve, in 5 (5.3) the seventh nerve, in 4 (4.2) the eighth nerve, in 2 (2.1) the ninth and tenth nerves are involved.

Concurrence of MS and migraine was previously assessed and different rates were reported. The objective of this study was to assess relative frequency of migraine in MS patients and to compare the migraine rates in MS to age and gender matched controls. Eligible patients were over 18 years of age and had a diagnosis of definite MS according to Mc Donalds criteria. Presence and subtypes of headache in patients were evaluated according to the ICHD II criteria and patients with other than migraine headaches were excluded. Prevalence and clinical characteristics of migraine in patients with MS were compared with aged and sex matched control subjects.

During the evaluation of the results, it was investigated whether migraine characteristics are related to concurrency of migraine in MS patients comparing to an MS control group without headache. Quality of life is impaired due to characteristic features of the disease in MS but headache could also impact on quality of life. To understand whether migraine in MS patients is a coincidence or comorbidity would be crucial in recognizing and managing this issue.

A Case of A Migraine With Radiologically Isolated Syndrome (RIS)
Tiltak A
Department of Neurology, Education and Research Hospital, Antalya, Turkey

Background: The use of MRI in a patient presenting with complaints except for the symptoms of multiple sclerosis (MS) may allow the detection of demyelinated lesions randomly. This is a case who was investigated for migraine headache and followed as a RIS.

Case: A 20-year-old girl experienced migraine headache two or three times in a month last three years. Neurological examination and fundus was normal. Brain MRI was consistent with demyelination with T2 and Flair hyperintensities, there was an evident contrast enhancement in one plaque, cervical spinal cord MRI was normal. Oligoclonal band was Type II positive, IgG index was 1.22, P100 was found to be prolonged in the right eye. IFA panel was normal. This case was diagnosed as a RIS without clinical events associated with MS.

Conclusion: RIS represents a group that has high risk of developing clinically definite MS, therefore close clinical and radiological follow-up of patients with RIS is important. Thus appropriate treatment can be started in time.

Concurrent Occurrence of Multiple Sclerosis and Primary Central Nervous System Lymphoma: Report of Two Cases
Chitsaz A MD. Professor
Neurology, Isfahan University of Medical Sciences

Introduction: Primary central nervous system lymphoma (PCNSL) can be confused with multiple sclerosis (MS). MS is an autoimmune disease that immunosuppressant therapy in the treatment of MS may be a potential catalyst in the development of PCNSL. Early treatment with corticosteroids can dramatically improve patient’s symptoms in MS and PCNSL.

Methods: We reviewed two case with PCNSL or MS. In these cases, conventional diagnostic approaches were not definitive, thus further evaluation like high volume lumbar puncture, slit-lamp examination.

New CNS images techniques and repeated biopsy were helpful.

Case 1: The 26-year old woman reported blurry vision based on FLAIR MRI imaging was diagnosed to have MS, she received beta
interferon 1-a and 24 months later she developed headache, seizure left hemiparesis and epistaxis. The CSF analysis showed elevated of IgG but oligoclonal bands. The presumptive diagnosis was MS and high doses of methylprednisolone were given. Improvement was short–lived, and clinical condition was deteriorated. Repeated MRI demonstrated extension of primary lesion in the right side anterior BG, caudate nucleus and internal capsule. He was diagnosed primary angiitis of the CNS after biopsy.

**Conclusion:** Early definitive diagnosis of PCNSL is the key, if it has not been established, patients who have MS may undergo brain biopsy as part of their evaluation to rule out PCNSL.

**[P-124] Muscular Dystrophy in Multiple Sclerosis. Report of Three Cases**

Ebrahim Etaati1, Masoud Etemadifar2, Omid Mirmosayyeb1, Mehri Salar1, Hamidreza Jahanbani Ardakani1

1 Isfahan Neurosciences Research Center, Alzahra Hospital, Isfahan, Iran. Medical Students’ Research Center, Isfahan University of Medical Sciences, Isfahan, Iran.

2 Department of Neurology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

**Introduction:** Multiple sclerosis (MS) is an acquired disease of the central nervous system. MS is caused by dysregulation of peripheral immune system leading to demyelination and demyelination in the central nervous system. Muscular dystrophies are inherited disorders triggered by mutations in a number of genes. These genetic mutations cause either a dysfunction in, or lack of, proteins that are critical for muscle cell stability, leading to progressive destruction and weakness in the muscles.

**Case Report:** Herein, we report three cases presented muscular dystrophy with MS: one affected by Limb-girdle muscular dystrophy, one by Facioscapulohumeral Dystrophy (FSHD) and one by Myotonic Dystrophy type 2 (DM2).

**Discussion:** Unlike Muscular Dystrophies, genetic abnormalities that increase the risk of MS are not completely identified. It has been suggested that expression of either DUX4 or other genes in the vicinity to D4Z4 on 4q35 locus in FSHD patients and an expansion of a CCGT tetraplet repeat in intron 1 of the ZFN9 gene on chromosome 3q 21.3 in DM2 patients might confer susceptibility to MS. Co-occurrence of MS and muscular dystrophies is relatively rare. It would be important to determine whether there is an etiology behind this co-occurrence or it is just a coincidence. Large cohort studies are needed to test and validate these findings in terms of statistically significant associations.

**[P-125] Pediatric Tumefactive Demyelination; Biopsy Proven Primary angiitis of the Central Nervous System**

Sujin Lee1, Young-Do Kim2

1 Department of Neurology, International St. Mary’s hospital, Catholic Kwandong university

2 Department of Neurology, Incheon St. Mary’s hospital, Catholic university

**Differential diagnosis of tumefactive demyelinating lesion from other inflammatory brain diseases/neoplasms/abscesses remains challenging on neuroimaging. Here we report a pediatric case with a mass-like lesion, who was diagnosed primary angiitis of the CNS after biopsy. A previously well 14-year-old Korean male presented with confused mentality after generalized seizure. Magnetic resonance imaging (MRI) revealed T2-hyperintense, infiltrating lesion with focal enhancement in the right basal ganglia (BG), thalamus, and periventricular white matter (WM). Cerebrospinal fluid analysis revealed 79 leukocytes (62% lymphocytes), protein 41.6 mg/dl, and negative cultures. Because of mass-like lesion with extensive surrounding edema, the lesion was thought to be a tumor, and brain biopsy was performed. Pathologic studies revealed a lymphocytic vasculitis. He was treated with pulse intravenously methylprednisolone for 3 days, followed by a tapering dose of oral prednisolone. One month after completing prednisolone, he developed generalized seizures again. MRI displayed newly appeared lesion to be of increased signal on T2-weight/Flair images with faint enhancement in the right side anterior BG, caudate nucleus and internal capsule. He was diagnosed with primary angiitis of CNS, and treatment with lower dose of prednisolone and immunosuppressant therapy (azathioprine) was commenced. He remains well, without seizures 1.6 years after his initial presentation. Tumefactive demyelinating lesions are uncommon manifestation of demyelinating disease and can pose a diagnostic challenge in patients without a pre-existing diagnosis of multiple sclerosis. It is important that other pathologies such as vasculitis, granuloma, infection and malignancy are excluded. In this case, brain biopsy can be crucial in final diagnosis.

**[P-126] Hypoxia-like Tissue Injury and Glial Response Contribute to the Development of Balo’s Concentric Demyelination**

Y Takai1, T Misu1,2, S Nishiyama1, H Ono1, H Kuroda1, I Nakashima1, R Saito3, M Kanamori1, S Mugikura4, M Watanabe5, M Aoki1, K Fujihara6

1 Department of Neurology, Tohoku University Graduate School of Medicine, Sendai, Japan.

2 Department of Multiple Sclerosis Therapeutics, Tohoku University Graduate School of Medicine, Sendai, Japan.

3 Department of Neurosurgery, Tohoku University Graduate School of Medicine, Sendai, Japan.

4 Department of Diagnostic Radiology, Tohoku University Graduate School of Medicine, Sendai, Japan.

5 Department of Pathology, Tohoku University Graduate School of Medicine, Sendai, Japan.

6 Department of Multiple Sclerosis Therapeutics, Fukushima Medical University, Fukushima, Japan.

**Background:** Balo’s concentric sclerosis (BCS) is an inflammatory demyelinating disease which characterized by alternating demyelinating rings. A previous histopathological study reported that hypoxia-like tissue injury and tissue preconditioning is the central mechanism of alternating demyelination. However, a
hypothesis based on mathematical modeling of Liesegang ring formation suggests that preconditioning theory alone may be insufficient and both activating (currently unidentified) and protective agents (preconditioning proteins) might be necessary for the development of concentric rings in BCS.

**Objective:** To clarify the pathogenic factors and mechanisms underlying the development of concentric demyelination in BCS.

**Methods:** Serial clinical, MRI, and histopathological assessments of concentric lesion formation in a case of BCS.

**Results:** The patient experienced two attacks caused by left parietal and left frontal lesions in five years. In MRI, there were diffusion-restricted rings that antedated the appearance of gadolinium enhancement and typical concentric T2 lesions. Histopathological examinations revealed definite concentric demyelinating layers typical of BCS. Numerous hypertrophic astrocytes were observed beyond the edges of and within the demyelinating layers. The expression of hypoxia-inducible factor-1α (HIF-1α) was upregulated in glial cells located beyond the edge of the demyelinating layers but was also elevated in hypertrophic astrocytes on the inner sides of resected lesions and in oligodendrocytes in non-demyelinating layers. In addition, these astrocytes expressed CC motif chemokine 2 and/or interleukin-1β, which are inducible by HIF-1α and potentially promote demyelination.

**Conclusion:** A unique interplay between hypoxia-induced tissue preconditioning and proinflammatory cytokines derived from glial cells may contribute to the development of concentric demyelination in BCS.

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**P-127**  
**Serious Autoimmune Diseases in Patient Treated with Glatiramer-Acetate for Relapsing-Remitting Multiple Sclerosis – Case Report**  
Hradilek, Zapletalová, Woznicová, Zeman  
Dpt. of Neurology, University Hospital, Ostrava, Czech Republic  
**Background:** Glatiramer-acetate (GA) is commonly used in relapsing-remitting multiple sclerosis (RRMS). It is generally considered safe and well tolerated with low frequency of serious adverse events. However, some autoimmune diseases like erythema nodosum (EN) or lupus-like panarteritis are rarely described.

We report a case of 42-year-old woman with RRMS presenting with serious autoimmune disease after 10-months treatment with GA. She suffered from intensive cutaneous lesions after injections and even some abscesses occurred. Detailed dermatological exam including cutaneous biopsy revealed suspicion to systemic lupus erythematosus (SLE), but finally diagnostic criteria were not met. Dermatologists made the diagnosis of EN. Furthermore, intermittent fever complicated the situation and blood samples revealed severe pancytopenia. Subsequently the patient had several episodes of epistaxis and cutaneous haemorrhage and had to be treated with blood supplies. Anti-platelet antibodies were strongly and ANCA, ENA and anti-Ro antibodies slightly positive. The final diagnosis was: severe autoimmune pancytopenia with haemorrhagic complications – possibly drug-induced or paraneoplastic? Treatment with cyclophosphamide intravenously and oral steroids was initiated with stabilization of haematological parameters and also haemorrhagic complications. The course of MS switched into secondary progressive and last EDSS score of the patient is 6.0. MS lesions on brain MRI are stable. Patient is now treated with Cyclophosphamide and oral steroids.

**Conclusions:** We consider pancytopenia with haemorrhagic complications to be of autoimmune origin as well as EN. As both conditions occurred subsequently to GA treatment the relationship of these serious adverse events is possible. Furthermore, SLE or lupus-like panarteritis is still not excluded.

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**P-128**  
**A Case of Neuromyelitis Optica Spectrum Disorder Presented with Recurrent Area Postrema Syndrome**  
W-K Kim¹, D-K Kang¹, H J Park¹, K D Park¹, Y-C Choi¹  
¹Department of Neurology, Kangdong Sacred Heart Hospital, Seoul, Korea  
²Department of Neurology, Ewha Womans University College of Medicine, Seoul, Korea  
³Department of Neurology, Gangnam Severance Hospital, Yonsei University, Seoul, Korea  
**Background:** The discovery of aquaporin-4 (AQP4) antibodies as a highly specific biomarker separated neuromyelitis optica (NMO) from multiple sclerosis and also broadened the clinical spectrum of NMO. Area postrema, rich in AQP4, contains chemosensitive nausea and vomiting center. Disruption of AQP4 channels could constitute a distinct syndrome of intractable nausea, vomiting, and hiccups as a feature of neuromyelitis optica spectrum disorder (NMOSD). Here we described a patient with recurrent area postrema syndrome as the initial presentation of NMOSD.

**Case:** A 49-year-old man, was admitted with acute onset of nausea, vomiting and hiccups for one week. There was no fever, abdominal pain, or diarrhea. Three years ago, she presented with unexplained nausea and vomiting, and admitted in psychiatry ward with diagnosis of undifferentiated somatoform disorder for three times. During her third admission, nystagmus and truncal ataxia noted. Brain MRI showed right cerebellar infarction. Serum NMO-IgG was negative. Laboratory findings were suggestive of Sjogren syndrome. Since then, she was on azathioprine for 3 years. Unfortunately, she discontinued her medicine 2 months prior to the onset of recent event. There was no significant neurological deficit. Brain MRI and CSF exam was normal. Gastroenterological evaluation was negative. Area postrema syndrome was suggested and steroid pulse therapy was done. The symptoms were gradually improved. Test for AQP4-IgG revealed positive.

**Conclusion:** Although NMOSDs are rare, tests for AQP4-IgG should be considered for patients who present with unexplained, intractable vomiting. Detection of the antibody allows patients to receive immunosuppressive therapy before the development of neurologic disabilities.

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**P-129**  
**Neuromyelitis Optica Spectrum Disorders Seropositive Concomitant with Herpes Simplex Type 2**  
Jitpraipaksalan J¹, M.D., Siritho S², M.D., Prayoonwivat N¹, M.D.  
¹Division of Neurology, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand  
²Division of Neurology, Department of Medicine, Seoul National University College of Medicine, Seoul, Korea  
**Background:** The discovery of aquaporin-4 (AQP4) antibodies as a highly specific biomarker separated neuromyelitis optica (NMO) from multiple sclerosis and also broadened the clinical spectrum of NMO. Area postrema, rich in AQP4, contains chemosensitive nausea and vomiting center. Disruption of AQP4 channels could constitute a distinct syndrome of intractable nausea, vomiting, and hiccups as a feature of neuromyelitis optica spectrum disorder (NMOSD). Here we described a patient with recurrent area postrema syndrome as the initial presentation of NMOSD.

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**Conclusion:** Although NMOSDs are rare, tests for AQP4-IgG should be considered for patients who present with unexplained, intractable vomiting. Detection of the antibody allows patients to receive immunosuppressive therapy before the development of neurologic disabilities.
Background: Long extensive transverse myelitis (LETM) is a common presentation of seropositive neuromyelitis optica spectrum disorders (NMOSD). The mechanism of the disease is unknown. Several infections have been reported concomitant with NMOSD. Until now, herpes simplex type 2 (HSV2) has not been reported as such.

Case presentation: An 84-year-old Thai woman presented with acute quadriparesis for one week without fever or rash. Physical examination revealed no oral/genital ulcers or skin vesicles, intact cranial nerves and motor power grade 2-3/5 in the lower extremities. Spinal magnetic resonance imaging demonstrated cranial nerves and motor power grade 2-3/5 in the lower extremities. Spinal magnetic resonance imaging demonstrated LETM. Cerebrospinal fluid (CSF) analysis showed mild pleocytosis (WBC 8 cell/mm³ with 100% lymphocyte), protein 636 mg/dL and normal glucose. Cell-based assay was serum AQP-4 IgG positive. CSF polymerase chain reaction (PCR) for HSV type 1 was negative, but HSV2 was positive. Seropositive NMOSD was diagnosed.

Discussion: The diagnosis of HSV2 infection is supported by the 100% specificity of PCR for HSV2 with 120 copies of the virus detected. Methylprednisolone i.v. was given for 5 days. The motor power recovered to grade 4/5. The pathogenesis of parainfectious NMOSD may involve molecular mimicry or bystander activation in a genetically susceptible patient.

Conclusions: We report the first case of a concomitant HSV2 infection in a seropositive NMOSD patient. LETM should be investigated in both NMOSD and HSV2 infection. The association and possible role of HSV2 in the pathogenesis of NMOSD needs further study.

[P-130] Neuromyelitis Optica Spectrum Disorder only with Hypersomnia and Intractable Vomiting

Soon-Won Park, Ji-Young Jang, Young-Eun Park
Department of Neurology, Pusan National University School of Medicine, Busan, Republic of Korea

Neuromyelitis optica spectrum disorder (NMOSD) is a term used to describe a wide spectrum of clinical features including recurrent myelitis, recurrent optic neuritis, or both, and other neurologic manifestations. A 26-year-old woman presented with two episodes of acute demyelinating processes in central nervous system within one year. Firstly, she presented with hypersomnia and blurred vision for 3 weeks after fever and headache. Neurological examination revealed a marked decrease in visual acuity. Optic fundi were normal but a conduction defect in the visual evoked potential (VEP) system was detected. Brain MRI showed high-signal intensity lesions at thalamus, hypothalamus and medial temporal lobe in T2 weighted and FLAIR images. CSF analysis revealed unremarkable results, and oligoclonal band was negative. Since serum was positive for anti-aquaporin (AQP)-4 antibody, we then diagnosed the patient with NMOSD. One year after, the patient developed intractable nausea and vomiting. Brain MRI showed interval decreased in previous lesions but a newly developed lesion at the 1st cervical vertebrae to 7th thoracic vertebrae level. There were no oligoclonal bands. His muscle weakness improved gradually after steroid pulse therapy. After 5 months later, he developed headache and visual blurring. Neurological examination revealed a release of NMO and received steroid pulse therapy (1 g/day for 5 days). After steroid treatment, her symptoms were disappeared. One year later, follow-up brain MRI showed no leptomeningeal enhancement.

Conclusion: This case demonstrates that leptomeningitis could be a form of NMO relapse.

[P-132] A Pediatric Case of Seronegative Neuromyelitis Optica

Hyung Jun Park, MD1, Woo-Kyung Kim, MD2, Kee Duk Park, MD1
1Department of Neurology, Ewha Womans University College of Medicine, Seoul, Korea
2Department of Neurology, Hallym Neurological Institute, Hallym University College of Medicine, Seoul, Korea

Neuromyelitis optica (NMO) is an inflammatory central nervous system disease that primarily affects the spinal cord and optic nerves. Although NMO predominantly affects female adults with a median age at presentation in the late 30s, pediatric cases with NMO are occasionally reported. Herein, we describe a Korean case of pediatric NMO with longitudinally extensive transverse myelitis and optic neuritis.

Case Report: A 10-year-old boy was referred to our clinic due to gait disturbance and visual difficulty. Neurological examination showed mild spastic paraparesis and hypesthesia for all sensation below T10 level. Spinal MRI scan revealed long spinal cord lesion from the 1st cervical vertebrae to 7th thoracic vertebrae level. There were no oligoclonal bands. His muscle weakness improved gradually after steroid pulse therapy. After 5 months later, he developed headache and visual blurring. Neurological examination revealed a release of NMO and received steroid pulse therapy (1 g/day for 5 days). After steroid treatment, her symptoms were disappeared. One year later, follow-up brain MRI showed no leptomeningeal enhancement.

Conclusion: This case demonstrates that leptomeningitis could be a form of NMO relapse.
IgG was negative. After steroid pulse therapy, his visual acuity slowly improved.

**Conclusion:** NMO is a comparatively rare disease in children, but we keep in the mind NMO as a differential diagnosis of pediatric inflammatory demyelinating central nervous system diseases.

**[P-133]**

**An Extremely Long Interval Between a Benign Optic Neuritis and a Transverse Myelitis in a Patient with MOG Antibody**

Ryo Ogawa1, Ichiro Nakashima1, Tohisawa S1, Yamazaki T1, Yonehara Y1, Bokuda K1, Kaneko K1, Nakashima I2, Isozaki E1

1Department of Neurology, Tokyo Metropolitan Neurological Hospital, Tokyo, Japan

2Department of Neurology, Tohoku University Graduate School of Medicine, Sendai, Japan

**Background:** Myelin oligodendrocyte glycoprotein (MOG) antibodies are found in the serum of patients with optic neuritis (ON), acute demyelinating encephalomyelitis, and neuromyelitis optica spectrum disorders (NMOSD). The long-term clinical course of MOG antibody-seropositive cases is unclear.

**Objective:** To report a case of NMOSD with MOG antibodies that was diagnosed with 25 years after the initial ON event.

**Case:** A 40-year-old male that exhibited positivity for MOG antibodies (titer during a cell-based assay: 1:4,096) and negativity for anti-aquaporin-4 antibodies was admitted to our hospital. He had experienced two episodes of ON 25 and 16 years ago. His symptoms completely disappeared after a course of high-dose intravenous methylprednisolone (IVMP) therapy, and he received no further medication. He developed dysesthesia of the lower extremity. The dysesthesia expanded below the second cervical cord level (C2), and paraplegia and urinary retention developed within 10 days. Magnetic resonance imaging showed moderate pleocytosis and mildly elevated total protein.

**Conclusions:** Our case suggests that a severe transverse myelitis can be occurred even after a long period in benign optic neuritis patients if it’s related to MOG antibody. Although pathological roles and clinical importance of MOG antibody are not completely revealed, long-term follow-up with titration of MOG antibodies may be required even in cases with benign optic neuritis.

**[P-134]**

**Adult MOG-IgG-Positive, Benign, Unilateral, Cerebral Cortical Encephalitis with Epileptic Seizure**

Ryo Ogawa1, Ichiro Nakashima1, Toshiyuki Takahashi2, Hirohiko Ono1, Kimihiko Kaneko1, Tetsuya Akaishi1, Kazuhiro Kurosawa1, Yoshiki Takai1, Douglas Kazutoshi Sato1, Shuei Nishiyama1, Tatsuro Misu1, Hiroshi Kuroda1, Kazuo Fujihara1, Masashi Aoki1

1Department of Neurology, Tokyo Metropolitan Neurological Hospital, Tokyo, Japan

2Department of Neurology, Tohoku University Graduate School of Medicine, Sendai, Japan

**Background:** Oligodendrocyte glycoprotein-IgG (MOG-IgG) is a glycoprotein located on the myelin sheath of the central nervous system (CNS). Recently, anti-MOG antibody had been detected in the serum of various CNS demyelinating diseases.

**Design/Methods:** We tested for IgG1 subclass of MOG-IgG using a cell-based assay in consecutive 24 adult patients with encephalitis of unknown etiology seen at Tohoku University Hospital, between 2008 and 2014. The clinical, radiological and laboratory features of MOG-IgG-positive cases were retrospectively analyzed.

**Results:** Total 4 male case were MOG-IgG positive (age median 37, range 23-39). The major symptom of 4 cases was generalized epileptic seizure. Three patients exhibited emotional behavior, two developed optic neuritis, and one had dysuria in addition. In all cases, brain MRI showed characteristic unilateral cerebral cortical FLAIR-high intensity lesions, which corresponded to hyperperfusion in SPECT study. Spinal cord lesions were not detected in any of 4 cases. Cerebrospinal fluid (CSF) study showed moderate pleocytosis and mildly elevated total protein level but normal myelin basic protein concentration. IgG bands were negative in all. Antibodies against aquaporin-4, glutamate receptor, and voltage-gated potassium channel were negative in both sera and CSF of all the cases.

**Conclusion:** We have detected MOG-IgG in patients with steroid responsive autoimmune encephalitis with unique clinical features. Although it is unknown whether the MOG-IgG is pathogenic, it may have the potential to be a specific marker for the autoimmune encephalitis with good prognosis.

**[P-135]**

**Effects of Topiramate on Pain in Patients with Neuromyelitis Optica**

Sakamaki Masanori
Department of Neurology, Musashi Kosugi Hospital of Nippon Medical School, Kanagawa, Japan

**Background:** Pain is a common symptom in neuromyelitis optica (NMO). It is severely affects for quality of life in a patient with NMO and often refractory to treatment. Antiepileptic agents are used to treat pain in patients with NMO. However, it is not known whether topiramate is effective for refractory pain in patients with NMO.

**Objectives:** To assess the analgesic efficacy of topiramate for neuropathic pain in NMO.

**Methods:** Two case reports in which topiramate were used for pain in patients with NMO. The visual analogue scale (VAS) was used to evaluate the pain intensity during a pain episode.

**Result:** A 44-year-old woman had 3-year history of NMO with terrible, burning and tingling sensations around her chest. Topiramate 50 mg every day was started. Regardless of nausea that is side effect of topiramate, she continued to take topiramate because of improvement of refractory pain. Her VAS was changed from score of 4.5 to 2.1. Patient 2 was a 49-year-old woman with 3-year history of NMO who developed pain in the left upper limb. Topiramate was initiated at 50 mg every day and increased to 150mg every day. Her VAS was changed from score of 8.6 to 2.6.

**Discussion:** Topiramate acts enhancing the gamma-aminobutyric acid (GABA) concentration, and decreasing the α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA)/kainate-glutamate function. It might be reason why topiramate is effective for refractory pain in patients with NMO.
Conclusions: Our case reports suggest that topiramate may be effect for treatment of refractory pain in NMO patients.

Poster Session 15
Case Reports: ADEM and Myelitis

[P-136]
Acute Disseminated Encephalomyelitis (ADEM) Associated with Bacterial Meningitis
Akgün Hakan, Çetiz Ahmet, Demirkaya Şeref
Gülhane Military Medical Faculty, Ankara, Turkey

Background: Acute disseminated encephalomyelitis (ADEM) is an immunological and inflammatory disorder of the central nervous system (CNS) characterized by demyelination of the white matter of the brain and spinal cord. In patients with bacterial meningitis parainfectious inflammatory syndromes such as vasculitis and ADEM may occur.

Objective: In this case report we discussed an ADEM patient occurred after bacterial meningitis with neurological examination, laboratory and imaging findings.

Methods: Case report

Results: A 20-year-old man was admitted to our hospital because of headache, fever, vomiting, diarrhea and meningism. CSF analysis revealed pleocytosis with gram-positive cocci. After initiation of appropriate antibiotic therapy magnetic resonance imagining (MRI) showed white matter lesions hyperintense in T2 and FLAIR. His neurological examination revealed; confused consciousness, neck stiffness, left hemiparesis and ataxic gait. Cerebral arterial and venous angiography showed no vasculitis or atherosclerosis. Significant improvement in clinical and MRI findings was observed after 7 days of corticosteroid-pulse treatment.

Conclusions: Infectious diseases prior to ADEM can be seen. However, bacterial meningitis associated with ADEM is a very rare comorbidity. Physicians need to keep in mind ADEM in the differential diagnosis of bacterial meningitis.

[P-137]
Concurrent Acute Disseminated Encephalomyelitis and Anti-GT1a Antibody Positive Guillain Barre Syndrome
Juyoung Lee, Jong Seok Bae
Department of Neurology, Kangdong Sacred Heart Hospital, Hallym University College of Medicine

Background and Significance: Previous reports regarding the coexistence of acute disseminated encephalomyelitis (ADEM) and Guillain Barre syndrome (GBS), suggest that certain immunogenicity within central and peripheral nerves may share a common autoimmune process during the disease course. Here we report a patient with simultaneous development of ADEM and GBS.

Case Presentation: A previous healthy 20 years old man came to our clinic because of symptoms suggesting meningencephalitis, such as headache, myalgia and fever. A few days later, he developed flaccid quadriparesis, facial diplegia, and external ophthalmoplegia. Nerve conduction study revealed motor dominant neuropathy. Brain MRI showed symmetrical lesions in bilateral basal ganglia and brain stem. After immunological treatment, his neurological features recovered remarkably.

Conclusion: Our case suggest that certain component of autoimmunity simultaneously result in the inflammation of both central and peripheral nerves. Specific immunological mechanism is remained to be elucidated. Although we could not conclude whether cellular component or humoral component is dominant for our case, the presence of anti GT1a antibody suggest a role of humoral mechanisms. In clinical aspect, clinicians should keep in mind of occasional co-existence of CNS and PNS inflammatory disorders.

[P-138]
A Case of Pediatric Multiple Sclerosis First Presenting Acute Disseminated Encephalomyelitis
JW Jung, SM Kim, HY Shin
Department of Neurology, Yonsei University College of Medicine, Seoul, Korea

Background: Multiple sclerosis (MS) is chronic inflammatory disease of central nervous system. We documented patient with features mimicking acute disseminated encephalomyelitis (ADEM), but were ultimately diagnosed MS.

Case: 7-year-old female was admitted with fever, headache and lethargy. Cerebrospinal fluid (CSF) findings were: white blood cell count 38/μL, red blood cell 92/μL and bacterial culture were negative. Brain magnetic resonance imaging (MRI) showed multifocal hyperintense in bilateral cortex, brainstem and thalamus. Spine MRI showed hyperintense lesions in whole spinal cord. We suspected ADEM and intravenous (IV) steroid, immunoglobulin were used. She was admitted again with fever and lethargy. CSF analysis was normal and oligoclonal band also negative. Several new lesions on brain MRI (subcortex, internal capsule). Same treatment were used again.

The girl was admitted for third time with ataxia. Brain MRI revealed improved multifocal hyperintense lesions compared to previous but signal change along right optic nerve. Visual evoked potential (VEP) revealed conduction defect of bilateral optic nerves. She was treated IV steroid and discharged 10 days later. Her last admission was vertigo and diplopia. Brain MRI showed newly multifocal hyperintense lesions in right pons and left cerebellar peduncle. IV steroid was given and her symptom was improved. We are under observation in outpatient without medication now.

Conclusion: Differentiation of pediatric MS from ADEM has important because the long term prognosis of ADEM is more benign compared with MS. Because final diagnosis can be established only at follow up, children should be monitored closely for early treatment for high risk patients.

[P-139]
Atypical Demyelinating Lesions Due to Synthetic Cannabinoids
A. Soysal, Z. Özdemir, F. Eren, N. Sakalli, M. Tütüncü, N. Kale
Bakıkoş Training and Research Hospital for Psychiatry, Neurology and Neurosurgery, İstanbul, Turkey

Background: In this report, we present a patient with atypical demyelinating lesions and a history of synthetic cannabinoid abuse.

Case Report: 34-year-old male presented with slowing of movements and speech problems for the last 3 days. The patient had a history of smoking but initially no illicit drugs however when
Background: Patient who presented with Tetraplegia Cervical and Thoracic

Conclusions: Recently increased substance abuse and related CNS side effects are not rare. Synthetic cannabinoids are cheap, easy to obtain and are commonly abused resulting in systemic CNS side effects are not rare. Synthetic cannabinoids are cheap, easy to obtain and are commonly abused resulting in systemic

Methods:

Results:

Conclusions: MRI lesions persisted with regression.

Methods:

Results:

Conclusions: OCB (-) and IgG index was normal. Patient was treated with high dose steroids for 10 days followed with oral prednisolone taper.

Methods:

Results:

Conclusions: ADEM patient presented with tetraplegia and magnetic resonance imaging (MRI) revealed high signal changes in Cervical and Thoracic Spine.

Methods:

Results:

Conclusions: Patient considered as ADEM and corticosteroid-pulse treatment for hepatitis C, there has been no recurrence of myelitis.

Methods:

Results:

Conclusions: Hepatitis C should be in the differential diagnosis for recurrent myelitis with no clear etiology.

Methods:

Results:

Conclusions: Low Serum Vitamin D Levels and Anti-N-Methyl-D-Aspartate Receptor Encephalitis: A Case-Control Study.

Methods:

Results:

Conclusions: Hepatitis C should be in the differential diagnosis for recurrent myelitis with no clear etiology.

Methods:

Results:

Conclusions: Normal serum vitamin D levels and anti-NMDA receptor antibodies are independent risk factors for ADEM which could be a different form of ADEM. This is the largest case-control study of vitamin D levels and ADEM.

Methods:

Results:

Conclusions: Low Serum Vitamin D Levels and Anti-N-Methyl-D-Aspartate Receptor Encephalitis: A Case-Control Study.

Methods:

Results:

Conclusions: Movement disorders have been described in demyelinating disease, mainly multiple sclerosis. The most frequent movement disorders in demyelinating diseases are paroxysmal dystonias, also called tonic spasm. We report a case of myelitis associated with painful paroxysmal dystonia.

Methods:

Results:

Conclusions: Paroxysmal dystonia is rarely described in multiple sclerosis and neuromyelitis optica. These results indicate that paroxysmal dystonia should be considered as possible cause of acute myelitis.

Methods:

Results:

Conclusions: Hepatitis C should be in the differential diagnosis for recurrent myelitis with no clear etiology.
though relatively uncommon, these conditions usually indicate antibody–mediated central nervous system (CNS) disorders, Chitsaz, A, MD. Professor Cases of Review of Articles Autoimmune Channelopathies: Anti-GLYR-Alpha-1

These channelopathies are chronic or relapsing–remitting, one associated disorder that can mimic the multiple sclerosis (MS). GLYR alpha 1a is not associated with tumor and there is no evidence to data for main pathogenic mechanism. Typical symptoms of GLYR–alpha 1a are excessive startle, rigidity, myoclonic jerks. GLYRS are primarily express in spinal cord, brainstem, caudal brain and retina, Anti GLYRS alapla encephalitis can mimic MS with progressive encephalomyelitis, rigidity and myoclonus (PERM).

18 cases of Anti-GLYR–alpha 1 from review of articles showed the following symptoms: Spasms / stiffness/ rigidity / excessive startle, limb or gait ataxia / limb paresis / pyramidal signs/ walking difficulties / falls/ sensory symptoms and pain/ diplopia, nystagmus / bulbar motor disturbance, dysphagic, dysarthria, difficulty chewing, facial numbers and strimus.

Conclusion: Since the course of anti – GLYR – alpha 1a sometimes is relapsing and remitting and clinical symptoms are very resembling with MS and since they are era of immunotherapy – responsive CNS disease and immunotherapy reduce antibody levels and improve clinical outcomes, in patients with mimic MS consider in mind anti – GiYR – alpha la encephalitis.


Introduction: Central pontine myelinolysis (CPM) typically present in a devasting fashion as quadriplegia and pseudobulbar palsy. Predisposing factors include severe underlying medical illness, nutritional deficiency and changes in serum sodium concentration. The pathology of CPM is demyelination without inflammation in the base of the pons, extrapontine demyelinolitic foci in the deep cerebral white matter and corpus callosum named as extrapontine myelinolysis and these partial forms may mistake with massive pontine demyelination in acute or chronic relapsing multiple sclerosis (MS) in a form of pure pontin syndrome.

Case Report: A 44-year old woman present to neurologic clinic with left lower limb weakness in neurologic exam she had absent of abdominal cutaneous reflexes and left babinsky sign, the rest of neurologic exam was normal, she had abnormal brain stern auditory response and axial T2 weighted brain MRI reveals a symmetrical area of abnormal high signal intensity within the basis pontis. After high dose of methylprednisolon weakness of left lower limb were disappear.

I past history, 8 years ago she had blurred vision in right eye that without treatment her vision returned to normal.

CSF examination showed positive oligoclonal bands. Six months after treatment with beta interferon 1-b, repeat brain MRI showed that lesion of the basis pontis were very smaller than first MRI.

Conclusion: Since in variants of CPM develop of pontine myelinolysis is not rapidly and in acute or chronic relapsing multiple sclerosis rarely massive pontine demyelination produces pure pontine syndrome we must consider in mind differentiation of them, the clinical features and contex provide the clues to correct diagnosis.

[P-146] Acute Idiopathic Blind Spot Enlargement Syndrome: A mimic of Recurrent Optic Neuritis Woojun Kim,1 Seung-Yong Choi,2 SeongHee Ho,1 Jong Yoon Lee,1 Jee Eun Lee,1 Hyun Jo Lee,1 Kwang-Soo Lee1

1Department of Neurology, The Catholic University of Korea, Seoul, Korea
2Department of Ophthalmology, The Catholic University of Korea, Seoul, Korea

Background: Optic neuritis, one of the most common neuro-ophthalmic conditions, is the presenting feature of multiple sclerosis or neuromyelitis optica spectrum disorder. However, there could be a possibility of alternative diagnosis.

Case: A 33-year-old woman presented with a 2-week history of blurred vision affecting her right eye in August 2016. She had similar symptoms in 2007, 2012, and 2014, respectively, and was diagnosed with optic neuritis. High-dose steroid therapy was performed only in 2007, and her symptoms had improved in
several months each time. Magnetic resonance imaging of the optic nerve and the brain revealed no abnormalities correlated to her symptoms. On the eye examinations, best corrected Snellen acuities were 20/25 in the right eye and 20/25 in the left. Pupil reactions and the dilated fundus examination were normal in both eyes. Humphrey visual field tests showed an enlarged temporal scotoma associated with the physiological blind spot in the right eye. Retinal nerve fiber layer measured by optical coherence tomography were normal in both eyes. Fluorescein angiography showed mild hyperfluorescence in the right eye, and indocyanine green angiography disclosed multiple hypofluorescent spots in both eyes, more severe in the right eye. Based on her clinical symptoms and detailed ophthalmologic examinations, the diagnosis was changed to acute idiopathic blind spot enlargement syndrome.

Conclusions: Acute idiopathic blind spot enlargement syndrome should be a possible diagnosis when the diagnosis of optic neuritis is not clear.

[P-147]
CADASIL Mimicking Multiple Sclerosis
Lee SM, Joo IS
Department of Neurology, Ajou University School of Medicine, Suwon, Korea

Background: Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy (CADASIL) is an autosomal dominant vascular disorder caused by mutations of the Notch3 gene. CADASIL and multiple sclerosis (MS) share similar clinical manifestations in that recurrent and remitting episodes of neurologic symptoms occur.

Objective: To report a patient who experienced recurrent transient loss of consciousness, headache, dysphagia, intermittent confusion and progressive bilateral lower limb weakness for 5 years and had been misdiagnosed as multiple sclerosis.

Methods: A detailed clinical history and clinical examination were performed. Routine blood tests, CSF and electrophysiological studies including evoked potentials were obtained. Brain and spinal MRI were also taken. Genetic test for white matter changes was done.

Results: The patient showed the relapsing focal neurologic deficit such as transient loss of consciousness and bilateral lower limb weakness. Marked spastic gait and impaired cognitive function were found. Blood tests and CSF analysis were normal. IgG index was 0.72 and CSF oligoclonal band was negative. Somatosensory and magnetic evoked potentials were abnormal. Brain MRI showed bilateral asymmetric linear and nodular T2 high signal lesions along pons, medulla, and periventricular and subcortical white matters with diffuse brain atrophy. Notch3 genetic screening showed a variant of unknown significance in exon 24, c.4039G>C(p.Gly1347Arg).

Conclusions: CADASIL should be considered in the differential diagnosis of MS, especially in patients who do not have any known familial history of similar clinical episodes.

[P-148]
Atypical Demyelinating Disease in A 40-Year-Old Man Responsive to Intravenous Immunoglobulin (IVIG) Treatment
Akgün Hakan, Çetiz Ahmet, Demirkaya Şeref
Gülhane Military Medical Faculty, Ankara, Turkey

Background: Intravenous immunoglobulin (IVIG) treatment has been shown as a therapeutic option in different types of MS in several published studies.

Objective: In this case report we discussed a patient with atypical demyelinating lesions who did not benefit from high corticosteroid-pulse treatment but responsive to IVIG.

Methods: Case report

Results: A 40-year-old male patient was admitted to our hospital with left hemiparesis and blurred vision of the left eye. Magnetic resonance imaging (MRI) of the brain showed multiple white matter lesions forming clusters with each other in the periventricular area and a large lesion in pons. Cervical MRI showed multiple gadolinium enhanced lesions on multiple levels. NMO IgG was negative and oligoclonal bans were type 4 negative. His complaints partially declined after 10 days of corticosteroid-pulse treatment but 15 days later hemiparesis progressed and developed vision loss of the left eye. He had another 10 days of corticosteroid-pulse treatment but he did not benefited properly. By the time on follow up brain MRI revealed new lesions and still showing gadolinium enhancement in white matter of the brain and cervical spinal region. Plasmapheresis treatment was started but in the second session complications occurred in the form hypotension. IVIG treatment for 5 days 0.4 g/kg was administered. He benefited IVIG and no new complaints occurred for a month.

Conclusions: IVIG may be a treatment option in the treatment of progressive demyelinating disease and in patients who did not receive plasmapheresis because of complications.

[P-149]
Primary CNS Lymphoma Mimicking Neuromyelitis Optica Spectrum Disorder with Aquaporin-4 IgG Antibody
Young-do Kim1, Su-jin Lee2, Tae-Won Kim3
1Department of Neurology, Incheon St. Mary's Hospital, the Catholic University of Korea
2Department of Neurology, International St. Mary's Hospital, the Catholic Kwandong University of Korea

Primary CNS lymphoma (PCNSL) is a rare disorder defined by involvement of the cerebral parenchyma, leptomeninges, eyes or spinal cord without evidence of systemic disease. For histological diagnosis of PCNSL, the procedure of choice is a stereotactic needle biopsy because patients derive no clinical benefit from surgical resection. A 66-year-old woman presented with 7 days of binocular diplopia and mild ataxic gait. Brain MRI showed small high SI lesion on T2 and FLAIR image with enhancement in right middle cerebellar peduncle around 4th ventricle. CSF study and serum vasculitis laboratory were normal. But, serum aquaporin-4 IgG antibody (AQP4-IgG) was positive. At that time, possible diagnosis was considered neuromyelitis optica spectrum disorder (NMOSD) with AQP4-IgG. After treatment with intravenous high-dose corticosteroids, the patient recovered completely within a few days. One month later, the patient required hospitalization because of a severe acute ataxia and drowsiness. Brain MRI showed that the lesion was more enlarged and enhanced with gadolinium. The lesion was demonstrated PCNSL by stereotactic needle biopsy. Our case report shows that PCNSL, especially with positive AQP4-IgG located in the brainstem, can also meet the criteria of NMOSD with AQP4-IgG and should be kept in mind as a possible differential diagnosis.
Intravascular Large B-cell Lymphoma Presenting as Seronegative Neuromyelitis Optica Spectrum Disorder

Kanokkawinwong N, M.D. Jitprapaikulsan J, M.D., Prayoonwiwat N, M.D.
Division of Neurology, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand

Background: Intravascular large B-cell lymphoma (IVLBCL) is a rare type of lymphoma whose presentation often imitates other diseases. It may present with myelopathy. We describe an unusual presentation of IVLBCL as seronegative neuromyelitis optica spectrum disorders (NMOSD).

Case Presentation: A 70-year-old Thai man presented with severe paraparesis and fever for 3 weeks. Spinal magnetic resonance imaging (MRI) demonstrated a hyperintense signal lesion in the T2-weighted image from T4 to T6 with gadolinium enhancement. Cerebrospinal fluid (CSF) analyses were unremarkable except for CSF oligoclonal band positivity. CSF PCR for Mycobacterium tuberculosis (TB) was negative. Cell-based assay was serum AQP-4 IgG negative. While waiting for the laboratory result, his paraparesis was worsening, so i.v. methylprednisolone was given for 5 days. The clinical result was slightly improved. He had pulmonary infiltration and positive sputum PCR for TB. Pulmonary TB and probable spinal intramedullary tuberculosis were diagnosed. One month later, he had worsening paraparesis, visual loss and fever. Thoracic myelopathy was increased from T1 to T8 with gadolinium enhancement. Seronegative NMOSD was diagnosed. Methylprednisolone and plasma exchange caused no clinical improvement. He developed cerebral ischemia. Thus, IVLBCL was suspected and diagnosed by skin biopsy.

Discussion: IVLBCL can present with subacute long extensive transverse myelitis and visual loss similar to NMOSD. The red flag sign of NMOSD is persistent fever and progressive course. The mechanism is spinal cord and orbit infiltration of lymphoma cells.

Conclusions: IVLBCL can initially mimic seronegative NMOSD by presenting with subacute long extensive transverse myelitis and visual loss.

HTLV-1-Associated Myelopathy Accompanied by Thymic Hyperplasia: A Case Report

Hayashi S1,2, Nagamine S2, Okamoto K3
1Department of Neurology, Gunma Rehabilitation Hospital, Agatsuma, Japan
2Department of Neurology, Gunma University Graduate School of Medicine, Maebashi, Japan
3Department of Neurology, Geriatrics Research Institute and Hospital, Maebashi, Japan

Backgrounds: We report a case of human T-lymphotropic virus type 1 (HTLV-1)-associated myelopathy (HAM) accompanied by thymic hyperplasia, who underwent a thymectomy with favorable response.

Case: A 30-year-old Japanese male presented with a 3-month history of gait disturbance. He had spasticity and hyperreflexia of the lower extremities (LEs), and Babinski reflexes were positive bilaterally. Dysesthesia of the LEs and periproctal region were noted, and vibratory sensation was markedly disturbed in the LEs. His neurological function corresponded to 6.0 on the Expanded Disability Status Scale of Kurtzke (EDSS). Antibodies against HTLV-1 were positive in both the serum (PA, x4,096) and CSF (PA, x256). Thoracic spinal MRI showed T2 high-intensity lesion in the dorsal funiculus without contrast enhancement. He was diagnosed with HAM, and prednisolone (60 mg/day) and vitamin C (1,800 mg/day) were administered orally, resulting in the partial amelioration (EDSS 4.0). Chest CT showed a thymic mass and he underwent extended thymectomy, which showed thymic hyperplasia histologically. Immunohistochemical examinations revealed that CD3- (T cells), CD20- (B cells), CD1a- (dendritic cells), and CD8-immunoreactive cells were markedly present in the medulla, especially around Hassall’s capsules. Following the thymectomy, his symptoms ameliorated, and he remains stable (EDSS 3.5) at 16 years after onset.

Conclusions: Given that CD8-ir cells are aggravating factors of chronic spinal inflammation in patients with HAM, the patient’s favorable response to thymectomy might have contributed to the removal of these cells in the thymus, which lessened the recruitment of CD8-ir cells into the central nervous system.
EUROPEAN CHARCOT FOUNDATION SYMPOSIUM

Progressive MS
Chairperson: Giancarlo Comi (Italy) & William Carroll (Australia)

Progressive MS in Asia
Kazuo Fujihara (Japan)
*Information not available at time of printing.*

Pathogenesis
Hans-Peter Hartung (Germany)
*Information not available at time of printing.*

Treatment in Progressive MS
Giancarlo Comi (Italy)
*Information not available at time of printing.*
Using MRI to Diagnose MS and Related Disorders
Chairperson: Jacqueline Palace (United Kingdom) & Kazuo Fujihara (Japan)

MS MRI Features and Its Differentiation from Vascular Disease and Aging
Olga Ciccarelli (United Kingdom) 
University College London (UCL) Institute of Neurology, London, United Kingdom

The most common, differential diagnosis of white-matter lesions in patients suspected of having MS is the possibility that these lesions are caused by small- vessel disorders. These disorders cause hypoxic-ischaemic cerebral lesions, which are usually asymptomatic, and can lead to transient ischaemic attacks, stroke, subcortical arteriosclerotic encephalopathy, and headache. Several MRI features are commonly associated to hypoxic-ischaemic lesions, including the presence of cortical infarcts, borderzone or watershed lesions, lacunes, and multifocal basal ganglia lesions. In addition, there are more typical features that support a more specific diagnosis. These include haemorrhage (amyloid angiopathy), multiple microhaemorrhages (CADASIL), cortical or subcortical lesions crossing vascular territories (mitochondrial disease), substantial asymmetry of the white-matter lesions (ipsilateral carotid disease), and involvement of the external capsules and temporal poles (CADASIL). MS lesions have a typical perivenular distribution, whilst hypoxic-ischaemic lesions are usually dominated by arterial anatomy, such as cortical infarcts, basal ganglia lesions (including lacunar infarcts), or borderzone or watershed abnormalities.

Infratentorial lesions are specific for MS, but may occur in small-vessel disorders. However, in MS lesions are typically located at the surface of the pons and at the base of the fourth ventricle, whilst lesions in subcortical arteriosclerotic encephalopathy are usually centrally located in the pons. MS lesions typically involved the corpus callosum, which is spared by small-vessel disease and CADASIL lesions. MS patients often show lesions in the spinal cord, whilst patients with hypoxic-ischemic disease do not usually have spinal cord lesions. Furthermore, incidental spinal cord matter lesions do not occur with ageing.

Differentiating the Imaging Features of MS from NMOSD and ADEM
Jacqueline Palace (United Kingdom) 
Neurosciences, Oxford University Hospitals Trust, UK

The diagnosis of multiple sclerosis (MS) is usually straightforward with the majority of patients presenting with a typical clinical history and confirmatory investigations. However clinical mimics can make the differentiation challenging and MRI becomes an important diagnostic tool. The neuromyelitis optica spectrum disorders (NMOSD) are divided between those with aquaporin 4 antibodies (AQP4-AbS) who make up about 60% of cases, and those without. Around 20-30% of those with seronegative NMOSD have myelin oligodendrocyte glycoprotein antibodies (MOG-Abs) and these antibodies are also identified in a subgroup of patients with acute disseminated encephalomyelitis (ADEM). Although the initial diagnostic criteria required patients to have a normal brain MRI (outside of optic nerve abnormalities) and subsequently to have a non MS-like brain MRI, it is now recognized that NMOSD patients can have imaging features which fulfil the MS brain imaging diagnostic criteria, and a greater proportion have non-specific white matter lesions. However, there are imaging features which are useful differentiators with various specificities and sensitivities.

On the brain MRI, the presence of Dawson’s fingers, lesions adjacent to the lateral ventricles and in the inferior temporal lobe, S-shaped U-fibre lesions, cortical lesions and the majority of lesions having central veins support a diagnosis of MS, whereas peri-ependymal lesions, particularly in the area postrema, and diencephalic lesions are more specific for NMOSD. Posterior, bilateral, long optic nerve lesions often involving the chiasm are typical of NMOSD optic neuritis.

Spinal cord MRI associated with transverse myelitis typically demonstrates short asymmetrical lesions in MS and longitudinally extensive central cord lesions (≥3 vertebral segments), often with acute T1 hypointensity in NMOSD. Atrophy outside of lesion related damage, widespread abnormalities of normal appearing brain tissue and silent activity is well recognized in MS but is probably uncommon in NMOSD. Fluffy cerebral brain lesions, deep grey matter lesions, longitudinally extensive transverse myelitis, and conus involvement are typical of ADEM and MOG-Ab disease. Of note the imaging features of patients with AQP4 and MOG antibodies overlap.

Case Examples of Other MS Mimics
Kazuo Fujihara (Japan) 
Department of Multiple Sclerosis Therapeutics, Fukushima Medical University School of Medicine and MS & NIMO Center, Southern TOHOKU Research Institute for Neuroscience (STRINS)

In making the diagnosis of multiple sclerosis (MS), we need to evaluate clinical, MRI and laboratory findings to demonstrate inflammatory demyelinating CNS lesions disseminated in space and time. However, not a single biomarker is perfectly sensitive and specific to MS, and a variety of diseases may be confused with MS. CNS pathologies to consider include other inflammatory or immune-mediated, demyelinating diseases, vascular diseases and migraine, infections, neoplasms, and neurodegenerative diseases. Genetic diseases, nutritional deficiencies, and psychiatric diseases may also present in a similar manner to MS. The diagnosis of MS should be questioned in cases with few or no specific characteristics of MS lesions in the absence of typical and convincing symptoms and/or objective neurological findings.

In this presentation, cases of MS mimics manifesting cerebral and brainstem syndrome, optic neuropathy and myelopathy except cerebrovascular diseases, NNOSD and ADEM will be presented, and a practical clinical and neuroimaging framework of differential diagnosis of MS will be discussed.
**B Cell Biology in NMOSD: From Pathology to Innovative Therapeutics**

Chairperson: Ho Jin Kim (Republic of Korea)
Friday, 28 October 2016, 8:30-10:00

**B Cell Basics and Implications in Autoimmune Disease**
Amit Bar-Or (Canada)
*McGill University, Montreal, Canada*

Elucidating how B cells contribute to the autoimmune disease and, in particular, to the spectrum of CNS inflammatory demyelinating disease, has become of major interest. In part, this interest has been fueled by the success of B cell depleting therapy in limiting multiple sclerosis (MS) relapses. Additional reasons, however, include the growing recognition that B cells may contribute to CNS inflammatory conditions through multiple distinct mechanisms which may, in turn, contribute to the pathophysiologic heterogeneity that appears to exist across the disease spectrum, for example in the context of NMO spectrum disorders; NMO-SD. This introductory lecture will provide a brief overview of the range of B cell responses that may participate in CNS inflammatory disease including NMO-SD. Since the roles of antibodies in NMO will be expanded upon in a separate presentation, here we will highlight some of the non-antibody dependent mechanisms underlying B cell involvement in the disease spectrum, including how B cells may shape T cell and myeloid cell responses in ways that are relevant to CNS inflammation.

**Pathogenic Autoantibodies in the Pathogenesis of NMOSD**
Sasitorn Siritho (Thailand)
*Faculty of Medicine, Siriraj Hospital, Mahidol University, Thailand*

Information not available at time of printing.

**The MOG Antibody and NMOSD**
Ichiro Nakashima (Japan)
*Department of Neurology, Tohoku University School of Medicine*

Anti-myelin oligodendrocyte glycoprotein (MOG) antibody, which is specifically detected using a cell-based assay (CBA), has been identified in various demyelinating diseases, including neuromyelitis optica (NMO) spectrum disorders, acute idiopathic optic neuritis (ON), and pediatric multiphasic disseminated encephalomyelitis (MDEM). Although its pathogenic role has not been established, antibody seropositive cases appear to share several characteristic features, such as a preferable response to steroid therapy and a good prognosis. Antibody detection at the onset of a demyelinating disease is important to predict the prognosis. The cytokine profile of anti-MOG antibody associated disease was similar to that of anti-aquaporin-4 (AQP4) antibody positive NMO and was different from that of multiple sclerosis. Further analysis of the clinical features and investigation of the pathogenic roles of the antibody are required to establish the disease spectrum associated with the antibody. Although the associated diseases appear to have a relatively good prognosis, treatment recommendations are offered for patients with severe symptoms or frequent relapses.

**What New Therapies for NMOSD are on the Horizon?**
Ho Jin Kim (Republic of Korea)
*Department of Neurology, Research Institute and Hospital of National Cancer Center, Goyang, S. Korea*

Neuromyelitis optica spectrum disorder (NMOSD) is a rare, disabling autoimmune disease associated with serum aquaporin-4 immunoglobulin G antibodies. Disability in NMOSD occurs as a result of acute attacks. Therefore, suppressing the frequency and severity of attack is the prime goal of treatment. Retrospective case series data for a range of immunosuppressive medications have demonstrated a reduction in annualized relapse rate and stabilization of expanded disability status scale scores; however, none of which have been validated in a prospective randomized controlled trial. Several trials of new biological therapies such as monoclonal antibodies against complement protein C5 (Eculizumab), anti-interleukin-6 receptor antibody (SA237), or anti-CD19 antibody (MEDI-551) are currently underway. Results from these studies will hopefully help guide future management decisions.
The Changing Treatment Landscape in MS; 
Immunosuppression vs Immunomodulation
Chairperson: William Carroll (Australia)
Friday, 28 October 2016, 17:00-18:30

Immunosuppression vs Immunomodulation;
An Immunologist’s Perspective
Amit Bar-Or (Canada)
Information not available at time of printing.

Immunosuppression vs Immunomodulation;
A Neurologist’s Perspective
Anthony Traboulsee (Canada)
Information not available at time of printing.