January 27, 2024 | KKL Luzern

State of the Art

Symposium 2024

«Treatment Algorithms & Deescalation»
Abstract Book

Swiss
Multiple Sclerosis
Society

MS State of the Art Symposium 2024

«Treatment Algorithms and Deescalation»

Dear Colleagues,

It is with great pleasure that we invite you to this year's 26th edition of the MS State of the Art Symposium. The symposium is organized by the Swiss MS Society and its Medico Scientific Advisory Board.

The symposium is dedicated to discussing **«Treatment Algorithms and Deescalation»**, a topic that deserves close examination with the advancement of new, potent MS medications and increasingly precise methods for diagnosis and disease course prognostics.

The morning session features internationally renowned speakers such as **Fredrik Piehl (Stockholm)** on the benefit-risk balance in MS treatment, **Christine Lebrun-Frenay (Nice)** on RIS and early treatment, as well as **Andrew Chan (Bern)** with an update on MS medication and treatment.

Disease modifying therapies during pregnancy will be the topic of a podium discussion under the lead of **Caroline Pot (Lausanne)**. Neurologists, gynaecologists and pharmacologists will discuss the national consensus recommendations that have recently been developed in Switzerland.

During the coffee and lunch breaks you will have the opportunity to view the **Poster Presentations** of the researchers currently funded by the Swiss MS Society, and discuss their projects.

The afternoon session, with two sets of parallel **Workshops**, will address specific topics relevant to daily practice, and encourage you to ask your own questions and engage in the discussion.

On behalf of the organisers and speakers, we hope that the programme meets your interest, and are looking forward to meeting you in Lucerne.

Prof. Dr. med. Jürg H. Beer
President of the Swiss MS Society

Dr. Christoph Lotter
Co-Director of the Swiss MS Society

PD Dr. med. Sandra Bigi
Head of the Programme Committee and Member of the Medico Scientific Advisory Board

General Information

Date

Saturday, January 27, 2024, 09.30 – 16.00

Venue

KKL Lucerne, Europaplatz 1, CH-6005 Lucerne

Programme Committee

Sandra Bigi, Luzern; Adam Czaplinski, Zurich; Britta Engelhardt, Bern; Jens Kuhle, Basel; Caroline Pot, Lausanne

Organisation

Swiss Multiple Sclerosis Society and its Medico Scientific Advisory Board

Contact

Swiss Multiple Sclerosis Society
Josefstrasse 129, CH-8031 Zurich
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Credits

The Swiss Neurological Society awards 6.0 credit points.

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Contributors

Programme Committee and Chairpersons

Sandra Bigi, Lucerne
Adam Czaplinski, Zurich
Britta Engelhardt, Bern
Jens Kuhle, Basel
Caroline Pot, Lausanne





Welcome Speech

Jürg H. Beer, Baden & Zurich
Christoph Lotter, Zurich


Speakers & Poster Presentations

Lectures

Andrew Chan, Bern
Christine Lebrun-Frenay, Nice
Fredrik Piehl, Stockholm
Caroline Pot, Lausanne

Podium Discussion

Andrew Chan, Bern
Michael Graber, Bern
Alice Panchaud, Bern & Lausanne
Daniel Surbek, Bern
Caroline Pot, Lausanne (Moderation)

Workshops

Lara Diem, Lucerne
Renaud Du Pasquier, Lausanne
Lars Hemkens, Basel
Ilijas Jelcic, Basel
Iris-Katharina Penner, Bern
Jean-Michel Pignat, Lausanne
Arseny Sokolov, Lausanne
Özgür Yaldizli, Basel

MS Researcher Poster Presentations

Sara Da Costa Pereira, Zurich
Giulio Disanto, Lugano
Sarah Guimbal, Bern
Stefania Iaquinto, Zurich
Benjamin Ineichen, Zurich
Isabele Jacot de Alcântara, Geneva
Perrine Janiaud, Basel
Samuel Jones, Lausanne
Daniela Latorre, Zurich
Jesús López-Alcalde, Zurich
Tradite Neziraj, Basel
Johanna Oechtering, Basel
Elisabeth Pössnecker, Basel
Mina Stanikic, Zurich
Nina Steinemann, Zurich
Lenka Sukenikova, Zurich
Juan Villar-Vesga, Zurich
Viktor von Wyl, Zurich

RG now

Network for young persons with MS

Many questions follow the diagnosis - and above all is the wish to be understood.

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more on **rgnow.ch**

get better together

MS Swiss Multiple Sclerosis Society

Plenary Sessions

9.30 – 10.00	Coffee and Gipfeli
Session 1	**Chairpersons:** Jens Kuhle, Basel Caroline Pot, Lausanne
10.00 – 10.15	Jürg H. Beer, Baden & Zurich Christoph Lotter, Zurich **News from the Swiss MS Society**
10.15 – 10.45	Fredrik Piehl, Stockholm **Optimizing the Treatment Benefit-Risk Balance over the MS Disease Course**
10.45 – 11.15	Christine Lebrun-Frenay, Nice **RIS and Early Treatment**
11.15 – 11.45	Coffee Break MS Researcher Poster Presentation
Session 2	**Chairpersons:** Sandra Bigi, Luzern Adam Czaplinski, Zurich
11.45 – 12.15	Andrew Chan, Bern **MS Treatment Update 2024**
12.15 – 12.30	Caroline Pot, Lausanne **DMT Use in Pregnancy**
12.30 – 13.00	**DMT Use in Pregnancy: Podium Discussion** with Andrew Chan, Bern | Michael Graber, Bern | Alice Panchaud, Bern & Lausanne | Daniel Surbek, Bern Moderation: Caroline Pot, Lausanne
13.00 – 14.15	Lunch Break MS Researcher Poster Presentation

Fredrik Piehl

«I did my undergraduate studies in medicine in parallel with a PhD in basic neuroscience at the Karolinska, followed by a 3-year post-doc in experimental neuroimmunology in the group of Tomas Olsson. Over the course of two decades my research focus has moved from experimental systems to clinical research on neurodegenerative aspects of neuroinflammation, biomarkers and effects of disease modulatory treatments. I have been head of the MS clinic at Karolinska 2008-2017, and I am now head of research at the Academic Specialist Clinic, our hospital-affiliated outpatient clinic where we provide care for about 2,600 people with MS.»

Optimizing the Treatment Benefit-Risk Balance over the MS Disease Course

Multiple Sclerosis (MS) is an inflammatory, demyelinating and neurodegenerative disease usually diagnosed in early mid-life, but with a wide age range. It is well established from large natural cohort studies that aging impacts on disease manifestations of MS. Thus, inflammatory disease activity manifesting as relapses and focal brain lesion accrual is negatively correlated with age, while the risk of progressive worsening of disability instead increases.

Accumulating data suggest that infection with Epstein-Barr virus is a strong driver of dysregulated adaptive inflammation in MS, perhaps due to a chronic infection of B cells. Depletion of B cells with antiCD20 treatment show striking efficacy for preventing relapses and focal lesion accrual, even in early disease phases with high disease activity.

Here Sweden remains unique in its high use of B cell depletion as a first line treatment for MS, which is associated with beneficial long-term disability outcomes and improved control of inflammatory disease activity compared to alternative treatments, as seen in one of the world´s largest prospective real world drug studies; CombatMS. In this context, our data has been important for the inclusion of the antiCD20 monoclonal rituximab on WHO´s list of essential medicines for MS, in spite of lacking a formal approval for this indication.

However, B cell depletion is associated with increased infection risk and risk mitigation strategies are needed to retain a beneficial benefit-risk balance over time, not least since our data indicate that systemic infections increase the risk of worsening of MS disability.

We have recently shown that extension of antiCD20 infusion intervals in stable patients is not associated with signs of return of inflammatory disease activity, while at the same time improving humoral vaccination responses. As a result we have transitioned to an infusion once every two years in a majority of patients in clinical practice. In ongoing work we aim to address why disability accrual with time occurs in a proportion

of patients by leveraging our large and well characterized cohorts and technical developments in genetics, blood biomarkers and brain image profiling, including use of state-of-the-art 7T MRI. Such information will be important for finding markers to evaluate treatment effects and to individualize therapy with novel drug classes impacting CNS inherent disease processes, therefore potentially being more suitable in later disease stages.

Fredrik Piehl
- *Karolinska Institutet, Stockholm SE*
- *Karolinska University Hospital, Stockholm SE, Department of Neurology*

Notes

Christine Lebrun-Frenay

«As a Neurologist and Oncologist, my research interest includes therapeutical and MRI studies in MS with a specific implication in the description of Radiologically Isolated Syndrome (RIS). I am in charge of the inflammatory neurological disorders clinical research unit and MS Center at the University of Nice Cote d'Azur Hospital.»

RIS – Radiologically Isolated Syndrome and Early Treatment

Even before the introduction of RIS criteria, longitudinal clinical data from individuals with incidentally identified T2 lesions suggestive of Multiple Sclerosis (MS) were described. Healthy individuals who do not exhibit signs of neurological dysfunction commonly have brain MRI studies performed for a reason other than an evaluation for MS that reveal unexpected anomalies highly suggestive of demyelinating plaques, given their size, location, and morphology. These healthy subjects lack symptomatology suggestive of MS and fulfill formal criteria for the radiologically isolated syndrome (RIS). This recently described MS subtype expands upon the phenotype of at-risk individuals for future demyelinating events. A formal description of RIS was first introduced in 2009 by Okuda et al. to define this relevant cohort of individuals at risk for future demyelinating events. In European or North American observational studies, the authors have found that up to 30-45% of patients presenting with a RIS will show clinical progression. The presence of asymptomatic lesions in the cervical cord increases the risk of progression, either to relapsing or to progressive MS.

The consortium studying the epidemiology of RIS worldwide (RISC) presented its first retrospective cohort. The 5-year and 10-year observed conversion rates to the first clinical event were 34% and 51%. In the multivariate model, age, sex (male), oligoclonal bands, and lesions within the spinal cord were identified as significant predictors for developing a first clinical event. The ARISE study demonstrated the efficacy of dimethyl fumarate on the occurrence of a clinical event, with a decreased risk of over 80% to evolve to MS for the treated arm. The TERIS study evaluating the efficacy of teriflunomide in RIS showed a risk reduction of 72% over placebo. These two results significantly advance our conviction that early treatment for MS is necessary and potentially impacts long-term disability. Despite advancements in the characterization of RIS subjects and our understanding of risk factors for initial symptom development, we need to define risk profiles for a seminal neurological event to propose treatment to at-risk RIS subjects.

Christine Lebrun-Frenay
– *Nice Côte d'Azur University Hospital, Nice FR, MS Clinic*

Notes

Andrew Chan

«I act as Head of the Medical Division Neuro (Depts. Neurology, Neurosurgery, Neuroradiology), Inselspital, University Hospital of Bern. After studying medicine and obtaining a doctorate at the University of Hamburg, I completed my specialist training at the University of Würzburg and continued my professional development as Senior Physician at the Universities of Göttingen and Bochum. I have published widely in the field of MS, including papers on molecular markers of disease progression and risk of immunotherapy, treatment optimization and patient monitoring. I have been the principal investigator for several clinical studies in MS. I have also been involved in the development of national treatment guidelines.»

MS Treatment Update 2024

In view of the large variety of disease modifying therapies, benefit risk assessment over the long term, treatment switch algorithms as well as conditions for discontinuation of therapy are currently in the focus of discussions on MS management. Given increasing financial restraints and restricted access to therapy in many parts of the world, also the aspect of generic drugs/biosimilars becomes increasingly important.

Whereas there is broad agreement that focal MS disease activity (i.e. relapses, new MRI lesions) is relatively well targeted by current (highly efficacious) immunotherapies, more recent appreciation of disease progression also without focal activity («progression independent of relapse activity, silent progression») as a major and early driver of disability points to a major unmet medical need.

Underlying pathophysiology may entail at least partly distinct mechanisms and inflammatory cell populations. These may be targeted by a novel class of substances – newer generation Bruton's tyrosine kinase (BTK) inhibitors – for which pivotal phase III trial data are expected to be announced beginning of 2024.

Inhibition of the costimulatory CD40/CD40L pathway necessary for adaptive and innate immune cell activation represents a potentially novel mechanism of action, currently being explored in phase II/III study programmes.

Andrew Chan
– *University Hospital Bern, Inselspital, Department of Neurology*

Notes

Caroline Pot

«I am a clinician-scientist specialized in neuroimmunology with a strong expertise Multiple Sclerosis. I trained as a neurologist at the Geneva University Hospitals (HUG). In parallel, I completed my MD-thesis at the University of Zurich and performed a research fellowship at Harvard Medical School in Boston, USA. In 2015, I joined the Service of Neurology at the Lausanne University Hospital (CHUV), awarded by a Swiss National Science Foundation Professorship, and focus my research on establishing the role of lipid metabolism and of the gut-brain axis in driving MS. I was nominated associate Professor in 2019 and I am responsible for the Day Hospital and the Neuroimmunology and Multiple Sclerosis Unit at the CHUV.»

DMT Use in Pregnancy

Multiple Sclerosis usually manifests in the second to fourth decade of life and shows a female predominance. Until the 1990's, women with MS were discouraged to consider pregnancy.

Over the last three decades it has become clear that pregnancy is not associated with a worse MS disease outcome. In parallel, we have seen a significant expansion of disease modifying therapies (DMTs) with different mechanisms of action and modes of application. Furthermore, we experience a change in treatment paradigms. Early and aggressive treatment has become our current belief and is associated with less disease burden and better functional outcome. As specific DMT risk profiles have emerged, individual benefit-risk considerations also need to consider family planning.

In this presentation, I will discuss the international recommendations and guidelines as well as our recent Swiss recommendations for the use of DMTs in the context of family planning, pregnancy and lactation.

Caroline Pot
– Lausanne University Hospital (CHUV), Service of Neurology

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DMT Use in Pregnancy: Podium Discussion

A comprehensive team of professionals is needed for an optimal management of persons with MS. Family planning is an example of this complexity of care. In the podium discussion we will debate, with different experts that all contributed to the elaboration of the Swiss recommendations presented in the preceding speech by Caroline Pot, the use of DMTs in the context of family planning, pregnancy and lactation: Andrew Chan and Michael Graber, neurologists from the University Hospital Bern; Alice Panchaud, clinical pharmacist and pharmacologist from the Lausanne University Hospital and the University of Bern who is an expert in safety and effectiveness of drugs in the real-life setting and on teratogen risk; and Daniel Surbek, gynecologist and obstetrician, Head of the Deptartment of Obstetrics and Gynecology at the University Hospital Bern.

Andrew Chan
– *University Hospital Bern, Inselspital, Department of Neurology*

Michael Graber
– *University Hospital Bern, Spital Riggisberg, Department of Neurology*

Alice Panchaud, Bern & Lausanne
– *Lausanne University Hospital (CHUV), Maternity Sector, Service of Pharmacy*
– *University of Bern, Institute of Primary Health Care (BIHAM)*

Daniel Surbek, Bern
– *University Hospital Bern, Inselspital, Clinic for Gynaecology*

The discussion will be moderated by:
Caroline Pot, Lausanne University Hospital (CHUV), Service of Neurology

Notes

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Workshops

These workshops invite discussion and the attendees are encouraged to participate actively.

Workshop A
14.15 – 15.00

Renaud Du Pasquier, Lausanne
Ilijas Jelcic, Basel
Vaccinations in the Context of MS: New Insights

Vaccination for people with MS has gained growing attention since the approval of effective therapies with increasing immunosuppressive potential and since the COVID pandemic. We will discuss current general recommendations for vaccinating people with MS and lessons learned from the COVID pandemic.

Workshop B
14.15 – 15.00

Lara Diem, Lucerne
Jean-Michel Pignat, Lausanne
Fatigue: The Invisible but Debilitating Symptom

Fatigue affects at least 75% of persons with MS. Obviously, MS-related fatigue has socioeconomic consequences leading to increased sick leaves and a higher probability of unemployment. In this workshop, we will discuss the current status regarding pathophysiology, diagnosis and therapy of fatigue.

15.00 – 15.15

Coffee Break

Workshop C
15.15 – 16.00

Lars Hemkens, Basel
Özgür Yaldizli, Basel
Pragmatic Trials Adding to Treatment Personalisation

We will explore the MultiSCRIPT trial within the Swiss MS Cohort Study as innovative approach for a continuous learning system, where a series of pragmatic trials evaluate personalized strategies for patient care. We will describe the approach, next steps and the outlook to systematically improve care of persons with MS.

Workshop D
15.15 – 16.00

Iris-Katharina Penner, Bern
Arseny Sokolov, Lausanne

Cognition in MS: How to Screen, Assess and Treat in Clinical Routine?
We will first introduce the topic of cognitive impairment in MS and highlight its impact on daily life. We will then look at common testing procedures together, perform and evaluate them, and discuss potential pitfalls. Finally, we will provide an outlook on new non-pharmacological treatment strategies currently under study in Switzerland.

16.00

Farewell Apero

Renaud Du Pasquier
«I am Chairman of Neurology at the Lausanne University Hospital (CHUV) and Director of the neuro-immunology laboratory. I see all kind of patients with neuro-inflammatory conditions. My main topic of research is about the viral causes of demyelinating diseases (MS-EBV, PML-JCV).»

Ilijas Jelcic
«I am Head of the Neurocenter Basel, Head of the aHSCT-in-MS Service, Neurocenter Bellevue and Klinik Hirslanden, Zurich. I provide care to patients with Multiple Sclerosis and related disorders (MOGAD, NMOSD, neuro-sarcoidosis, etc.) as well as neuro-infectious diseases (PML, neuroborreliosis, etc.) and am specialized in the care of MS patients during and around autologous hematopoietic stem cell transplantation (aHSCT). My main research interest is antiviral immunity in these conditions.»

Workshop A

Vaccination in the Context of MS: New Insights

Immunomodulatory treatment with inducing varying degrees of immunosuppression constitute now the standard of care of MS patients. These treatments need a careful management. In particular, the clinician should know what effects vaccines have on MS and on the course of the disease under a given DMT; which vaccines are recommended or not depending on the DMT the patient is on; what is the optimal timing to vaccinate, etc. This field became more complex with the onset of COVID-19 and related vaccines. Here, we will review these different aspects under the light of the recent literature and try to provide clear take-home messages, useful for the clinician.

Renaud Du Pasquier
– *Lausanne University Hospital (CHUV), Department of Clinical Neurosciences, Service of Neurology, University of Lausanne*

Ilijas Jelcic
– *Center for Multiple Sclerosis, Neurocenter Basel and Neurocenter Bellevue, Zurich,*
– *Clinic Hirslanden, Zurich, Department of Neurology*

Notes

Lara Diem

«I currently work as a senior physician at the Lucerne Cantonal Hospital. My daily clinical work includes individual MS patient care. My special interests include fatigue syndrome. I am involved in the care, information and counselling of people with MS and fatigue syndrome. Scientifically, I am interested in the fatigue syndrome and its cause, e.g. connection between hypogammaglobulinemia and fatigue.»

Jean-Michel Pignat

«My current position is senior physician in the Department of Neurorehabilitation at CHUV, Lausanne. I am a neurologist specialized in cognitive disorders, including fatigue, caused by brain lesions, with extensive experience in assisting patients in their return to work. Scientifically, my primary interest lies in understanding the connection between cognitive impairment and brain networks.»

Workshop B

Fatigue: the Invisible but Debilitating Symptom

Multiple Sclerosis (MS) is the most common cause of mental and physical disability in young adults affecting approximately 10'000-15'000 persons in Switzerland (incidence 16/100000; prevalence 190/100000). MS-fatigue affects at least 75% of the MS-patients (affected persons in Switzerland 7'500-11'250). Obviously, MS-related fatigue, as in other neurological diseases, has socioeconomic consequences leading to increased sick leaves and a higher probability of unemployment. Nonetheless, fatigue in MS remains poorly understood and often underemphasized for several reasons. Fatigue is a subjective symptom without a unified definition, and ambiguity also arises because no gold standard exists by which to measure fatigue.
Finally, fatigue in MS patients may be multifactorial. In addition to immunologic abnormalities, Multiple Sclerosis is associated with an increased prevalence of other conditions that contribute to fatigue, including depression, cognitive impairment, metabolic disorders, sleep disorders, etc. Though there have been advancements in more effective immunotherapies for managing autoimmune neuroinflammation and MS disease activity, treatment options for MS-fatigue are

limited, even though physical exercise, psychopedagogy and stimulant drugs of the central nervous system may improve fatigue. Unclear understanding of the underlying mechanisms, coupled with non-MS-related factors, such as biological dysfunction (including thyroid dysfunction, anaemia), cognitive deficits, mood disorders or sleep impairment, explains the limitation of the therapeutic choice. In this workshop, we will discuss the current understanding of pathophysiology, diagnosis and treatment options of fatigue in MS.

Lara Diem
– *Cantonal Hospital of Lucerne, Neurology and Neurorehabilitation Clinic*

Jean-Michel Pignat
– *Lausanne University Hospital (CHUV), Service of Neuropsychology and Neurorehabilitation*

Notes

Lars Hemkens

«I am a physician and clinical epidemiologist, currently leading the Pragmatic Trials and Real World Evidence workstream at the Research Center for Clinical Neuroimmunology and Neuroscience Basel (RC2NB). My primary mission is to create evidence that matters for patients. I focus on developing digital biomarkers and digital health applications for Multiple Sclerosis and co-lead the MultiSCRIPT project, a nationwide learning health care system and pragmatic trial platform within the Swiss MS Cohort.»

Özgür Yaldizli

«I graduated in medicine at the University of Düsseldorf in 2001 and specialised in neurology at the University Hospital Essen. I joined the MS center in Basel in 2009 and am currently working as a senior consultant neurologist at the University Hospital Basel. I lead the MultiSCRIPT Study - a pragmatic randomized controlled trial embedded in the Swiss MS Cohort.»

Workshop C

Pragmatic Trials Adding to Treatment Personalisation

Pragmatic randomized trials inform decisions about health-related interventions in routine care. They are essential for providing reliable evidence to make better treatment decisions but are not yet commonly used to improve the care of persons with MS. Pragmatic trials can substantially benefit from high-quality routinely collected data, which are available in Switzerland for MS through the Swiss Multiple Sclerosis Cohort (SMSC).

In this workshop, we will explain the concept of pragmatic trials, provide a systematic overview of their current application in MS, and introduce the MultiSCRIPT project, the world's first nationwide pragmatic trial in MS.

MultiSCRIPT is a learning healthcare system for persons with MS. It continuously evaluates which new personalized care strategies ensure no evidence of disease activity, while achieving better patient outcomes, fewer adverse events, and improved care. MultiSCRIPT uses the procedures and high-quality real-world data collection of the SMSC usual care to avoid almost all the burden for participants that traditional clinical trials would require. This innovative approach will make clinical research part of usual care in MS to continuously improve health of all persons with MS.

We will explain the first cycle of MultiSCRIPT which evaluates the use of serum neurofilament light chain (sNfL) as a sensitive measure of disease activity. In this first part of MultiSCRIPT, all patients with RRMS in the SMSC for at least a year can participate – we hope to include at least 915 persons.
We will show how we have developed consensus-based algorithms for treatment decisions to facilitate the use of sNfL as supporting information for decisions on the escalation and de-escalation of disease-modifying therapies.
Overall, there is an urgent need to leverage the potential of pragmatic trials to generate useful randomized real-world evidence, and this workshop illustrates the steps we are taking in Switzerland to achieve this ambitious goal.

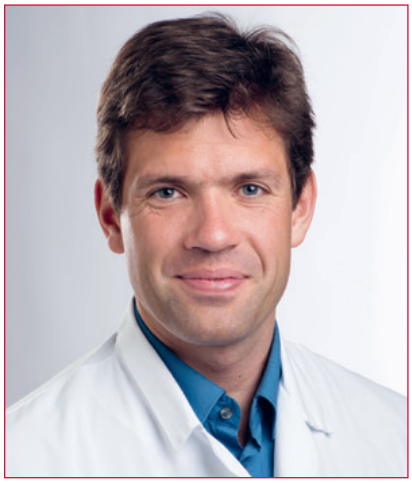
Lars Hemkens
– *RC2NB – Research Center for Clinical Neuroimmunology and Neuroscience Basel; University of Basel and University Hospital Basel*

Özgür Yaldizli
– *RC2NB – Research Center for Clinical Neuroimmunology and Neuroscience Basel; University of Basel and University Hospital Basel, Neurologic Clinic and Policlinic, Departments of Clinical Research and Biomedical Engineering*

Notes

Iris-Katharina Penner

«I am a cognitive neuroscientist and neuropsychologist with more than 20 years of experience in neurocognitive research and clinical care. From 1999 to 2015 I worked at the University and the University Hospital Basel, where I completed my PhD and my habilitation with a focus on cognition, cognitive rehabilitation, fatigue and brain imaging in MS. In 2015, I moved to the Neurology Department of University Hospital Düsseldorf and was the director of the COGITO Center for applied neurocognition and neuropsychological research. Since January 2022 I am the Head of Neuropsychology at the Department of Neurology, Inselspital, Bern where I am responsible for the whole spectrum, from bedside to ambulatory neuropsychology. My clinical and scientific focus is concentrated on cognitive processes, fatigue and brain plasticity in inflammatory and neurodegenerative diseases of the CNS.»



Arseny Sokolov

«I am a cognitive neurologist in charge of the Department of Neuropsychology and Neurorehabilitation and an Associate Professor at the University Hospital of Lausanne (CHUV). I am specialized in cognitive and behavioural neurorehabilitation, and my research focuses on the implementation of novel technology in neuropsychology and neurorehabilitation, and on social cognition in neurological patients. Before returning to the CHUV, I have completed a PhD at the University College London, a postdoctoral fellowship at the University of California San Francisco, and served as Vice Director of the University Neurorehabilitation at the Inselspital Bern.»

Workshop D

Cognition in MS: How to Screen, Assess and Treat in Clinical Routine?

Cognitive impairment is one of the most debilitating symptoms for patients living with Multiple Sclerosis (plwMS), since it affects people in their most productive phase of life and it has tremendous effects on employment and daily living. Despite the high prevalence, the majority of neurologists is still not aware of the relevance of these symptoms nor are they familiar with screening instruments allowing to objectify the cognitive problems in standard clinical care and to integrate results into treatment decisions.
Therefore this workshop will first briefly provide some background information on cognition in MS, focusing on impact and cognitive domains being typically affected. With this in mind, we will introduce several instruments which represent the state-of-the-art to screen for cognitive issues in MS. We will perform some of these tests hands-on during the workshop, in order to familiarize attendees with the testing procedure, the evaluation of test results and their interpretation. In a last step, we will discuss indications for in-depth neuropsychological examination, and give an outlook on two cognitive neurorehabilitation approaches currently being studied in Switzerland.

Iris-Katharina Penner
– *Bern University Hospital, Inselspital, Department of Neurology*

Arseny Sokolov
– *Lausanne University Hospital (CHUV), Department of Clinical Neurosciences, Service of Neuropsychology and Neurorehabilitation*

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MS Researcher Poster Presentations

The Swiss MS Society supports research projects in the field of Multiple Sclerosis with considerable financial contributions.

A selection of current projects is displayed during the coffee and lunch break of the symposium.

Do not miss the opportunity of viewing these posters and discussing the projects with the researchers.

01 | Sara Da Costa Pereira

Human Organotypic Retina Cultures to Study Pathophysiology of Neuromyelitis Optica Spectrum Disorder

Background — Multiple Sclerosis is a prevalent chronic CNS inflammatory disorder characterized by the transition from relapsing-remitting MS (RRMS) to a progressive form (PMS), marked by notable neurodegeneration leading to irreversible disability accumulation. Despite recent RRMS treatment advancements, approved PMS therapies offer limited efficacy, lacking predictive biomarkers for the transition. Cumulative inflammatory damage and ageing are primary risk factors for PMS development. In both MS and its animal model, experimental autoimmune encephalomyelitis (EAE), innate immunity and monocyte-derived phagocytes significantly contribute to neuroaxonal damage. In the context of broader changes such as ageing or chronic inflammation, innate immune cells demonstrate adaptive states that mirror the integration of various inputs. We envisage that chronic inflammation and ageing play a substantial role in the transition to progressive MS.

Methods — To explore the effect of ageing on neuroinflammation, we induced an established experimental model of neuroinflammation, namely adoptive transfer EAE, based on the transfer of syngeneic in vitro restimulated MOG35-55-specific T cells obtained from immunised young adult (2-3 months-old) Bl/6 mice, in young adult and middle-aged (11 months-old) female Bl/6 mice, recapitulating the age of onset of PMS in humans. Resorting to multiparametric spectral flow cytometry and algorithms-guided analyses, we charted systemic and local innate immune response of neuroinflammation in ageing, from the systemic (femur) and CNS-border bone marrow (skull) niches to the CNS at the peak of disease.

Results — We observed a precocious onset and higher cumulative and max EAE clinical score in the aged group. Interestingly, at the peak of EAE, we detected an increase of specific CNS infiltrating monocyte-derived macrophage (moMac) subsets, that also up-regulate phagocytosis receptors in aged mice, alongside phenotypic changes in CNS-resident microglia. The analysis of the systemic and CNS-border BM niches at the peak of the disease, revealed a myeloid skewing in both niches and ageing-assoociated changes in the spatio-temporal dynamic of the monocyte lineage.

Conclusions — Altogether, we confirmed that ageing exacerbates neuroinflammation and described at unprecedented resolution the systemic and CNS immune landscape underlying the ageing-driven worsening of neuroinflammation, identifying ageing-specific CNS-infiltrating moMAC.

Sara Da Costa Pereira
– *University of Zurich, Institute of Experimental Immunology*

Research Team Members:
– *Sara Da Costa Pereira, Rachel Lindemann, Laura Oberbichler, Donatella De Feo*

02 | Juan Villar-Vesga

Phagocyte-MerTK: The Hero or the Villain of a Neuroinflammation Story

Background — Multiple Sclerosis is the most common demyelinating and neuroinflammatory disease of the central nervous system (CNS). In the CNS, phagocytes constitute an important subset of immune cells that play a crucial role in tissue homeostasis. Both CNS resident and infiltrating phagocytes have been described as important contributors to MS pathophysiology. The phagocyte receptor MerTK (Mer Tyrosine Kinase) is used by phagocytes for the recognition of myelin and apoptotic cells. MerTK has been identified as a strong MS-associated risk locus, and its protein expression is increased in MS lesions. The receptor is expressed in microglia, border-associated macrophages, and monocyte derived cells (MdCs) -infiltrating cells. However, its role in CNS neuroinflammation remains largely unknown.

Methods — In this study, we investigate the impact of phagocytic MerTK expression by conditional gene ablation in microglia and in MdCs during experimental autoimmune encephalomyelitis (EAE), the preclinical mouse model of MS.

Results — Strikingly, we observed an opposing effect of MerTK ablation in microglia and MdCs: MerTK ablation in microglia led to an increase in disease severity, while MerTK ablation in MdCs ameliorated clinical symptoms.

Conclusions — Our current results suggest that MerTK can have a protective or pathogenic role in phagocytes during neuroinflammation. Further steps aim to understand this opposing role and test the therapeutic potential of MerTK ablation in MdCs.

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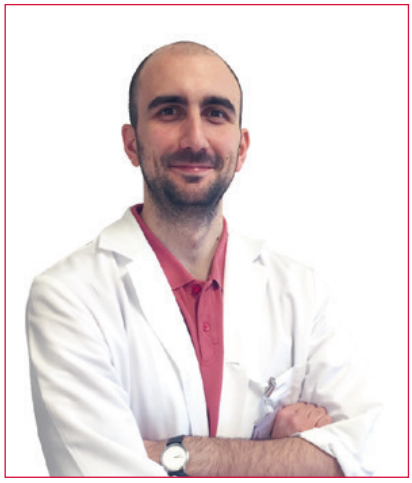

03 | Giulio Disanto

Monitoring of COVID-19 Vaccinations in Multiple Sclerosis Patients Under Different Disease-Modifying Treatments

Background — Some disease modifying treatments impair response to SARS-CoV-2 vaccines in Multiple Sclerosis, potentially increasing the risk of breakthrough infections. We investigated longitudinal SARS-CoV-2 antibody dynamics, memory B cell and T cell responses after repeated mRNA vaccine doses.

Methods — We performed a prospective observational cohort study in MS patients undergoing SARS-CoV-2 mRNA vaccinations. Anti-spike IgG titers were measured by chemiluminescence microparticle immunoassay. Frequencies of spike-specific memory B cells were measured upon polyclonal stimulation of peripheral blood mononuclear cells (PBMCs) and screening of secreted antibodies by ELISA. CD4+ T cell responses were measured upon stimulation of PBMCs with SARS-CoV-2 Spike Recombinant Protein.

Results — We recruited 120 MS patients (58 on anti-CD20, 9 on S1P-modulators, 15 on cladribine, 24 on teriflunomide and 14 untreated), and collected 392 samples up to 10.8 months after two vaccine doses. As compared to untreated patients, anti-CD20 antibodies (β=-2.07, p<0.001) and S1P-modulators (β=-2.02, p<0.001) were associated with lower anti-spike IgG, while teriflunomide and cladribine were not. Anti-spike IgG decreased with months since vaccine (β=-0.14, p<0.001), independently of treatments. Within anti-CD20 patients, anti-spike IgG remained higher in those with greater baseline B cell counts. Spike-specific memory B cell responses were weaker on S1P-modulators and anti-CD20 than on teriflunomide, and influenced by post-vaccine anti-CD20 infu-

sions. SARS-CoV-2 CD4+ T cell responses were mainly of Th1 phenotype, strong in anti-CD20 and teriflunomide treated patients, but diminished in S1P-modulators. The frequency of breakthrough infections was comparable between DMTs, but risk of COVID-19 was predicted by the last measured anti-spike IgG titer before infection (OR=0.56, 95%CI=0.37-0.86, p=0.008).

Conclusions — Post-vaccine anti-spike IgG titers decrease over time regardless of MS treatment, and are associated with breakthrough COVID-19. Within anti-CD20 treated patients, B cell count at first vaccine determines anti-spike IgG production, post-vaccine anti-CD20 infusions negatively impact spike-specific memory B cells, whereas the CD4+ T cell response is strong. Humoral, specific memory B and CD4+ T cell responses against SARS-CoV-2 are diminished by treatment with S1P-modulators.

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04 | Sarah Guimbal

New Molecular Underpinnings of BBB Dysfunction in Multiple Sclerosis

Background — Blood-brain barrier (BBB) breakdown is amongst the earliest pathological hallmarks observed in Multiple Sclerosis. The mechanisms leading to BBB dysfunction are incompletely understood and are generally thought to be a consequence of the autoimmune neuroinflammatory process in MS. We challenge this view and ask if intrinsic alterations in BBB endothelial cells manifested at the genetic or epigenetic, transcriptional, and ultimately phenotypic level cause or contribute to altered BBB function.

Methods — To do so, we made use of human induced pluripotent stem cells (hiPSCs) derived from 6 healthy controls (HC) and 10 MS patients and differentiated them into brain microvascular endothelial cell (BMEC)-like cells as in vitro model of the BBB. We performed a transcriptomic analysis on the donors available (3 HC and 4 MS patients) via RNA sequencing on HC and MS-derived BMEC-like cells stimulated with TNF-α and IFN-γ and unstimulated.

Results — The RNA sequencing analysis showed an increase of regulated genes in unstimulated BMEC-like cells compared to the stimulated condition, which strengthened that BBB may contribute directly to MS pathology. More interestingly, it also revealed a strong modulation of the Semaphorin-4D (SEMA4D) signalling pathway in unstimulated MS-derived BMEC-like cells compared to the controls. We confirmed, via western blot and immuno-staining, the expression of SEMA4D and its downstream effectors, RHOB and ROCK2. HC- and MS-derived BMEC-like cells were then treated with a recombinant protein for SEMA4D and showed a decreased mRNA expression of SEMA4D.

Conclusions — Our study suggests that SEMA4D and its downstream effectors could play a role in BBB dysfunction in the context of MS.

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05 | Benjamin Ineichen

Assessing the Predictive Translational Power of Animal Models in MS Drug Development: A Systematic Review and Meta-Analysis

Background — Despite some success in drug development for Multiple Sclerosis, it is unclear how well drug testing in animal studies predicts successful bench-to-bedside translation. Understanding which experimental factors of MS animal research govern successful development of treatments would allow a more efficient drug discovery, while reducing the number of animals used in research. Thus, here we aim to identify predictors of successful animal-to-human translation for MS, we systematically compared animal studies of approved MS disease-modifying therapies (DMTs) to those DMTs that failed in clinical trials for efficacy/safety reasons.

Methods — Approved and failed DMTs for MS were identified through literature review. Animal studies for these DMTs were identified from searches in PubMed and EMBASE. Machine-learning methods were exploited for abstract screening and data extraction. A random effect meta-analysis was fitted to the data to compare outcome effect sizes for approved vs. failed DMTs.

Results — We included 477 animal studies, covering 15 approved and 11 failed DMTs, tested in approximately 30'000 animals. DMTs were tested in a small repertoire of experimental parameters, i.e., about 87% and 79% of studies used experimental autoimmune encephalomyelitis (EAE) and mice, respectively. Clinically pertinent outcomes of animal studies were not associated with successful translation.

However, testing a DMT under more diverse experimental settings, e.g., across different labs or animal models, was associated with successful approval. Surprisingly, 90% of animal studies have been conducted after official FDA approval.

Conclusions — Our systematic review underscores specific challenges in translating animal research to clinical practice. Notably, many animal studies lack translational validity, even with seemingly pertinent outcomes, and there is a limited range of experimental methods and a disconnect between preclinical and clinical studies. To optimize the value of animal research for patient care, we recommend introducing greater variability in experimental conditions and strengthening ties between preclinical and clinical researchers.

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06 | Isabele Jacot de Alcântara

Encompassing the Complexity of Personality to understand its Impact on Disability in Multiple Sclerosis

Background — Although certain personality facets have been linked to disability in Multiple Sclerosis, the influence of their combinations (i.e. personality profile) has yet to be explored. The objective of the present study is to test whether precise personality profiles are differently associated with disability.

Methods — For this purpose, 41 patients with relapsing remitting MS (30 females; Mage = 42.63 years, MEDSS = 1.92) were assessed with the NEO Personality Inventory 3rd edition and the Expanded Disability Status Scale. Cluster and regression analyses were performed to explore personality profiles and their associations with disability.

Results — Analysis revealed two personality profiles that differed on eleven personality facets. The personality profile characterized by higher levels on facets of Neuroticism and Agreeableness as well as lower levels on facets of Conscientiousness and Extraversion displayed higher disability. Additionally, the Warmth facet had a contrasting association with disability depending on the profile, which underscored that this facet is only protective if it is not combined with high Tender-Mindedness.

Conclusions — Our findings suggest that personality profiles based on facets are important to understand the complexity of personality in MS.

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07 | Perrine Janiaud

Personalized Treatment Decision Algorithms for the Clinical Implementation of Serum Neurofilament Light Chain in MS: a Modified Delphi Study

Background — Serum neurofilament light chain (sNfL) is a biomarker of disease activity which predicts disease worsening in patients with Multiple Sclerosis (PwMS). sNfL is increasingly being used as a marker of treatment response and may play a crucial role in tailoring treatments to individual patients, ensuring disease stability, minimizing adverse events, and enhancing quality of life. We conducted a modified Delphi study to facilitate the implementation of sNfL as supporting information for decisions on escalation and de-escalation of disease modifying therapies (DMTs).

Methods — Candidate treatment decision algorithms on how to use sNfL within the most common clinical scenarios were developed by a core team based on their expertise and the literature. In a sequence of three rounds of voting, 10 international and 18 Swiss MS experts, and 3 patient consultants rated their agreement on a 9-point Likert scale (1-Strongly disagree to 9-Strongly agree) on decision algorithms on DMT change in situations where sNfL levels were considered high (>90th percentile based on age and body mass index in controls) or normal (<80th percentile). Consensus thresholds were specified as 50 to 80% (moderate), 80 to 95% (broad), >95% (strong consensus), and 100% full agreement. When the agreement did not reach the majority (<50%), algorithms were excluded.

Results — The Delphi process resulted in a consensus on DMT classification into low, medium and high efficacy and 23 decision algorithms were agreed upon: 9 treatment escalation algorithms (e.g., escalating from low to medium or high DMT based on high sNfL; 1 full; 4 strong; 2 broad; 2 moderate consensus); 11 switch algorithms (e.g., switching anti-B cell therapy for another high efficacy DMT based on high sNfL; 2 strong; 7 broad;2 moderate consensus); and 3 de-escalation algorithms (e.g., stopping DMT or extending interval in anti-B cell therapy based on normal sNfL; 1 broad; 2 moderate consensus).

Conclusions — Consensus among experts and patients has been achieved for a set of treatment decision algorithms which may represent a step towards more precise and personalized treatment choices. The algorithms are now implemented in the MultiSCRIPT trial, a pragmatic randomized clinical trial embedded in the Swiss MS Cohort assessing the superiority on quality of life and disease activity of 6-monthly sNfL monitoring compared with usual care.

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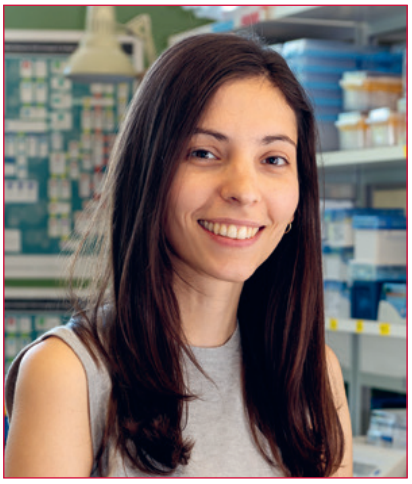

08 | Tradite Neziraj, Elisabeth Pössnecker

The Role of B Cell Activating Factor (BAFF) in Predicting Treatment Response in B Cell-Depleted MS Patients

Background — Multiple Sclerosis is a chronic inflammatory disease of the central nervous system. The strong involvement of B cells in the pathogenesis of MS has been underscored by the success of CD20 B cell-depleting treatments. Initiation of B cell-depleting treatments lead to a significant increase of B cell activating factor (BAFF) in the serum of MS patients. BAFF is a crucial factor for strengthening B cell self-tolerance and for inducing regulatory B cells. Yet, the role of BAFF as a predictive factor for treatment response in B cell-depleted MS patients remains unclear.

Methods — We retrospectively determined quantitative BAFF serum levels of 166 MS patients from two different centres using commercial ELISA before and under treatment with the monoclonal CD20 depleting antibodies Ocrelizumab and Rituximab. We analyzed the changes in BAFF levels under therapy based on disease subtype, disease duration as well as prior therapies. Further, we investigated the prognostic value of serum BAFF levels for EDSS worsening and long-term progression independent of relapse activity (PIRA).

Results — BAFF levels increased significantly with a peak within 6-12 months after the initiation of a B cell-depleting therapy. Overall, BAFF increases were lower in progressive MS patients compared to relapsing-remitting MS patients (RRMS). In RRMS, serum BAFF increases following anti-CD20 therapy tended to be lower in patients showing EDSS worsening and PIRA under B cell depletion.

Conclusions — BAFF serum levels might serve as a novel prognostic biomarker for long-term clinical outcome in B cell-depleted RRMS patients. Since PIRA is considered as a clinical correlate of grey matter (GM) pathology, these clinical observations might indicate that high BAFF levels correlate with less GM pathology.

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09 | Johanna Oechtering

Complement Activation is Associated with Brain Atrophy and Paramagnetic Rim Lesions

Background — Intrathecal complement activation (C4a, C3a, Ba, Bb) is increased in Multiple Sclerosis and is associated with clinical outcomes reflecting disease severity. The rate of brain volume loss and paramagnetic rim lesions (PRLs) are supposed to reflect MS severity, degeneration and smoldering inflammation. We aimed to investigate whether intrathecal complement activation is associated with increased atrophy and PRL counts.

Methods — Complement components (CC) and their activation products (CAP) (Factor H and I, C1q, C3, C4, C5, Ba, Bb, C3a, C4a, C5a, sC5b-9) were measured in cerebrospinal fluid (CSF) of patients with a clinically isolated syndrome (CIS) or MS followed in the Swiss MS cohort. Standardized MRI protocols included 3D T1-weighted, 1mm isotropic magnetization-prepared rapid gradient-echo and 3D 1-mm isotropic fluid-attenuated inversion recovery images. Brain parenchymal fraction (BPF) estimation was based on the SPM12 toolbox using the lesion-filled T1-weighted image. To study differences in atrophy rates, we built individual mixed models for each parameter (12 CC/CAP) with an interaction between time of follow-up and the

(log2-transformed) parameter and (log2)BPF as dependent variable adjusted for age, sex, MRI, magnetic field strength (1.5 vs 3T), (log2)albumin-quotient, disease course and dominant disease-modifying treatment (DMT) category during follow-up. PRLs were quantified in MRIs with susceptibility-based images and were used as dependent variables in negative binomial models with the same independent variables as described above, adjusted for age, sex, (log2)albumin-quotient and dominant DMT category.

Results — 121 patients, median age 36.8 (IQR 28.5-47.2) years, follow-up of 6.7 (IQR 4.3-9.9) years and 7 (IQR 5-8) prospective annual MRIs were included. Doubling of C4a levels was associated with an additional annualized brain volume change of −0.24% [95%-confidence interval −0.31, −0.16], doubling of: Ba of −0.22% [−0.29, −0.15], C3a: −0.13% [−0.21, −0.06], Bb: −0.12% [−0.17, −0.07], C5a: −0.07% [−0.11, −0.04], and sC5b-9: −0.06% [−0.09, −0.03] (all p<0.001). Doubling of C3a levels was associated with a 2.6-fold incidence ratio (IR) of PRLs (CI: 1.7-3.9, p<0.01), Ba 2.3-fold (CI:1.3-4.3) p<0.01) and C5a with an IR of 1.25 (CI:1.0-1.5; p=0.0264).

Conclusions — Intrathecal complement activation was associated with accelerated brain volume loss and higher PRL counts. Our results support the concept that complement activation plays an important pathophysiological role in MS and is associated with a more severe disease course.

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SFCNS Swiss Brain Health Plan

The Swiss Brain Health Plan 2023-2033

The SBHP (Swiss Brain Health Plan) is a comprehensive initiative in Switzerland to promote brain health and prevention of brain disorders across all stages of life. More awareness, education, and research about the burden of brain disorders, brain health, mechanisms of brain disorders and opportunities for their prevention are needed. In addition, the SBHP aims at establishing a person-centered, integrated, coordinated and cost-effective public health approach based on novel and strong synergies between healthcare professionals, scientists, patients, caregivers, insurance providers, commercial, societal and governmental stakeholders, and emphasizing gender perspectives, equity, and humans rights.

The first activities of the SBHP after its launch in November 2023 will include the (co-)organization of educational and scientific events across the country, a systematic analysis of the global burden of brain disorders in Switzerland, the launch of an international Certificate of Advanced Studies on Brain Health, and the creation of international collaborations.

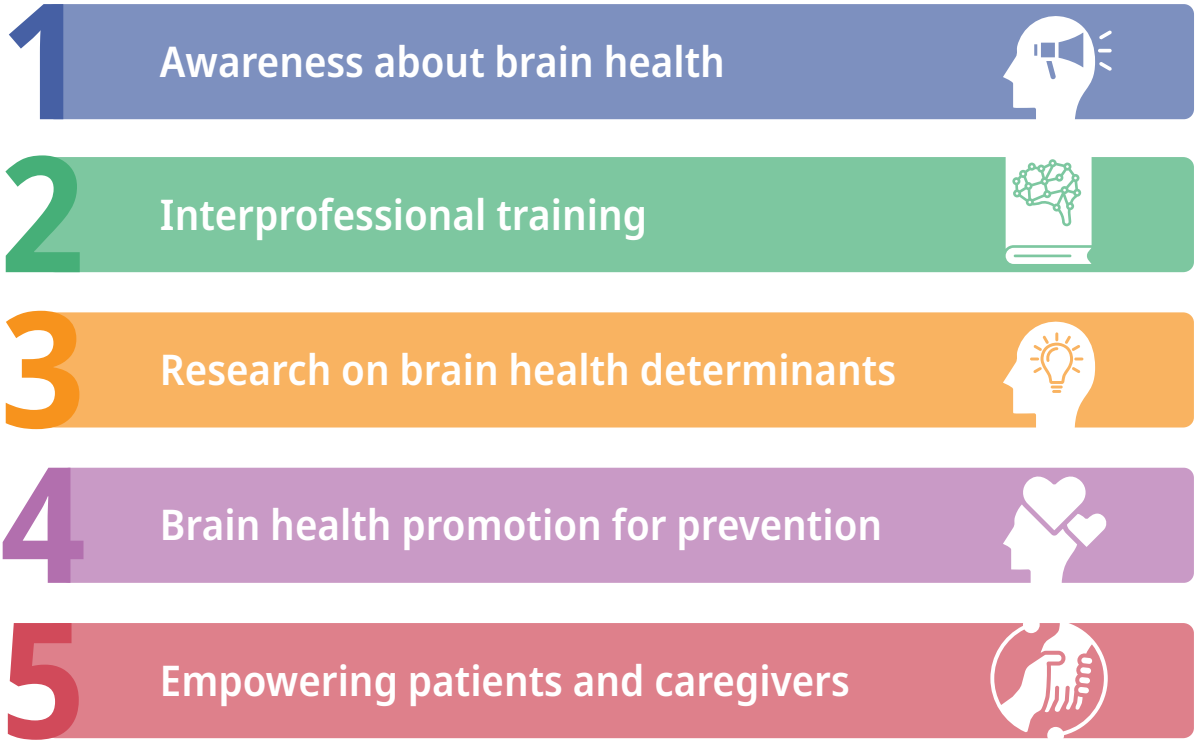

Figure - The five strategic objectives of the Swiss Brain Health Plan
The Swiss Brain Health Plan 2023-2033
Clin. Transl. Neurosci. 2023, 7, 38. https://doi.org/10.3390/ctn7040038

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SFCNS Swiss Federation of Clinical Neuro-Societies

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10 | Samuel Jones

Identification of Clonally Expanded CD8+ T Cells in MS Patients after Co-Culture with Autologous Neurons and Astrocytes

Background —Multiple Sclerosis pathogenesis is most certainly driven by autoreactive immune cells infiltrating the brain and inducing inflammatory demyelinating lesions. CD8+ T cells are the most predominant lymphocytic population in these lesions and are clonally expanded suggesting that an in-situ antigen is driving CD8+ T cell activation and proliferation. However, no antigen/epitope targeted by CD8+ T cells has yet been formally identified in human MS. Our objective is to screen for the presence of autoreactive CD8+ T cells recognizing autologous neurons and astrocytes in MS patients and compare them with the response in healthy donors (HD).

Methods — To expand and detect brain-reactive CD8+ T cells, we have developed a co-culture assay between peripheral blood mononuclear cells (PBMC) and autologous human-induced pluripotent stem cell (hiPSC)-derived neurons and astrocytes from either HD or MS patients. First, an expansion step is initiated where ex vivo PBMC and autologous HLA-I-enhanced neurons or astrocytes are cultured together for 14 days in the presence of IL-2 to induce proliferation of antigen-specific CD8+ T cells. Second, either directly ex vivo or after 14 days of expansion, CD8+ T cells are isolated and undergo bulk T cell receptor (TCR) sequencing to assess for clonally expanded TCR-α and -β chains.

Results — First, we have generated and characterized hiPSC from a cohort of 8 MS patients and 6 age- and sex-matched HD. Second, we demonstrate that hiPSC-derived neurons and astrocytes efficiently upregulate HLA class I expression upon exposure to IFN-γ and TNF-α and activate cognate CD8+ T cells. Finally, using our 14-day neuron/astrocyte-PBMC co-culture system, we have assessed the CD8+ T cell TCR-α and -β repertoire (ex vivo and at day 14 of co-culture) in all 6 HDs and 3/8 MS patients. After 14 days of culture with neurons or astrocytes, clonally expanded TCR-α and -β chains were identified in both HD and MS patients. However, when comparing TCR repertoires between HD and the preliminary MS patient group, we observed an increase in TCR-β chain clonality predominantly in the MS patient group.

Conclusions — Overall, we now have at hand a co-culture system allowing us to successfully expand and identify autoreactive CD8+ T cells from any donor. We are now screening the remaining MS patients to assess if we identify significant differences in TCR repertoires between HD and MS patients. Additionally, we are currently performing TCR-specificity validation assays by pairing of identified clonally expanded TCR-α and -β chain sequences from our cohort. Ultimately, our novel hiPSC-based platform will offer unique perspectives in identifying TCRs and ultimately antigens that would be pathogenic in MS patients.

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11 | Daniela Latorre, Lenka Sukenikova

Exploring Lipid-Reactive T Cells in Multiple Sclerosis

Background — Multiple Sclerosis is the most prevalent chronic demyelinating disorder of the central nervous system (CNS) affecting over 2 million individuals. Despite extensive research in animal models suggesting an autoimmune origin driven by aberrant T cell responses against CNS myelin proteins, the immune-mediated mechanisms underlying the disease are still far from clear. Starting from the knowledge that myelin is mainly composed by lipids (70-80%) and from increasing evidence suggesting an involvement of T cells recognizing self-lipids displayed on group 1 CD1 molecules in human autoimmunity, this project will address the novel hypothesis that T lymphocytes targeting myelin lipids of the CNS may contribute to MS pathophysiology.

Methods — In this work we aim at developing a novel sensitive and unbiased experimental approach based on the combination of in vitro stimulation assays, ex vivo tetramers staining and single cell RNA sequencing to study lipid-specific T cells in biological samples from MS patients and controls.

Results — By performing MHC-class II knockout and stable over-expression of co-stimulatory molecules (CD80, CD86, and 4-1 BBL), we have recently generated «universal» CD1a-, CD1b- and CD1c- expressing cells lines that may efficiently be used in in vitro stimulation assays to screen for the presence of lipid-reactive T cells in biological samples from virtually all donors. Simultaneously, we have optimized a tetramers staining approach to explore the existence of T cells reactive to the self-glycosphingolipid sulfatide, which is known to be enriched in CNS myelin, in the blood and cerebrospinal fluid (CSF) samples from MS patients and controls.

Conclusions — Here we show that sulfatide-reactive T cells are detected in the blood and CSF of MS patients as well as in the blood of healthy donors (HD). Such cells comprise mostly CD4+, double positive CD4+ CD8+ T cells and, at lower frequency, CD8+ T cells, are mostly restricted to CD1a and -b molecules and show a slightly higher frequency in MS patients at disease onset compared to HD. In summary, our preliminary data offer a novel perspective on the complexity of MS and paves the way for new discoveries with potential translational impact into clinical settings.

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12 | Stefania Iaquinto, Viktor von Wyl

Estimating the Burden of MS: Prevalence Estimation for MS in Switzerland in 2021

Background — Multiple Sclerosis is the most prevalent chronic inflammatory and neurodegenerative disease of the central nervous system, affecting more than 2 million people worldwide. Quantifying the prevalence and burden of MS is of utmost importance for healthcare planning, to help identify trends and patterns of disease occurrence, and to gain a better understanding of the real-life impacts of MS. In Switzerland, the latest estimate of MS prevalence dates back to 2016, assuming approximately 15'000 individuals living with MS. This study provides an updated prevalence estimate for MS in Switzerland for the year 2021.

Methods — We estimated the prevalence of MS in Switzerland for 2021 using a 7-step framework (developed by Kaufmann et al, https://doi.org/10.3389/fneur.2019.00953), allowing us to combine data from three distinct data sources: the Swiss MS Registry, the Swiss national treatment registry, and the MediService database. The core estimation approach is based on the benchmark-multiplier method. It uses information about the treatment status of persons with MS (pwMS) in 2021 from the different data sources. Results were discussed with disease experts and compared to the Swiss estimate from 2016 and to current prevalence estimates from other countries.

Results — In 2021, the prevalence of pwMS in Switzerland is estimated to be between 17’400 and 18'700, corresponding to a period prevalence of 199.3-214.1/100’000 inhabitants. The comparison between the age- and sex-specific prevalence per 100’000 inhabitants in 2016 and 2021 mainly shows an increase of MS diagnoses in women under the age of 60.

Conclusions — MS affects around 18’000 persons in Switzerland. The estimated national MS prevalence for 2021 indicates an increasing prevalence, which coincides primarily with a higher number of MS diagnoses in women.

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13 | Mina Stanikic

Disease-Modifying Therapies in Persons with MS Aged 55 and Above: Real-World Insights from the Swiss MS Registry

Background — The lack of consensus and clear guidance on the utilization or discontinuation of disease-modifying therapies (DMTs) in older adults with Multiple Sclerosis may contribute to widely varying real-world DMT use in this population. We aimed to investigate DMT utilization in older adults enrolled in the Swiss MS Registry (SMSR) and identify factors associated with DMT use.

Methods — The SMSR participants aged 55 and above who responded to the most recent annual follow-up survey were categorized into two groups based on their current DMT use and compared descriptively. These groups included «No DMT» (indicating no current DMT use, including newly reported treatment stops) and «DMT» (indicating current use of a DMT, both continuously used and newly reported). The most frequently used and discontinued DMTs were reported. Logistic regression models were employed to identify factors associated with DMT use.

Results — Out of a total of 400 participants 217 (54.2%) reported DMT use, including 20 (5.0%) who had switched medication in the last 3 years. Of the 183 participants (45.8%) not using DMTs, 54 (13.5%) had ceased medication use in the past 3 years. Those not using medication were older (median [interquartile range (IQR)] age of 65 [58 to 69] years compared to 60 [57 to 63]), had longer disease duration (median [IQR] of 25 [18 to 35] years compared to 19 [14 to 27]), and had progressive MS types more frequently (primary progressive MS N = 34 (18.6%) compared to N = 25 (11.5%); secondary progressive MS N = 90 (49.2%) compared to N = 65 (30.0%)). Among DMT users, ocrelizumab was the most commonly reported medication, with 82 (37.8%) participants, followed by fingolimod and dimethyl fumarate, each accounting for approximately 15% of reports. Among those who stopped medication use within the last 3 years, ocrelizumab was also the most frequently reported (N = 19, 35.2%), followed by fingolimod (N = 10, 18.5%) and interferon beta 1a (N = 8, 14.8%). On multivariable regression, longer MS duration was associated with the absence of DMT use (odds ratio = 1.05, 95% confidence interval [1.02 to 1.07]). Furthermore, progressive MS types were associated with no DMT use compared to relapsing-remitting MS, while regular visits to neurologists were associated with DMT use.

Conclusions — More than half of the surveyed participants aged 55 and above used DMTs, predominantly ocrelizumab. Around one-tenth of participants stopped DMT use in the past three years, also predominantly ceasing ocrelizumab usage. Those not using DMTs were older, had longer MS duration, and more often had progressive MS. However, while longer MS duration was associated with no DMT use, older age was not.

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14 | Nina Steinemann, Jesús López-Alcalde

Symptom Profiles and Use of Complementary Therapies in Persons with MS in Switzerland

Background — The use of complementary therapies (CTs) might help alleviate symptoms in persons with Multiple Sclerosis (PwMS) in addition to conventional therapies. The participatory evidence synthesis in MS and complementary therapies (PEMS) research project aims to enhance the relevance and access of clinical research in MS and complementary medicine. Here we will focus on real-world patterns and motivations for use of complementary therapies by PwMS in Switzerland.

Methods — The Swiss MS Registry conducted a survey on CT use by PwMS in Switzerland. The survey was developed and tested in a participatory approach with stakeholders. We invited 2261 PwMS to participate in the survey either online or on paper. Descriptive analyses were performed to assess CT use (divided into five subgroups «manual therapies», «mind body therapies», «natural substances», «diet», «exercise»), symptom mitigation, expectations on the effectiveness and safety of CTs as well as the reasons for CT use.

Results — 888 PwMS were included in this analysis. Of these, 74% were female and the median age was 54 years. Furthermore, 547 PwMS (61.6%) reported having relapsing-remitting MS (RRMS) and 266 (30%) a primary or secondary progressive disease course (PMS). Of all participants, 49.4% used CTs in the past 6 months. The most common reasons stated were «to improve my quality of life» (44%), followed by «to relieve my MS symptoms» (38%), and «to curb MS progression» (33%). Participants with RRMS reported using CTs most commonly for the following symptoms: fatigue (18.6%), stress (18.6%), weakness (17.9%), gait problems (17%), sleep problems (16.8%) and balance disorders (16.8%). In contrast, participants with PMS reported using CTs for the symptoms gait problems (32.7%), weakness (30.8%), spasms (30.8%), balance disorders (27.1%) and bladder disorders (22.2%).

Conclusions —Almost half of the study participants used CTs in the past 6 months, primarily for quality of life reasons. The most common symptoms for CT use varied between RRMS and PMS participants.

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We thank you for your participation in the symposium.

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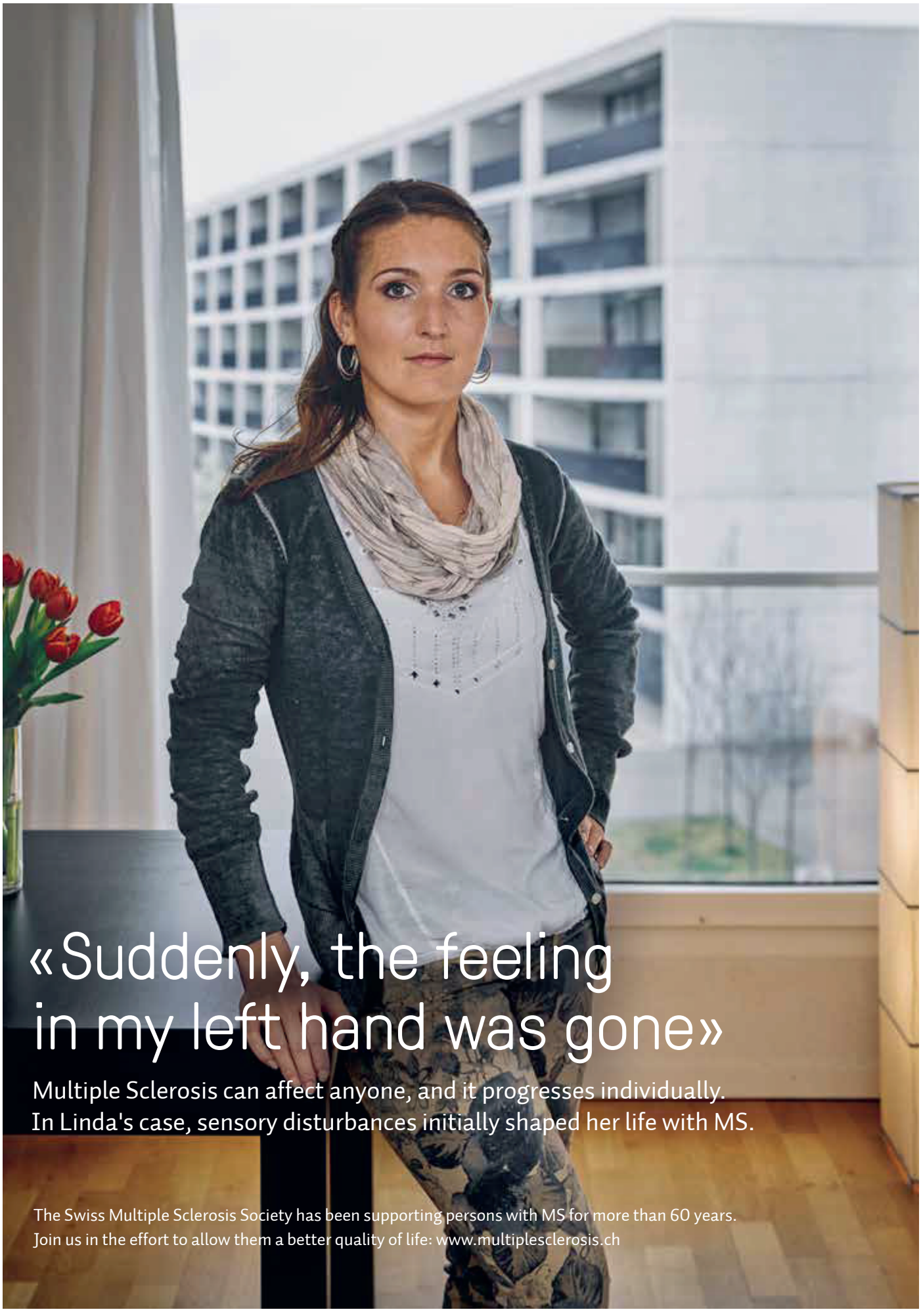
See you next year at the 27th MS State of the Art Symposium, Saturday, January 25, 2025

Kind regards
Swiss Multiple Sclerosis Society



MS Swiss Multiple Sclerosis Society

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