

# CLOSTRIDIUM DIFFICILE INFECTION AND NEUROLOGICAL DISORDERS - A CASE REPORT

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**Conference presentation / Izlaganje na skupu**

*Permanent link / Trajna poveznica:* <https://urn.nsk.hr/urn:nbn:hr:267:654271>

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*Download date / Datum preuzimanja:* **2025-04-02**

*Repository / Repozitorij:*

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# ABSTRACT BOOK 2023



**Mind&Brain**  
*International  
Neuropsychiatric Congress*

*Main Theme* | **Bridging between  
Neurology & Psychiatry**

**MIND & BRAIN**

**62<sup>nd</sup> INTERNATIONAL NEUROPSYCHIATRIC CONGRESS**

**Pula - Croatia**

**MAY 18<sup>th</sup> – 21<sup>st</sup>, 2023.**

**ISSN 2469-5748**

**[www.pula-cong.com/abstract-book-2023](http://www.pula-cong.com/abstract-book-2023)**

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**ISSN 2459-5748**

**[www.pula-cong.com/abstract-book-2023](http://www.pula-cong.com/abstract-book-2023)**

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**WORLD FEDERATION OF NEUROLOGY**



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May 18<sup>th</sup> - 21<sup>th</sup>, 2023

Park Plaza Histria

Pula - Croatia

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### **Publisher**

International Institute for Brain Health

Ulica grada Vukovara 271/4  
Zagreb, Croatia

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### **Design & Layout**

International Institute for Brain Health

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**ISSN 2469-5748**

**Abstract Book (International Neuropsychiatric Congress. Online)**

**Abbreviation: Abstr. book (Intern. Neuropsychiatr. Congr., Online)**

**mizmo.ibrain@gmail.com**

**www.pula-cong.com**

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## PROGRAM

### Thursday, May 18<sup>th</sup>, 2023.

17:00-19:00      **Registration**

### Friday, May 19<sup>th</sup>, 2023.

09:00-10:00  
Hall A      **OPENING CEREMONY**

10:00-11:40  
Hall A      **MAIN THEME**  
Chairpersons: V. Demarin & O. Sinanović

Vida Demarin (Zagreb, Croatia): How the brain is affected by arts

Radwa Khalil (Bremen, Germany): Creative Therapy in Health and Disease: Inner Vision

Osman Sinanović (Tuzla, BiH): Restless Legs Syndrome: Disorder between Neurology and Psychiatry.

Zdravko Lacković (Zagreb, Croatia): Botulinum toxin and depression: clinical and preclinical evidence

Ervina Bilić (Zagreb, Croatia): Non-motor signs of myasthenia gravis

11:40-12:00      **Coffee Break**

12:00-13:00  
Hall A      **GRAZ STROKE SYMPOSIUM: DIAGNOSIS, CLINICAL MANAGEMENT AND TREATMENT OF INTRACRANIAL HEMORRHAGE**

Chairpersons: K. Niederkorn & T. Gatttringer

Thomas Gatttringer (Graz, Austria): Neuroimaging of intracranial hemorrhage

Kurt Niederkorn (Graz, Austria): Clinical management of intracranial hemorrhage

Hannes Deutschmann (Graz, Austria): Neurointerventional treatment of macrovascular causes of intracranial hemorrhage

12:00-13:00  
Hall B      **"LETS TALK ABOUT OLD AGE PSYCHIATRY" SYMPOSIUM**

Chairperson: N. Mimica

Ninoslav Mimica (Zagreb, Croatia): The role and place of old age psychiatry today

Petrana Brečić (Zagreb, Croatia): Affective disorders and suicidality in the elderly

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Program

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Marija Kušan Jukić (Zagreb, Croatia): Delirium and dementia

Zrnka Kovačić Petrović (Zagreb, Croatia): Addictions in the elderly

13:00-14:00 **Lunch**

14:00-15:30 **NEURODEGENERATIVE SYMPOSIUM**

Hall A

Chairpersons: V. Vuletic & M. Cuturic

Miroslav Cuturic (Columbia, USA): Huntington's Disease: Clinical Research and the Road Ahead

Gabriela Novotni (Skopje, N. Macedonia): Inflammaging and the Brain

Maja Relja (Zagreb, Croatia): Could we improve dystonia management in Europe?

Vladimira Vuletić (Rijeka, Croatia): Invasive methods in Movement disorders

14:00-17:00 **PULA PSYCHOPATHOLOGY SUMMER SCHOOL 2023- FOCUS ON SCHIZOPHRENIA**

Hall B

Chairpersons: Karl Bechter, Dominique Endres, Martin Brüne

Dominique Endres (Freiburg, Germany): Autoimmune Psychosis as a new differential diagnosis of Schizophrenia Spectrum

Norbert Müller (Munich, Germany): Neuroinflammation in Schizophrenia-actual status of knowledge

Paolo Enrico (Milan, Italy): Neural and immunological similarities/differences - schizophrenia vs. bipolar disorder

Margherita Bechi (Milan, Italy): Empathy for psychological and physical pain in borderline personality disorder

Giulia Agostoni (Milan, Italy): Looking into the brain through the language window

Monika Zdravkovic (Leiden, Netherlands): Linking adverse childhood experiences to borderline personality features

Martin Brüne (Bochum, Germany): Insights from behavioral ecology regarding somatic comorbidity in borderline personality disorder

15:30-16:30 **PULA MS SYMPOSIUM**

Hall A

Chairpersons: V. Bašić Kes & U. Rot

Jörg Kraus (Austria): Overview of modern and upcoming MS treatment

Vanja Bašić Kes (Zagreb, Croatia): MS and pregnancy

Uroš Rot (Ljubljana, Slovenia): TNF alpha inhibitors and demyelinating/inflammatory diseases of the nervous system

16:30-17:00 **NOVARTIS Satellite Symposium**  
Hall A Vladimira Vuletić (Rijeka, Croatia): Innovation in MS together

17:00-17:15 **NOVARTIS Satellite Symposium**  
Hall A Sanja Tomasović (Zagreb, Croatia): Innovation in Migraine together

17:30-19:00 **POSTER SESSION**  
Chairpersons: K. Bechter, I. Šain, K. Niederkorn, H. Budinčević

**Saturday, May 20<sup>th</sup>, 2023.**

09:00-11:00 **MAIN THEME**  
Hall A Chairpersons: K. Bechter & M. Brüne

Oxana Kosenko (Ulm, Germany): Gerd Huber (1921-2012): Pioneer of Schizophrenia Research

Karl Bechter (Günzburg, Germany): What mean the frequent CSF pathologies in affective and schizophrenic spectrum disorders?

Paolo Enrico (Milan, Italy): Stratification of first-episode psychotic patients based on immuno-imaging markers

Norbert Müller (Munich, Germany): Current State in Inflammation research and Anti-inflammatory Treatment in Major Depression

Francesco Benedetti (Milan, Italy): Circulating immune cell composition and activation status associate with brain white matter microstructure in Mood Disorders

Martin Brüne (Bochum, Germany): Gut-brain-interaction in psychiatric disorders

Milan Latas (Belgrade, Serbia): Benzodiazepines in 21th century - option or a big mistake

11.00-12.00 **MIGRAINE SYMPOSIUM**  
Hall A Chairpersons: B. Zvan & M. Zaletel

Marjan Zaletel (Ljubljana, Slovenia): Can Calcitonine gene related peptide be causally related to migraine aura?

Bojana Žvan (Ljubljana, Slovenia): What is the right choice for the treatment of episodic and chronic migraine in people at cardiovascular risk?

Mariana Ciobanu (Nashville, USA): Management of refractory migraine in adolescents and young adults- challenges and rewards

Hrvoje Budinčević (Zagreb, Croatia): The potential role of Anti-CGRP Inhibitors in treatment of post-traumatic headache

- 11.00-12:30  
Hall B **SPORT PSYCHIATRY SYMPOSIUM**  
Chairpersons: D. Marčinko, V.Z. Markser, T. Franić
- Martin Brüne (Bochum, Germany): Cardiovascular risk factors in young people with borderline personality disorder: why there is a need for more sports, not less
- Tomislav Franić (Split, Croatia): How to assess mental health in athletes – the role and problems of assessment and screening tools
- Stipe Drmić (Zagreb, Croatia): Mental benefit of sports – sports therapy in mental illness
- Darko Marčinko (Zagreb, Croatia): Healthy and pathological narcissism in football players
- 12.00-12.30  
Hall A **ACADEMIC LECTURE**  
Leontino Battistin (Padua, Italy): Reflections of a clinician on the actual trends in clinical neurosciences
- 12:30-13:00  
Hall A **MOLEAC Satellite Symposium**  
Anita Arsovska (Skopje, N. Macedonia): Neuroaid: The latest clinical data in stroke, TBI and AD?
- 13:00-14:00 **Lunch**
- 14.00-15.30  
Hall A **EPILEPSY SYMPOSIUM**  
Chairperson: S. Bašić
- Zrinka Čolak Romić (Zagreb, Croatia): Management of epilepsy in the elderly
- Iris Zavoreo (Zagreb, Croatia): Neuroimmunological aspects of the status epilepticus - treatment perspectives
- Željka Petelin Gadže (Zagreb, Croatia): Epilepsy and psychosis - treatment challenges
- Ana Sruk (Zagreb, Croatia): Sleep and epilepsy are correlated in both directions.
- 14.00-15.30  
Hall B **SYMPOSIUM - PROFESSIONAL MEDICAL ETHICS: CURRENT VIEWS, APPROACHES, AND CHALLENGES**  
Chairperson: M. Ćurković
- Marko Ćurković - (Bio)ethics and professional medical ethics - a very short introduction
- Ana Borovečki, Ivan Pavao Gradiški: Duties of physicians towards oneself
- Marko Ćurković, Diana Špoljar: Ethics at the end-of-life
- Sunčana Roksandić Vidlička, Aleksandar Maršavelski: Medical professionalism – legal framework
- Kristijan Sedak, Marko Marelić, Tea Vukušić Rukavina: E-professionalism - professional medical



Program

ethics in emerging digital landscapes

15:30-15:45

Hall A

**MEDIS Satellite Symposium**

Ana Sruc (Zagreb, Croatia): Brivaracetam: How to Get the Most Out of It in Everyday Clinical Practice.

15:45-17:30

Hall A

**CEESS STROKE SYMPOSIUM**

Chairpersons: A. Arsovska & M. Mijajlović

Milija Mijajlović (Belgrade, Serbia): Cerebrovascular disorders associated with COVID-19 infection

Anita Arsovska (Skopje, N. Macedonia): Rare Causes of Stroke

Frederic-Ivan Silconi (Pula, Croatia): Posterior circulation stroke

Jan Kobal (Ljubljana, Slovenia): Significant lowering of fatal outcomes due to Cerebral venous thrombosis in Slovenia

Vesna Đermanović Dobrota (Zagreb, Croatia): Metabolic syndrome and cognitive impairment

Sandra Morovic (Zagreb, Croatia): The role of HISPA in cardiovascular prevention.

15:30-17:00

Hall B

**SELECTED ORAL PRESENTATIONS SYMPOSIUM**

Chairperson: I. Šain

Kenan Galijašević (Zenica, BIH): The influence of daily life activities on the mental health of students

Jure Koprivšek (Maribor, Slovenia): Do changes in learning and training of staff communication skills affect the incidence of aggressive behavior associated with certain mental disorders in hospital intensive psychiatric settings

Lea Murn (Zagreb, Croatia): Will Artificial Intelligence Treat Mental Disorders efficiently as Professionals?

Igor Mosaic (Rijeka, Croatia): “Thukdam” - introduction to the post-mortem altered state of the mind

17:00-18:30

Hall B

**FREE TOPICS SYMPOSIUM**

Chairpersons: S. Butković Soldo & D. Vidović

Domagoj Vidovic (Zagreb, Croatia): Psychoneuroimmunology of sleep deprivation

Silva Butković Soldo (Osijek, Croatia): Neurorehabilitation in MS

Valentino Rački (Rijeka, Croatia): Obtaining a Genetic Diagnosis of Dystonia - A Single Tertiary Centre Experience

Eliša Papić (Rijeka, Croatia): Functional disorders in Parkinson's disease patients with deep brain stimulation – a case series

17:30-18:30 **WORKSHOP – MULTIDISCIPLINARY APPROACH TO ACUTE STROKE**

Hall A

Chairpersons: D. Janko Labinac & H. Budinčević

Dolores Janko Labinac (Pula, Croatia): Headache in Emergency Room

Hrvoje Budinčević (Zagreb, Croatia): How to accelerate the route to mechanical thrombectomy?

18:30-19:30 **BEST POSTERS AWARDS PRESENTATIONS**

Hall A

Chairpersons: V. Demarin & F. Benedetti

**Sunday, May 21<sup>st</sup>, 2023.**

09:00-10:00 **INPC Kuratorium, MIZMO & CEES Meeting**

Hall A

10:00-11:00 **CLOSING**

Hall A

**PLENARY LECTURES****Vida Demarin: HOW THE BRAIN IS AFFECTED BY ART**

Croatian Academy of Sciences and Arts, Zagreb, Croatia; International Institute for Brain Health, Zagreb, Croatia

A lot is happening both in the mind and the body when we make art and it can be used for therapeutic means, both in rehabilitation medicine and on our own. It has been found out that creativity in and of itself is important for remaining healthy, remaining connected to ourself and connected to the world. There is an increasing amount of scientific evidence that proves art enhances brain function. It has an impact on brain wave patterns and emotions, the nervous system, and can actually raise serotonin levels. Art can change a person's outlook and the way we experience the world.

Neuroscientists' research has proved that awe, wonder and beauty promote healthier levels of cytokines and suggests the things we do to experience these emotions – a walk in nature, losing oneself in music, beholding art – has a direct influence upon health and life expectancy. We can increase our well-being with awe-inspiring art. Any type of creative expression allows us to imagine new ways to communicate and engage with the world, as well as engages the brain's neuroplasticity, helping patients recover from traumatic brain injuries, stroke or more.

Many medical related articles provide evidence that points to the physical benefits derived from experiencing awe-inspiring moments on a routine basis. A recent study from the University of California-Berkeley found that “participants who experienced more awe-struck moments had the lowest levels of interleukin-6, a marker of inflammation.”

Making art is good for everyone, not just our patients in the field of rehabilitation medicine. Here are a few of the benefits and ways the brain is affected by art: lowers stress, deep focus, process emotions, imagine a more hopeful future .... Creating art allows us to make decisions and interpret images, figuring out what it means and helping us face potential futures as well as imagine better, more hopeful ones.

Art accesses many of the advanced processes of the human brain, such as intuitive analysis, expressivity and embodied cognition. Artists are often better observers and have better memory and this may be due to how art affects the brain's plasticity.

Results of numerous studies showed that listening to music can improve cognition, motor skills and moods, enhancing recovery after brain injury. In the field of visual art, the brain lesion can lead to the visuospatial neglect, loss of details and significant impairment of artistic work, while activation of neuroplasticity restore the skill and function again. All kinds of art, music, painting, dancing... stimulate the brain. They should be the part of treatment processes.

And as Semir Zeki points out, the brain is a perfect natural bridge between sciences, concerned with the nature of life and the universe, and the humanities, concerned with the nature of human existence.

And what are neurobiological principles underlining creativity in art, love, literature, happiness...

Appreciate Beauty!

After all, why live longer with a healthy brain if all we do is just think?!

**Radwa Khalil, Vida Demarin: CREATIVE THERAPY IN HEALTH AND DISEASE: INNER VISION**

Constructor University, School of Business, Social and Decision Sciences, Bremen, Germany

Can our current knowledge of the psychological and neuroscientific literature about creativity allow us to comprehend the distinctive mechanisms of de novo abilities? This review outlines the state-of-the-art in the neuroscience of creativity and points out crucial aspects that still demand further exploration. The progressive development of current neuroscience research on creativity will open several opportunities and possibilities for valuable therapy in health and disease. Therefore, we discuss directions for future studies, identifying a focus on pinpointing the neglected beneficial practices for creative therapy. We focus on the neglected neuroscience perspective of creativity on health and disease and how creative therapy could offer limitless possibilities to improve our well-being and give hope to neurodegenerative disease patients to express their hidden creativity.

**Zdravko Lacković: BOTULINUM TOXIN AND DEPRESSION: CLINICAL AND PRECLINICAL EVIDENCE**

University of Zagreb School of Medicine, Department of Pharmacology, Zagreb, Croatia

**Introduction/Objectives:** Botulinum toxin type A (BoNT-A), best confirms the age-old rule that dose makes the difference between medicine and poison: the most toxic substance in nature, in extremely small doses, is a useful medicine, especially in neurology. In cosmetics, the use of BoNT-A, primarily to reduce wrinkles, is sometimes promoted almost as part of personal hygiene. In addition to effects on spasticity, certain forms of pain, and vegetative disorders, clinical observations and controlled experiments have been gradually appearing in the last few years that BoNT-A could have an antidepressant effect. There are, nearly 800 such reports, including controlled trials (Phase II). Effectiveness is also confirmed by the latest meta-analysis (Wollmer et al. *Toxins* 2022). Regarding the mechanism of action, there are two possibilities: feedback mechanisms (the perception of ugliness creates emotional trauma) and an insufficiently defined molecular mechanism by which the toxin causes changes in neurotransmitters in the brain. Here we examine whether there are possibilities for molecules of peripherally applied botulinum toxin to interact with neurons in the brain, especially in regions crucial for our emotions.

**Participants, Materials/Methods:** We searched the literature and synthesized the results from our Laboratory, including ongoing research.

**Results:** Clinical publications mention mainly psychological and psychosocial reasons why self-perception of ugliness generates negative feelings. The cosmetic effects of BoNT-A would alleviate this. The molecular basis of the BoNT-A effect is possible primarily because our findings during the last almost 20 years point to the axonal transport of botulinum toxin from the periphery to the CNS, where it mediates the antinociceptive action (Bach Rojecky and Lackovic, *Pharmacol Biochem Behav.* 2009, Matak and Lackovic, *Prog Neurobiol* 2014). BoNT-A also reaches the motor regions, but the function of BoNT-A in the CNS motor system is not yet clear. Tracking the toxin after application to different parts of the cerebrospinal fluid shows that it reaches regions that are not associated with pain or motility. After peripheral administration, we found an increase of NA in the striatum and serotonin in the hypothalamus (Ibragić et al *Neurosci Lett* 2016). Recently Li et al (*Neurosci Bull.* 2009) confirmed that. Ongoing experiments in our laboratory show that toxin also comes to the parts of the brain involved in the processing of emotions.

**Conclusions:** Presented results indicate that the antidepressant effect of BoNT-A may be related to the direct molecular effects of BoNT-A on neurons in brain regions involved in the processing of emotions.

**Ervina Bilic: NONMOTOR FACES OF MYASTHENIA GRAVIS**

Medical School University of Zagreb, Clinical Hospital Center Zagreb, Department of Neurology, Zagreb, Croatia

**Introduction/Objectives:** Myasthenia gravis (MG) is a neurological disease traditionally considered to have exclusively oscillatory motor symptoms, usually including weakness of the face muscles. The most representative antibody has been recognized as that to the muscle nicotinic acetylcholine receptor (anti-AChR antibody), which resides at the neuromuscular junction. It is well known that approximately 8-10% of MG patients have additional autoimmune disorders, such as thyroid or collagen diseases.

**Participants, Materials/Methods:** However, symptoms of non-motor complications, even though quite frequently present, may often be missed or underestimated, which can severely affect the activities of daily living and quality of life of MG patients. We are witnessing to a growing knowledge about nonmotor faces of MG itself which may be divided into several groups: comorbid autoimmune diseases (Thyroid diseases, alopecia areata, vitiligo, gastrointestinal autoimmune diseases, other autoimmune neurological disorders), malignant diseases frequent in MG

patients (breast cancer, lung cancer, skin cancer), autonomic disturbances, cytokine mediated central nervous system involvement (memory changes, sleep alterations, chronic pain), gut microbiota changes (with overlapping pathophysiological background shared with other immune mediated diseases), endocrinologic alterations and fertility problems, infections, dry eyes and dry mouths, oral health issues, pregnancy specific challenges, body composition changes and many others.

**Results:** Above listed jointed MG symptoms and faces are not important just from clinical, observational point of view, they are important therapeutic field to act, as well. Of course, all the above mentioned nonmotor faces of MG may be additionally modified by chronic drug administration, especially glucocorticoids. Monitoring the disease activity, planning regular clinical controls outside the neurologic evaluation and advising patients about aspects of their life choices (occupational, sports, dietary, family planning and others) should be planned and created based on multidisciplinary approach having in mind complexity of MG, far beyond motor weakness itself.

**Conclusions:** Specific multidisciplinary approach in persons with MG should be a standard way of clinical thinking and decision making, but an important part of neurologists education and professional growing, as well.

### **Oxana Kosenko, Florian Steger: GERD HUBER (1921-2012): PIONEER OF SCHIZOPHRENIA RESEARCH**

University of Ulm, Institute of the History, Philosophy and Ethics of Medicine, Ulm, Germany

**Introduction/Objectives:** Last year marked the tenth anniversary of the death of Gerd Huber (1921-2012), a West German psychiatrist and neurologist of the postwar period. Huber became internationally known primarily for his pioneering scientific work on schizophrenia. The anniversary gives us an opportunity to consider Huber's contributions to the development of schizophrenia research from a medical-historical perspective.

**Participants, Materials/Methods:** We analyzed Huber's writings, his private and professional papers from his private archive as well as research works. To examine these sources, we implemented the historical-critical method.

**Results:** Gerd Huber's first systematic study of schizophrenia aimed to use pneumoencephalography (PEG) to reveal brain structural changes in chronic schizophrenic patients. He found dilatation of the lateral ventricles and third ventricle in subgroups of schizophrenia-afflicted patients. Huber succeeded in correlating his encephalographic findings with the clinical manifestations of schizophrenia. A major project then was his catamnesis study of the course of schizophrenia, known as the "Bonn Long-Term Study," which Huber conducted with Gisela Gross and Reinhold Schüttler. Among the important results of the study was the description of the psychopathological predictors of the early detection of schizophrenic disorders and the finding that the deficits in thinking and perception were detectable, not post-psychotic at the end of the course, but also before psychotic initial manifestation in precursor syndromes (prodromes and outpost syndromes). The data collected during the study were later used for the development of the "Bonn Basic Symptom Scale", which was an instrument for the psychopathological early detection of schizophrenic psychoses. Huber developed the concept of basic symptoms and basic stages of schizophrenia ("basic symptom concept") with Lilo Süllwold (1930-2020) as a continuation of Kurt Schneider's (1887-1967) psychopathological concept.

**Conclusions:** Gerd Huber was an influential West German psychiatrist and neurologist of the postwar period. Especially his studies with imaging techniques on the question of brain atrophy, the long-term course, and the basic symptoms of schizophrenic disorders made a significant contribution to the research of schizophrenia and were discussed internationally.

**Norbert Müller: CURRENT STATE IN INFLAMMATION RESEARCH AND ANTI-INFLAMMATORY TREATMENT IN MAJOR DEPRESSION**

Department of Psychiatry and Psychotherapy, Ludwig-Maximilians-University, München

The vulnerability-stress model for depression hypothesizes that an individual vulnerability, such as genetic susceptibility or negative childhood experiences facilitates the development of depression, especially in case of high stress levels. Stress is well known to contribute to a pro-inflammatory immune state in major depressive disorder (MDD), and higher levels of pro-inflammatory cytokines and glucocorticoids are found in both chronic stress and depression. Various studies have provided support for this model. Immune activation, such as treatment with interferon alpha, was shown to cause depressed states and suicidality. A large-scale Danish study demonstrated a clear link between infections and autoimmune diseases, which are associated with an immune activation, and an increased risk for depression; the type or localization of the infection or autoimmune disease was thereby irrelevant, but the proximity in time to the infection was associated with the risk for MDD. Meta-analyses of studies in patients with MDD showed higher levels of C-reactive protein (CRP) and pro-inflammatory cytokines, including IL-6, and lower levels of some anti-inflammatory cytokines in the blood and cerebrospinal fluid (CSF). A possibly central role for the pro-inflammatory immune state plays the dissociation of CRP to monomeric CRP at the site of inflammation. Results from neuroimaging studies also point to an association of moderate to severe MDD with activation of microglia, the “immune cells” of the central nervous system (CNS), and to a role of IL-6 in the volume loss in the CNS associated with depression. Accordingly, anti-inflammatory features have been shown for both traditional antidepressants and non-pharmacological antidepressant treatments, such as electroconvulsive therapy. Several therapeutic studies with the anti-inflammatory cyclo-oxidase-2 (COX-2) inhibitor celecoxib found a benefit of add-on celecoxib in patients receiving an antidepressant. Moreover, a meta-analysis of randomized clinical trials (RCTs) on different classes of non-steroidal anti-inflammatory drugs (NSAIDs) revealed an advantage of anti-inflammatory medication in MDD. In the subgroup of patients with high levels of CRP, an interesting randomized clinical trial (RCT) that studied a monoclonal antibody against tumor necrosis factor (TNF)-alpha showed a therapeutic effect in treatment-resistant MDD. These findings of studies on different aspects of inflammation in MDD underpin the important role of inflammation in the pathogenesis and treatment of MDD.

**Martin Brüne: GUT-BRAIN-INTERACTION IN PSYCHIATRIC DISORDERS**

LWL University Hospital Bochum, Department of Psychiatry, Psychotherapy and Preventive Medicine, Bochum, Germany

**Introduction/Objectives:** Research has shown that several psychiatric disorders are associated with alterations of the gut microbiota. The role of the microbiota and its metabolism in ameliorating symptoms has raised growing interest in the functioning of the gut-brain axis.

**Participants, Materials/Methods:** The present talk attempt to highlight the most important findings across a range of (neuroscience)psychiatric disorders.

**Results:** The majority of studies report differences in alpha- and beta-diversity between psychiatric patients and controls. This includes altered ratios of Bacteroidetes to Firmicutes, even though findings are mixed and not always consistent.

**Conclusions:** Even though the studies of the microbiota should be treated with caution and considered preliminary, they seem to indicate potential dysbiosis across a range of psychiatric conditions. One promising finding is that short-chain fatty-acid (SCFA)-producing bacteria could be substituted as an adjunct therapy for depression, anxiety disorders and personality disorders.

**SYMPOSIUMS' LECTURES****STROKE SYMPOSIUMS****Markus Kneihsl: CLINICAL MANAGEMENT OF INTRACRANIAL HEMORRHAGE**

Medical University of Graz, Department of Neurology, Graz, Austria

Recent developments have largely influenced treatment regimens for intracranial hemorrhages (ICH). The lecture „clinical management of intracranial hemorrhage” will highlight the most important findings on ICH treatment approaches over the past years: 1) Blood pressure management: Blood pressure therapy in patients with acute ICH has long remained controversial. While blood pressure lowering was obvious, it remained unclear to which extent blood pressure levels should be influenced. Large trials (INTERACT-2, ATACH-2) suggested target blood pressure levels of  $\approx 140$ mmHg as beneficial for most patients. However, recent post-hoc analyses of those trials allowed further insights on how to optimize blood pressure treatment in specific patient subgroups reporting on blood pressure variability and the impact of very intense blood pressure lowering. 2) ICH on antiplatelets/anticoagulants: With the invention of direct oral anticoagulants (DOACs) a new era of anticoagulation therapies started a few years ago. However, specific treatment approaches for DOAC-associated bleeding events were long missing. In recent years antidotes were developed to immediately stop the anticoagulatory DOAC-effect in patients with acute bleeding complications. The present lecture will report on current guidelines and practical treatment algorithms in such patients. 3) Surgical treatment strategies: Neurointerventional/surgical strategies are crucial to treat secondary ICH such as ICH based on arteriovenous malformations or ruptured aneurysms. The value of hematoma evacuation in primary ICH which is mostly related to arteriosclerosis or  $\beta$ -amyloid associated angiopathy still remains controversial. Although large trials (STITCH trials, MISTIE-III) were negative, post-hoc analysis identified subgroups that might benefit from surgical treatment. The lecture will therefore present an overview on the available evidence in this field.

**Hannes Deutschmann: NEUROINTERVENTIONAL TREATMENT OF MACROVASCULAR CAUSE OF INTRACRANIAL HEMORRHAGE**

Medical University Graz, Department of Radiology, Division of Neuroradiology, Vascular and Interventional Radiology, Graz, Austria

**Introduction/Objectives:** Intracranial cerebral aneurysm, dural fistula or AVM may be the underlying pathology in patients suffering from intracranial hemorrhage. Radiological diagnosis, interdisciplinary management and neurointerventional treatment play a crucial role in the management of these patients.

**Participants, Materials/Methods:** Overview of the diagnosis and treatment of different vascular pathologies.

**Results:** Patients suffering from acute intracranial hemorrhage should receive early vascular imaging by either CTA or MRA to facilitate interdisciplinary decision making and early treatment. Depiction of intracranial aneurysms, including 3D reconstruction, is necessary, to decide, whether the aneurysm may be treated endovascularly or surgically. If both methods are possible, endovascular treatment is the method of choice. Although not in the acute phase, in addition to endovascular and surgical treatment, decision making in the case of dural fistulas and AVMs should also take radiation therapy into account. Each treatment modality conveys separate challenges and risks. Interdisciplinary discussion of the options is of utmost importance. Technological progress in the treatment of cerebral aneurysms allows for treating even complex aneurysms with wide neck or side branches originating from the aneurysm sack. Several new devices may be used to occlude the aneurysm and to prevent rebleeding. Also, for the treatment of dural fistulas and AVMs, several different approaches to occlude the fistula or the AVM may be used.

**Conclusions:** Intracranial macrovascular lesions, such as cerebral aneurysms, dural fistulas or AVMs may lead to intracranial hemorrhage. Adequate imaging and interdisciplinary decision making is necessary to offer the best suitable treatment to the patients.

### **Milija Mijajlović: CEREBROVASCULAR DISORDERS ASSOCIATED WITH COVID-19 INFECTION**

Neurology Clinic, University Clinical Center of Serbia; Faculty of Medicine University of Belgrade, Department for Cerebrovascular Diseases, Belgrade, Serbia

COVID-19 is primarily a respiratory disease but up to two thirds of hospitalized patients show evidence of central nervous system damage, predominantly ischemic, in some cases hemorrhagic and occasionally encephalitic. Cerebral venous sinus thrombosis (CSVT) could also occur, especially in critically ill patients. Cerebral white matter is particularly vulnerable to ischemic damage in COVID-19. To date, it is still not clear whether cerebrovascular manifestations are caused by direct viral action or indirect action mediated by inflammatory hyper activation, recognized as a cytokine storm, causing severe dysfunction of the immune and coagulation systems, reflected through elevated D-dimer levels and intravascular disseminated intravascular coagulation (DIC). Another mechanism of cerebrovascular damage in COVID-19 is an endothelitis process. The final cerebrovascular damage would have clinical and neuroimaging pattern suggestive of a vasculitic process affecting the central nervous system. Data from postmortem brain magnetic resonance imaging (MRI) showed extensive signs of cerebrovascular involvement, including microbleeds with subcortical and posterior predominance. This multifocal pattern of hemorrhagic lesions could also be evocative of DIC-related lesions while prothrombotic state in COVID-19 is at least partially correlated with the occurrence of IS and CVST. Low platelet levels are found in patients with severe SARS-CoV-2, which may have triggered intracranial bleeding. COVID-19 is likely to leave an unexpected legacy of long-term neurological complications in a significant number of survivors. Cognitive follow-up of COVID-19 patients will be important, especially in patients who develop cerebrovascular and neurological complications during the acute illness.

### **Anita Arsovska: RARE CAUSES OF STROKE**

University Clinic of Neurology, University Ss. Cyril and Methodius, Faculty of Medicine, Department of Urgent Neurology, Skopje, North Macedonia

**Introduction/Objectives:** Stroke is classically characterized as a neurological deficit attributed to an acute focal injury of the central nervous system (CNS) by a vascular cause, including cerebral infarction, intracerebral hemorrhage, and subarachnoid hemorrhage, and is a major cause of disability and death worldwide. Clinical presentation span through a myriad of motor deficits, sensory deficits, seizures, personality/behavioral anomalies, dementia, brainstem stroke syndromes and herniation syndromes.

**Participants, Materials/Methods:** Conventional risk factors for stroke occurrence have also be described and grouped into modifiable and non-modifiable risk factors. Modifiable risk factors include hypertension, smoking, lifestyle, alcohol, high cholesterol, atrial fibrillation, obesity, diabetes, severe carotid stenosis, sleep apnea. Non-modifiable risk factors comprise of male gender, black race and age of more than 40 years. Besides conventional stroke causes, there are also rare causes of stroke which can be classified as noninflammatory blood vessel disorders, inflammatory blood vessel disorders, hematological disorders and miscellaneous disorders.

**Results:** Noninflammatory blood vessel disorders are CADASIL (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy), CARASIL (cerebral autosomal recessive arteriopathy with subcortical infarcts and leukoencephalopathy, Fabry's disease, hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu syndrome), fibromuscular dysplasia, MELAS (Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes), Moyamoya disease, cerebrotendinous xanthomatosis, reversible cerebral vasoconstriction syndromes,



radiation-induced vasculopathy, vasospasm after subarachnoid hemorrhage and Sneddon syndrome. Inflammatory blood vessel disorders are isolated angitis (vasculitis) of the central nervous system, giant cell (temporal) arteritis, vasculitis and Susac's syndrome. Hematological disorders are coagulation system disorders, antiphospholipid antibody syndrome and Sickle cell anemia. Miscellaneous disorders are migrenous strokes and cerebral venous sinus thrombosis.

**Conclusions:** Strokes with rare causes require heightened clinical awareness for recognition, evaluation and treatment.

### **Frederic-Ivan Silconi, Marjana Radić, Dolores Janko-Labinac: POSTERIOR CIRCULATION INFARCT**

General Hospital Pula, Department of Neurology, Pula, Croatia

**Introduction/Objectives:** Even though ischemic stroke represents a majority of strokes. In general, there is a small portion coming from a posterior circulation. Because of the different origin and particular territory involvement, this represents a difficult clinical task.

**Participants, Materials/Methods:** We compared relevant clinical data from literature with our patients results affected by the posterior circulation stroke (PCI ). We analyzed stroke admitted patients from 2018 to 2022, in the General Hospital of Pula, a touristic oriented county hospital in Croatia on the Adriatic Coast.

**Results:** In that period, we had admitted 1795 patients with ischemic strokes. 246 of those had originated from the posterior circulation. This makes a 16% of all strokes that is significantly less than other data we encountered. The predominance of those patients were males and equal 64%. Comparing the outcome, we found that the PCI had significantly better outcome (PCI 43% versus 32% of anterior circulation strokes). Death rate was similar in both, PCI 13% versus 15% in ACI. We also compared the outcome by infarct regions or compared with etiology. We also compared clinical particularities related by the territory of PCI involvement. We tried particularly to analyze the most noticeable PCI like in Wallenberg's syndrome or more diagnostical challenging ones like dissections strokes.

**Conclusions:** According to our results the patients with posterior circulation ischaemic stroke have a better outcome in comparison to ischemic stroke in anterior circulation strokes. The most frequent site of stroke was cerebellar strokes followed by pontine strokes. The highest death rate had those with multiple posterior circulation strokes. Initial NIHSS score was lower in posterior circulation strokes then in anterior circulation strokes, with an important impact on reperfusion therapy rates. So, it is crucial to have a comprehensive clinical evaluation of patients with posterior circulation ischaemic strokes.

### **Hrvoje Budincevic: HOW TO ACCELERATE THE ROUTE TO MECHANICAL THROMBECTOMY?**

Sveti Duh University Hospital, Department of Neurology, Zagreb, Croatia

The prompt response and proper treatment is crucial for stroke patients. The evidence clearly shows that mechanical thrombectomy improve functional outcome in stroke patients with large vessel occlusion. 20% of all strokes are caused by large vessel occlusion. Large vessel occlusion stroke is related to higher disability and mortality. The aim is to presents the overview of possible strategies how to improve stroke care by accelerating the route to mechanical thrombectomy. An improvement in accelerating route might be achieved by reducing pre-hospital, inter-hospital, and in-hospital delays. Organization of stroke care and especially transfer issues plays an important part in optimizing outcome parameters regarding mechanical thrombectomy. Improvements are requiring comprehensive and substantial efforts of medical professional and stakeholders to achieve defined goals for improvement of stroke care. Raising public awareness, using prehospital stroke scales, quality control, translation of experiences from acceleration of intravenous thrombolysis and organizational issues might be beneficial for the acceleration of mechanical thrombectomy too.

**Vesna Đermanović Dobrota: METABOLIC SYNDROME AND COGNITIVE IMPAIRMENT**

Clinical Hospital Merkur - University Clinic Vuk Vrhovac, Department of Diabetic Complications, Zagreb, Croatia

Metabolic syndrome (MetS) is characterized by several clinical conditions which include visceral or central obesity, hypertension, dyslipidemia, and impaired glucose tolerance, which is also associated with the development of type 2 diabetes mellitus (T2DM). Together they are known as “the deadly quartet”. These risk factors are also associated with cognitive disorders that occur at an increasingly early age: mild cognitive impairment (MCI), vascular dementia (VaD), and the development of Alzheimer's disease (AD). Therefore, we are seeing an increase in the metabolic syndrome and cognitive impairment at an alarming rate worldwide. Both conditions are multifaceted and interrelated. It is considered that there is a connection between MetS and mild cognitive impairment (MCI), and the question arises as to which of these factors develops first. MCI is considered a state between normal cognitive aging for age and education and a neurological neurocognitive state like Alzheimer's disease (AD). MetS with all its components causes changes in the brain in terms of neuroinflammation, hyperphosphorylation of the Tau protein, formation of beta amyloid plaques, and vascular changes which lead to altered signals in hormones such as adiponectin, leptin, and insulin. They clinically manifest as MCI, AD, and other major vascular neurocognitive disorders. Micro- and macrovascular changes of MetS, such as hypertension and diabetes, are always associated with brain alterations and vascular neurocognitive disorders, which have been seen on neurocranial MRI as brain white matter damage, lacunar infarcts, microhemorrhages, and microinfarcts. All these changes are called the cerebral small vessel disease (CSVD) and are characterized by the loss of smooth muscle cells in the middle of the tunic, deposition of fibro-hyaline material, and thickening of the blood vessel walls. There is a possibility to influence all components of MetS (hypertension, hyperglycemia, obesity, and dyslipidemia), and cognitive impairment, with adequate prevention and therapy. Changing lifestyle habits (diet and better nutrition, less calory intake, and more physical activity, less smoking and alcohol), and prescribing adequate therapy according to individual's indications goes a long way towards reducing risk factors.

**Jan Kobal: SIGNIFICANT LOWERING OF FATAL OUTCOMES DUE TO CEREBRAL VENOUS THROMBOSIS IN SLOVENIA**

UMC Ljubljana, Department of Neurology, Ljubljana, Slovenia

**Introduction/Objectives:** Cerebral venous thrombosis (CVT) is rare cerebrovascular disease with highly variable presentation and a variety of predisposing/provoking factors. Mortality is generally low, from 5% to 2-3%, in some studies even nil. To find out the mortality rate at the Department of Neurology, University Medical Centre Ljubljana we searched medical records of patients treated at our department from January 2008 till December 2022. There were in total 98 CVT patients hospitalized during this time.

**Participants, Materials/Methods:** In 4 of the patients (3 women) CVT ended fatally, which accounts a mortality rate of 4,08% in 15 year period. Each patient presented different predisposing/predicting factors ranging from pregnancy/hormonal contraception to interventional surgery and COVID-19 vaccination. The common clinical features of the patients were aggravating headache, bilateral neurological signs and altered mental status leading to coma. Raised D-dimer was a common laboratory finding and radiologically a haemorrhagic venous infarction was found in all 4 patients.

**Results:** The mortality rate was lowering during the observation time and it has dropped from 12% in the years 2008 – 2012 to 1.37% in the years 2013 – 2022 (P = 0.022).

**Conclusions:** We conclude that follow up and closer collaboration between neurology/neuroradiology wards has led to better alertness of attending neurologists/neuroradiologists and helped to improve the treatment of CVT. In fact, the only patient with fatal outcome in the years 2013-2022 was a young female who developed CVT after receiving COVID 19 adenovirus based

vaccine, mortality of similar cases in other European countries was high (e.g. in Norway 3 out of 4 patients ended in fatal outcome).

## NEURODEGENERATIVE DISEASES AND ALZHEIMER'S DISEASE SYMPOSIUM

### Miroslav Cuturic: UPDATE ON HUNTINGTON'S DISEASE

University of South Carolina Columbia, Department of Neurology, Elgin, United States

**Introduction/Objectives:** Huntington's disease (HD) is a hereditary neurodegenerative disorder with autosomal-dominant inheritance and complete expression. The genetic mutation consists of CAG trinucleotide expansion on the short arm of chromosome 4, resulting in production of mutant huntingtin protein. The illness usually emerges in middle age and is characterized by cognitive, motor, and psychiatric deterioration. In this presentation, we overview recent advancements in the knowledge about Huntington's Disease (HD) in the context of observational studies and clinical trials. We discuss the implications of the new findings in the context of other psychiatric and neurodegenerative disorders.

**Participants, Materials/Methods:** Review of literature and clinical trials database.

**Results:** Over the last fifteen years, multiple observational studies and clinical trials have been conducted in HD. The most significant outcomes have been the USFDA approvals for tetrabenazine and deutetrabenazine for the treatment of chorea. Emerging experimental treatment strategies are focusing on huntingtin protein lowering through gene therapy by using micro-RNA, antisense oligonucleotides, modulator genes expression, small molecules and DNA repair. Most recent clinical trials using huntingtin lowering approach resulted in ambivalent outcomes, requiring additional reconsiderations in overall approach to HD treatment. New emphasis is placed on identifying pre-symptomatic markers of HD development, DNA repair techniques, virtual visualization of huntingtin protein, and use of large data sets as well as artificial intelligence in HD modeling and research.

**Conclusions:** HD has a unique position among other neurodegenerative disorders as it bridges the boundaries separating disciplines of neurology, psychiatry, and genetics. With respect to research and drug development, HD is considered a model disorder that is pertinent to other trinucleotide repeat disorders, protein aggregation disorders, as well as dementias, movement disorders and psychiatric illness. In an autosomal dominant disorder such as HD, silencing of the mutant gene may potentially have a disease modifying or even curative effect. As the HD gene mutation can be identified decades before disease onset, the ultimate aim of therapy would be to delay the onset of the disease or possibly completely prevent it from emerging.

### Maja Relja: COULD WE IMPROVE DYSTONIA MANAGEMENT IN EUROPE?

University of Zagreb Medical School and Croatian Medical Academy, Department of Neurology, Zagreb

**Introduction/Objectives:** Lack of specific training in dystonia by general neurologist (GN), family doctors (GP) and health professionals was reported in a study performed by the European Network for the Study of Dystonia in 2016. Currently, the diagnosis of dystonia is largely based on clinical signs and dystonia is still diagnosed based on the examination of a specialist. Due to a lack of specific training in dystonia, a long time for diagnosis and treatment was reported. The aim of present study, as a part of European Brain Council-EBC Value of Treatment research project (VoT2 2018-2021), was to evaluate dystonia management from patients' own experience in four European countries with different health care systems regarding the delivery of services and education.

**Participants, Materials/Methods:** Dystonia survey was undertaken using a structured, validate on-line questionnaire (developed in Croatia, University of Zagreb Medical School) to assess patients' own experience of dystonia management and treatment in Croatia, Italy, Germany and the UK. with the intention to evaluate specifics across

countries with the UK as a reference. Questionnaire was divided into three parts (I. General questions: name, age etc. II. Specific questions: type of dystonia, time to correct diagnosis etc. III. Therapy, quality of life, etc.).

**Results:** A total of 1645 patients responded to survey: 379 (12.2%) from Croatia, 340 (10.9%) from Germany, 175 (5.6%) Italy and 751 (24.1%) from UK. Women outnumbered men in all countries cervical dystonia was the most prevalent type. Most patients (around 50%) from all countries were 41-50/51-60 years old. Although most patients across countries were diagnosed within 2 years since the first symptoms, significant number waited more than 10 years (7-15%). In comparison to UK participants Italian and Croatian patients reported shorter time to diagnosis. Croatian patients have experienced a 'more adequate' initial GP assessment. Botulinum toxin was the most common treatment reported (35-45%).

**Conclusions:** Sub-analysis of data obtained Germany, Italy and the UK did not show significant differences in the current state of dystonia management among countries, although significant difference exists in the healthcare system. But our findings showed that training on dystonia for GPs and GNs could improve dystonia care. It should be introduced in postgraduate education.

### **Gabriela Novotni, Antoni Novotni: INFLAMMAGEING AND THE BRAIN**

University Clinic of Neurology, Medical Faculty-University Ss Cyril and Methodius; Department for Cognitive Neurology and Neurodegenerative Diseases, Skopje, North Macedonia

**Introduction/Objectives:** Inflammation as an integral part of the healing process is essential to protect the organism against viral and/or bacterial infection. On the other hand, prolonged, chronic inflammation can be detrimental, causing oxidative stress and cell damage, especially in old age, when the effect of natural selection is no longer active, an explanation supported by the antagonistic pleiotropy theory of ageing. It is well known that ageing as a complex phenomenon is the major risk factor for developing neurodegenerative diseases. It is also well known that the brain is a highly immunologically active organ. Inflammageing as a term was coined 23 years ago by Claudio Franceschi, describing a chronic, low-grade inflammation that occurs with ageing, resulting in immune dysregulation with elevated pro-inflammatory markers

**Participants, Materials/Methods:** This talk aims to sublime latest publications in a review manner, on the implication of inflammageing on the brain, focusing on neurodegenerative diseases like Alzheimer's and Parkinson's disease.

**Results:** Evidence support that inflammageing is a risk factor for CVD, cancer, chronic kidney disease, dementia, and depression as well as multimorbidity, sarcopenia, frailty, and premature death. Though the causes for inflammageing are poorly understood, a complex interaction among genetic factors, visceral obesity, chronic inflammation, and microbiome alterations is brought in the frontline. Although a subject for thorough research during the last decade and more, the bidirectional crosstalk between CNS and the innate immune system has become one of the most intriguing topics in neurology research especially during the COVID-19 pandemic while exploring the possible mechanisms of long-COVID.

**Conclusions:** A logical question is raised while discussing the bidirectional connection neuroinflammation-neurodegeneration. Whether the inflammation is the cause, or the consequences and a biological marker of an existing underlying condition. Or it can be that both the possibilities are true, coexisting and leading to amplification, thus creating a vicious cycle. The discussion flows from causes to consequences, from microglia to inflammasomes and waves of inflammation, to sum up with the possibilities for treatment and prevention.

**Vladimira Vuletic: INVASIVE METHODS IN MOVEMENT DISORDERS**

Dept. of Neurology, UHC Rijeka, Medical faculty University of Rijeka, Rijeka, Croatia

Management of advanced Parkinson's disease is challenging. In that stage we can see motor fluctuation, nonmotor symptoms, insufficient control of motor symptoms with falls, freezing, festination, sudden ON and OFF etc. The severe nonmotor symptoms, especially neuropsychiatric problems, influence the quality of life of patients and their caregivers most. In that stage, multidisciplinary management is necessary. Beside known and available medications, there are a lot of possibilities like deep brain stimulation (DBS), continuous infusion therapy with levodopa-carbidopa intestinal gel, levodopa-carbidopa-entacapone intestinal gel or apomorphine in this stage which improve motor and non-motor symptoms differently. Modern treatment of advanced Parkinson's disease is holistic, individual, personalized and symptom orientated. Dystonia is also challenging in management and influence quality of life in our patients. In addition to drug therapy, DBS is very effective, especially in some forms of dystonia, and should not be delayed.

We highlight here the most relevant invasive treatment's effects in advanced and disabling movement disorders. Increased recognition of patients' differences and symptoms and their impact on treatment in advanced phase of movement disorders is very important for future studies and precise and personalized medicine.

In this article, we provide a review of invasive treatment in advanced movement disorders, mostly Parkinson's diseases.

**NEUROIMMUNOLOGY & MULTIPLE SCLEROSIS SYMPOSIUMS****Jörg Kraus: OVERVIEW ON MODERN AND UPCOMING MS TREATMENT**

Salzburger Landeskliniken, Paracelsus Medical University, Department of Laboratory Medicine, Paracelsus Salzburg, Austria

Department of Neurology, Medical Faculty, Heinrich-Heine-University, Düsseldorf, Germany

Multiple sclerosis (MS) is a chronic inflammatory disabling disease of the central nervous system leading to inflammatory lesions of predominately the white matter. In recent years a presumably secondary neurodegenerative pathway has been investigated in more detail. Since the approval of interferon-beta (IFN-beta) preparations and glatiramer acetate as the first proven disease modifying drugs for multiple sclerosis treatment in the 1990s, immunotherapy in MS has been a rapidly evolving field. Within the recent years several new drugs have become available for MS treatment. Amongst them are second-generation drugs, e.g. new formulations of IFN-beta, fumaric acid, advanced B-cell targeting CD20 depleting antibodies, or more-specific sphingosine-1-phosphate receptor modulators. And the next generation of drugs is already on the edge to be licensed for MS treatment. The probable most promising ones are the different Bruton's tyrosine kinase inhibitors that have a completely new mode of action. Another experimental field is the re-purposing of medications that are approved for other diseases and are now tested for MS. However, besides these great achievements predominately for patients with relapsing-remitting MS, several important issues have not been completely addressed in modern MS therapy such as only moderate efficacy for the progressive courses of MS or drugs that provide abilities for repair of the diseased CNS tissue.

## Uroš Rot: TNF ALPHA INHIBITORS AND DEMYELINATING/INFLAMMATORY DISEASES OF THE NERVOUS SYSTEM

University Medical Centre, Department of Neurology, Ljubljana, Slovenia

TNF alpha inhibitors are very successful in the treatment of many inflammatory systemic diseases such as rheumatoid arthritis, inflammatory bowel disease and psoriasis. They were also tested in multiple sclerosis, but worsening of the disease was unexpectedly found in clinical trials. In addition many neurological autoimmune diseases, central and peripheral, demyelinating and non-demyelinating were later described in patients with systemic diseases treated with TNF alpha inhibitors. Neurological conditions associated with TNF alpha therapy usually occur in first year of the treatment and patients are generally older than people with multiple sclerosis. The course of neurological diseases is monophasic in approximately two thirds of cases. Management of neurological symptoms includes withdrawal of TNF alpha inhibitor and corticosteroids. Stabilization is seen in 50% of patients after withdrawal of the TNF alpha inhibitor, resolution of symptoms in 25% of patients and the remaining have relapsing-remitting clinical course. There is growing evidence that the occurrence of neurological adverse events with the TNF alpha inhibitor treatment is not incidental and that there is a true association between TNF alpha inhibitor and neurological autoimmunity.

## MIGRAINE SYMPOSIUM

### Marjan Zaletel, Darja Visočnik, Matija Zupan, Bojana Žvan: CAN CALCITONINE GENE RELATED PEPTIDE BE CAUSALLY RELATED TO MIGRAINE AURA?

University Clinical Centre of Ljubljana, Department of Vascular Neurology, Ljubljana, Slovenia

**Introduction/Objectives:** In our study we presumed that eCGRP could evoke TVS in participants with MO and MA with vasodilatory response of the cerebral and meningeal arteries, including MCA and PCA. On the other hand, eCGRP could indirectly change cortical excitability via neurogenic inflammation induced by TVS because it can induce migraine aura. Indeed, the study showed a difference in cortical excitability between MA and MO. The aim of the study was to assess hemodynamic changes in cerebral circulation induced by eCGRP in MO and MA. We hypothesized that cerebral hemodynamic changes differ between MO and MA, reflecting a different degree of TVS. We hypothesized differences in hemodynamic response after eCGRP application between MA and MO groups, with a more pronounced response of arterial flow velocities in middle cerebral artery (MCA) and posterior cerebral artery (PCA) to eCGRP in MA.

**Participants, Materials/Methods:** We included twenty participants with migraine, of whom 15 (75%) had MO, and 5 (25%) had MA. An intravenous infusion of eCGRP was administered. Polymodal recording of mean arterial velocity in MCA (vm MCA) and PCA (vm PCA), end-tidal carbon dioxide partial pressure (Et-CO<sub>2</sub>), mean arterial pressure (MAP), and heart rate (HR) was employed using transcranial Doppler sonography (TCD). The parameters were determined at different time points with single responses vm MCA<sub>tot</sub>, vm PCA<sub>tot</sub>, Et-CO<sub>2</sub><sub>tot</sub>, MAP<sub>tot</sub>, and HR<sub>tot</sub>.

**Results:** The CGRP-IH appeared in five participants with MA (100%) and in 11 participants with MO (73.3%) ( $p = .530$ ). The difference of changes in vm MCA<sub>tot</sub> ( $p = .014$ ) and vm PCA<sub>tot</sub> ( $p = .004$ ) was significant, whereas in Et-CO<sub>2</sub><sub>tot</sub> ( $p = .658$ ), MAP<sub>tot</sub> ( $p = .392$ ), and HR<sub>tot</sub> ( $p = .686$ ), it appeared to be non-significant. We found significant associations between vm MCA<sub>tot</sub> and MA ( $p = .023$ ; OR = 0.88; 95% C.I. 0.78–0.98), and vm PCA<sub>tot</sub> and MA ( $p = .018$ ; OR = 0.85; 95% C.I. 0.74–0.97).

**Conclusions:** The main finding of our study is a greater decrease in vm MCA<sub>tot</sub> and vm PCA<sub>tot</sub> in MA compared to with MO. Our results, as well as reports from the literature, indicate TVS as the primary event and aura as a

consequential pathophysiological event. The central event might be neurogenic inflammation which evoked cortical spreading depression and headache. The finding could further add to clarifying the pathophysiology of MA and could serve as a clinical model for prophylactic treatment, including specific CGRP inhibition.

### **Bojana Zvan: MIGRAINE AND CEREBROVASCULAR RISK**

University Medical Centre Ljubljana, Department of Vascular Neurology - Center TeleKap, Ljubljana, Slovenia

**Introduction/Objectives:** Epidemiological studies have shown that migraine and stroke are among the most prevalent and disabling neurological diseases worldwide .

**Participants, Materials/Methods:** Migraines, especially those with aura, are more likely to develop subclinical infarct-like lesions in the brain that represent the cryptogenic or cardioembolic stroke. In some cases, migraine headache can be an introduction to an acute ischemic stroke or cerebral hemorrhage, and in rare cases, a migraine infarct can be directly attributed to a long-lasting migraine aura. Recent studies show that in the case of cerebral artery occlusion and a history of migraine, the progression of the infarction is more serious, which means a worse outcome of the disease. The mechanisms underlying the association between migraine and stroke are multifactorial, including cortical spreading depression, inflammatory and vascular factors, endothelial dysfunction, genetic factors, coagulation factors, and others.

**Results:** In treating patients with migraines, it is important to identify and modify any vascular risk factors such as hypertension, smoking, oral contraceptives use and lifestyle factors.

**Conclusions:** Conclusion: According to new drugs targeting the neural mechanisms of migraine, there is no evidence that gepants and anti-CGRP monoclonal antibodies should be contraindicated in patients with cardiovascular diseases, including stroke or myocardial infarction, although erenumab has been associated with hypertension. There are no cardiovascular safety concerns for lasmiditan and it could be used in patients with cardiovascular diseases. However, for their safer prescription, it is necessary to analyze long-term data from real life.

### **Mariana Ciobanu: MIGRAINE AT CROSSROADS : THE ACCESS TO HEADACHE CARE FOR PATIENTS WITH REFRACTORY MIGRAINE**

Monroe Carell Jr.Children's Hospital at Vanderbilt, Department: Pediatric Neurology, Gallatin, United States

**Introduction/Objectives:** Chronic migraine (CM), the suffering of 15 or more headache days with at least 8 of these migraine days, afflicts 1.2 % - 5.1% of the global population. Migraine is the second cause of disability worldwide and the first cause in patients under 50 years of age. Chronic migraine and refractory migraine (treatment resistant), especially when there is also analgesic overuse, are the most disabling forms of migraine and very difficult to treat. This oral presentation reviews quality improvement projects targeting improved access to headache care and different treatment modalities. Therapeutic options available are discussed and focused on a multidisciplinary approach, non-pharmacological interventions treatment of comorbidities and avoiding analgesic overuse.

**Participants, Materials/Methods:** Our hospital is a multispecialty children's hospital with 343 inpatient beds, 49 clinical divisions, and more than 500 physicians trained in pediatric and surgical subspecialties. The pediatric neurology division is one of the largest divisions of the hospital and has a robust outpatient and inpatient service with approximately 12,000 outpatient visits annually. Our SMART (Specific, Measurable, Actionable, Realistic, Time bound ) aim was to standardize treatment ,reduce time to access to a headache specialist and reduce visits to Pediatric Emergency Room .One of our pillar goal is to see new patients within 14 days from their initial referral date.

**Results:** The pediatric neurology 14 days access metric was at 32.1 % in 2021 and has been gradually increased through tireless quality improvement measures to 57.9 % in March ,2023

**Conclusions:** This presentation demonstrates that quality improvement projects have improved access to care for patients with migraine and follow-up care by identifying sources of delay and using targeted changes based on a set of access change principles. With appropriate guidance and data analysis, improvements in access can be made.

**Anita Marčinko Budinčević, Berislav Dalić, Matea Hudolin, Zurap Raifi, Hrvoje Budinčević: THE POTENTIAL ROLE OF ANTI-CGRP INHIBITORS IN TREATMENT OF POST-TRAUMATIC HEADACHE**

Sveti Duh University Hospital, Department of Neurology, Zagreb, Croatia; University J.J. Strossmayer, Faculty of Medicine, Department of Neurology and Neurosurgery, Osijek, Croatia; County Hospital Villach, Department of Neurology, Villach, Austria

Post-traumatic headache is classified as a secondary headache. It causes substantial disability and impairs quality of life. Commonly post-traumatic headache resembles migraine headache. Treatment of the headache is based on the headache phenotype which is represented. Since the post-traumatic headache share some some pathophysiology mechanisms with migraine. Anti-CGRP inhibitors might have potential role in treatment of post-traumatic headache. Currently, in non-randomized studies erenumab only showed efficacy in treatment of posttraumatic headache. Further randomized and double-blind studies are warranted to confirm these findings for erenumab and other anti-CGRP inhibitors

**EPILEPSY SYMPOSIUM**

**Zrinka Čolak Romić, Ivana Šušak Sporiš, Davor Sporiš, Silvio Bašić: MANAGEMENT OF EPILEPSY IN THE ELDERLY**

Clinical Hospital Dubrava, Department of neurology, Zagreb, Croatia

Management of epilepsy in older adults requires special attention with emphasis on individualised approach. Incidence and prevalence of epilepsy are highest in elderly people and the etiology differs from other age groups. Establishing the epilepsy diagnosis is challenging since a lot of the patients have atypical clinical presentation. Alterations in pharmacokinetic and pharmacodynamic parameters as well as comorbid medical conditions and co-medication can influence efficacy, tolerability and adherence of older patients which affects the choice of antiepileptic drugs. We are still lacking comprehensive guidelines specific to epilepsy in older patients, especially those with neurodegenerative disorders and psychiatric comorbidities but it is clear that our goal has to go beyond just seizure control.

**Iris Zavoreo: NEUROIMMUNOLOGICAL ASPECTS OF THE STATUS EPILEPTICUS – TREATMENT PERSPECTIVES**

University Hospital Centre Sestre milosrdnice, University Neurological Department, Zagreb, Croatia

Status epilepticus (SE) is a very heterogeneous clinical condition often refractory to all kinds of available treatment options. The effects of the variables of age, sex, underlying disease, and types of antiepileptic drug (AED) use showed no significant differences between the survivor and non-survivor groups. Importantly, the number of AEDs used in the first week and the use of thiobarbiturates predicted non-survival as well as etiology as the most important predictor of outcome, old age and medical comorbidity which are independent risk factors for mortality. According to animal models neuroinflammation arises in the brain during SE due to the activation of innate immune mechanisms in brain



parenchyma cells. Therefore there is a high variety in duration, and severity, refractoriness to treatments, and long-term neurological consequences. Clinical evidence shows that neuroinflammation occurs in patients with SE of diverse etiologies likely representing a common phenomenon, thus broadening the involvement of the immune system beyond the infective and autoimmune etiologies. Novel therapies for refractory SE that rely upon a better understanding of the previously mentioned basic mechanisms underlying this clinical condition. Preclinical and clinical evidence encourage consideration of specific anti-inflammatory treatments for controlling SE and its consequences in patients but still are under evaluation.

### **Ana Sruc: SLEEP AND EPILEPSY ARE CORRELATED IN BOTH DIRECTIONS**

Sveti Duh University Hospital, Department of Neurology, Zagreb, Hrvatska

Ten to fifteen percent of epilepsy is sleep-related. There are three subtypes of sleep-related epilepsy (SRE): sleep-associated, sleep-accentuated, and awaking epilepsy. Sleep-associated epilepsy refers to those in which seizures only or predominantly occur during sleep. Sleep-accentuated epilepsy is in which seizures occur both awake and asleep; however, epileptiform activity is frequently activated during sleep, and specific diagnostic seizure types are sometimes observed during sleep. Arousal epilepsy is characterized by the occurrence of most seizures immediately after awakening from sleep. Due to the fact that 30% of cases come from extra-frontal foci, seizures are linked to sleep rather than clock time, and hypermotor semiology predominates, it was suggested at an international consensus conference in 2016 to rename nocturnal frontal lobe epilepsy to sleep-related hypermotor epilepsy. Sleep deprivation induces seizures in some people with epilepsy. Genetic generalized epilepsies carry the highest risk, whereas focal epilepsies carry a significantly lower risk. Interictal epileptiform discharges (IEDs) and seizures are more likely to occur during NREM sleep than during REM sleep in both focal onset and generalized epilepsies. NREM sleep induces generalized discharges more than focal ones. The majority of sleep-related seizures are followed by arousal or awakening. IEDs cause arousals and, afterwards, are amplified. On polysomnography, patients with sleep-related seizures have more wake time after sleep onset than patients without sleep seizures. Adults with epilepsy are 2-3 times more likely to experience sleep/wake disorders than the general population. This category includes insomnia, restless legs syndrome, and sleep disordered breathing. These comorbidities are linked to a lower quality of life and may affect seizure control. According to a recent meta-analysis, obstructive sleep apnea is 2.4 times more prevalent in adult people with epilepsy than in healthy controls, affecting 33% of them. Treatment with CPAP was five times more likely to ameliorate seizure outcomes. Approximately 70% of all cases of SUDEP occur during sleep. Patients with nocturnal seizures have a 6.3-fold higher risk of dying in a prone position than those with diurnal seizures. In addition to NREM activation of seizures, other sleep-related physiological alterations that may predispose to SUDEP include decreased airway patency, reduced inspiratory drive, hypoxic and hypercapnic ventilatory responses, and a longer QT interval that lowers the threshold for malignant cardiac arrhythmia. To enhance epilepsy outcomes and provide patient and caregiver education and counseling, it is critical to recognize this bidirectional relationship.

### **Željka Petelin Gadže: EPILEPSY AND PSYCHOSIS – TREATMENT CHALLENGES**

Department of Neurology, University Hospital Centre Zagreb and School of Medicine, University of Zagreb  
Referral Centre of the Ministry of Health of the Republic of Croatia for Epilepsy, Affiliated Partner of the ERN  
EpiCARE

During recent years, there has been much focus on the comorbidity of psychiatric disorders in people with epilepsy, and observational studies have indicated a bidirectional relationship. According to clinical studies, the prevalence of any psychiatric disorder was observed in up to 43.3% of patients with epilepsy; the most common psychiatric

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disorders included mood disorders - affective disorders (up to 40%), anxiety disorders (up to 30.8%), personality disorders (up to 11% in juvenile myoclonic epilepsy) and psychotic disorders (in about 2-9% of patients), the latter being associated with a longer duration of epilepsy. Apart from a shared neurobiological susceptibility, the bidirectionality of epilepsy and psychosis may be influenced by various environmental factors, including the interaction of pharmacodynamic effects.

Psychosis in people with epilepsy can be divided into peri-ictal or interictal. Interictal psychosis occurs most often in patients with temporal lobe epilepsies. Almost all first and second generation antipsychotic drugs (APDs) increase the risk of epileptic seizures. It has been proven that dopaminergic activity has an impact on the development of psychosis, while dopamine antagonists have a proconvulsant and antipsychotic effect. Some antiseizure medications (ASMs) have an effect on increasing the risk of developing psychosis, with a prevalence of 2.5% for vigabatrin, 1.9-2.3% for zonisamide, 0.8% for topiramate, 0.3-0.7% for levetiracetam, and 0.5% for gabapentin.

Certain general risk factors for seizures should be considered when initiating antipsychotic therapy, including pharmacodynamic and pharmacokinetic interactions (resulting from a common metabolic pathway through cytochrome P450 isoenzymes), drug selection and dosing, as well as patient-related factors. APDs can lower the seizure threshold, but also have other side effects such as weight gain and sedation, especially when used simultaneously with ASMs such as valproate, vigabatrin, carbamazepine or barbiturates. Both first and second generation APDs can cause extrapyramidal syndrome as a side effect, especially the first generation. However, compared to the first generation, second generation antipsychotics cause more severe side effects in terms of weight gain and the development of metabolic syndrome. Other examples include the simultaneous use of carbamazepine with clozapine, which should be avoided because of the risk of bone marrow suppression.

In conclusion, psychiatric comorbidities, especially psychosis, represent a challenge in treating patients with epilepsy, along with the psychosocial consequences of both disorders. In this context, it is of great clinical importance to understand the interactions between antiepileptics and antipsychotics that can affect therapeutic efficacy or result in toxicity.

## “LETS TALK ABOUT OLD AGE PSYCHIATRY” SYMPOSIUM

### Ninoslav Mimica: THE ROLE AND PLACE OF OLD AGE PSYCHIATRY TODAY

University Psychiatric Hospital Vrapče, Department for Biological Psychiatry and Psychogeriatrics, Zagreb, Croatia

Many societies today, especially European ones, are faced with a growing number of elderly people; projections say that in the near future many countries will have up to one third of the population of elderly people. This change in the age structure of the general population will certainly change the overall morbidity. As a rule, elderly people have several chronic physical diseases, and quite often they also suffer from some psychological disturbances or psychiatric disorders. Therefore, psychiatry of the elderly already now, and even more so in the future, represents an important part of psychiatry and medicine. After retirement, in the future, people will increasingly need psychiatric care for various reasons. Of the affective states, depression should definitely be distinguished, and that which will result from prolonged mourning or some other reactive state, but also depression that will occur in involution without a visible reason or stressor. Dementia, for which the most significant risk factor is age, will of course be more common in the elderly, so it will be a significant percentage among the 80-year-olds, and the oldest old will affect almost half of the people. Psychotic states, of various causes, will also occasionally occur in the elderly population, as well as delirious states, which will require inpatient treatment. It is difficult to say how big a problem addiction will be in the elderly population, but it can be assumed that the single life of many elderly people will contribute to it. From all of the above, it follows that in the elderly population, society must plan preventive measures, measures to reduce the risk of dementia and mental disorders, and through numerous therapeutic activities of Centers of excellence, such as competent Reference Centers, specialized departments, etc., positively influence the quality of life of elderly people. The World Health Organization declared dementia a public health priority in 2012, and instructed all its members to

develop National strategies / Action plans to combat dementia. In Croatia, the Ministry of Health has recently established a Working Group for drafting proposals for an Action Plan to combat dementia, so we believe that Croatia will soon join the many advanced countries that have done so a long time ago and thus improve care for its elderly population.

**Marija Kušan Jukić, Ninoslav Mimica: DELIRIUM AND DEMENTIA**

Andrija Štampar Teaching Institute of Public Health, Center for mental health and prevention of addiction, Zagreb, Croatia

We would like to present psychiatric approach to delirium in people with dementia (PwDs). Delirium is a complex neuropsychiatric syndrome of acute brain failure characterized by a mix of cognitive and non-cognitive symptoms. The presence of symptoms of various psychiatric disorders in clinical picture of delirious patients leads to differential-diagnostic doubts, which are further complicated by the symptoms of comorbid physical or neurological conditions. Psychiatrists' skills in assessing cognitive function and psychopathology, along with their knowledge of the effects, side effects, and interactions of psychotropic medications, make a psychiatric approach important in the multidisciplinary care of patients with delirium. Delirium in 2/3 cases occurs in PwDs, and is followed with complications, prolong hospitalizations, greater risk of institutionalisation and lethal outcome. Psychiatrists also have an important role in assessing the risk to the safety of the patient himself and the person in environment. It is estimated that around 7% of patients attempt some form of deliberate self-harm during an episode of delirium. We would focus in our work on optimal management of delirious crisis and on a number of skills which are necessary to optimally overcome and resolve delirious crisis.

**Zrnka Kovačić Petrović: ADDICTIONS IN THE ELDERLY**

University of Zagreb School of Medicine; University Hospital Vrapče, Department of Psychiatry and Psychological Medicine; Addiction ward, Zagreb, Croatia

Although misuse of psychoactive substances (PS) among people over 60 is one of the fastest growing health problems, it is still underestimated, under-identified, under-diagnosed, and thus under-treated. The increase in the misuse of PS in the elderly is considered an "epidemic in the making", but the incidence and prevalence of the addiction in the elderly is unknown. Prevalence rate of PS misuse ranges from 1% to 67% and depends on the type of PS. The most commonly used PS in elderly are alcohol, nicotine, and prescribed drugs (benzodiazepines, hypnotics, sedatives, painkillers, etc.). Older people most often use prescription drugs such as benzodiazepines, sedative-hypnotics, and opiate painkillers. All of these drugs have addictive potential, very often elderly share them with other people, and use higher doses than prescribed or use them in a way of abuse or addiction. The risk factors for the occurrence of substance use disorders (SUD) among elderly are numerous, such as poor physical health, chronic pain, polypharmacy, psychiatric comorbidities, social isolation, disability, retirement, etc. Alcohol abuse and addiction are the most common SUD in the elderly, which are often not recognized by health professionals. These disorders in older age increase the possibility of the development of other mental disorders (depression, dementia) and physical illness (strokes, cardiovascular problems, heart diseases, malignant diseases, etc.). More than 10% of people over the age of 65 reported binge drinking in the past month, and this prevalence is steadily increasing. This is of particular concern because older people use a variety of medications that interact with alcohol, have health problems that can be exacerbated by alcohol consumption, and may be more prone to falls and other alcohol-related injuries. Since many physical and cognitive deficits in the elderly are related to the aging process, it is difficult to recognize the misuse of PS, including alcohol, which very often leads to failure to recognize the causes of the ailments. Although there is an increasing number of elderly people who come for treatment due to the misuse of alcohol and other PS, unfortunately a large number of them come at a stage when numerous consequences and complications of addiction are present.

Therefore, it is important that family medicine doctors recognize these disorders. Their interventions should be aimed to educate the elderly about the harmfulness of the misuse of PS, motivate them for change, and refer them to more intensive and specific treatment, when necessary.

## **PSYCHOPATHOLOGY SUMMER SCHOOL**

### **Norbert Müller: NEUROINFLAMMATION IN SCHIZOPHRENIA – ACTUAL STATE OF KNOWLEDGE**

Klinik für Psychiatrie und Psychotherapie der Ludwig-Maximilians-Universität München

Levels of proinflammatory markers, such as cytokines, have been found to be increased in the blood and cerebrospinal fluid of patients with schizophrenia. Furthermore, in animal models pre- or perinatal elicitation of the immune response may increase immune reactivity throughout life. Numerous epidemiological and clinical studies have provided evidence that a variety of infectious agents are risk factors for schizophrenia and other psychoses. For example, a large-scale epidemiological study performed in Denmark clearly showed that severe infections and autoimmune disorders are such risk factors. The vulnerability-stress-inflammation model may help to explain the role of inflammation in schizophrenia because stress has been shown to increase proinflammatory cytokines and may even contribute to a chronic proinflammatory state. The immune system itself is assumed to play an important role in schizophrenia, just as it does in autoimmune disorders, all of which involve genes, the environment, and the immune system. Changes in dopaminergic, serotonergic, noradrenergic, and glutamatergic neurotransmission have been found in low-level neuroinflammation and consequently may be key factors in the generation of symptoms of schizophrenia. Further support for the relevance of a low-level neuroinflammatory process in schizophrenia is provided by the loss of central nervous system volume and microglial activation demonstrated in neuroimaging studies. Last but not least, the benefit of anti-inflammatory medications found in some studies and the intrinsic anti-inflammatory and immunomodulatory effects of antipsychotics provide further support for the role of inflammation in this debilitating disease.

### **Margherita Bechi: EMPATHY FOR PSYCHOLOGICAL AND PHYSICAL PAIN IN BORDERLINE PERSONALITY DISORDER**

San Raffaele-Turro Hospital, Clinical Neuroscience Dept, Milano, Italy

**Introduction/Objectives:** Borderline Personality Disorder (BPD) is characterized by a severe impairment of the emotion regulation system, which significantly impacts interpersonal functioning. The ability to perceive and correctly interpret their own internal and external emotional stimuli as well as other ones seems to be altered in BPD. Empirical research observed in these patients an hyper-affective resonance with the mental state of others that could be determined by a dissociation between the cognitive and affective components of empathy. Moreover, BPD seems to be impaired in the ability to take the perspective of others in the perception of pain: as a matter of fact, people with BPD show a hyposensitivity and greater tolerance to physical pain and hypersensitivity to psychological pain.

**Participants, Materials/Methods:** the aims of this study are: 1. to investigate empathy for physical and psychological pain in sample of 50 subjects with BPD and 50 healthy controls, using a new German task: the Social Interaction Empathy Task (SIET); 2. to study the possible correlations of empathic abilities with other main components of the illness such as psychopathology, alexithymia and possible traumatic life events.

**Results:** Data analysis showed that patients rated neutral and psychologically painful situations as more painful than healthy controls, only in third- perspective, and they rated physical painful situations as less painful in first- perspective. Moreover, patients seemed to show an hyposensitivity to physical pain in first person perspective. In

contrast, controls did not differentiate either by pain intensity in different categories of stimuli, nor between the perspectives. Lastly, we observed a correlation with severity of symptoms, emotion recognition and alexithymia.

**Conclusions:** Overall, our data allowed for the first time to investigate empathy to physical and psychological pain in an Italian sample of BPD subjects. Even with a small sample, preliminary data gave an important contribute to clinical research showing a deficit in emotion recognition empathy correlated to relevant factors of the disorder.

### **Giulia Agostoni: LOOKING INTO THE BRAIN THROUGH THE LANGUAGE WINDOW**

IRCCS San Raffaele Hospital, Milan, Department of Clinical Neuroscience, Milano, Italia

**Introduction/Objectives:** People with schizophrenia display pronounced cognitive and linguistic-communicative deficits, especially in pragmatics, which is a sophisticated communicative ability that allows to appropriately use and interpret language in a wide range of contexts and situations. To date, these significant impairments, which deeply affect patients' functioning and quality of life, are not satisfactorily addressed by currently available treatments and contribute to the disability associated to the disease. To address these unmet clinical needs, the identification of reliable and easy-to-implement markers is crucial. In this view, Electroencephalography (EEG) represents a feasible, non-invasive, effective, and powerful tool that recently gained a renewed interest in research in psychiatry. Several EEG biomarkers have been highlighted with possible diagnostic value and linked to specific cognitive processes. Among the most replicated, Mismatch Negativity (MMN), assessing the ability to process an unexpected deviant stimulus, and alpha activity, a measure of cortical arousal and synchronization as well as of brain networks integrity, are both altered in schizophrenia and linked to cognitive processes. More recently, aperiodic activity, which seems to indicate the level of synchronization within neural networks, has gained popularity, although still poorly explored in schizophrenia, with no studies on the relation with cognition. Despite the promising relationship between EEG markers and psychopathological and cognitive features, to date a systematic assessment to identify a "neuropsychophysiological" profile (which combines clinically relevant EEG markers and neuropsychological data), consistent with the supposed altered process in schizophrenia is still missing. To fill this gap, the present study aims to identify brain signatures combining neurophysiological and neuropsychological measures in people with schizophrenia.

**Participants, Materials/Methods:** Fifty-six subjects with schizophrenia were enrolled and underwent a 128-channels EEG recording including a 5 minutes resting state with open eyes and a MMN task. Patients were also assessed for global cognition, pragmatic abilities, and psychopathology.

**Results:** EEG data for MMN amplitude, alpha and aperiodic indexes were obtained. Pearson correlation analysis between EEG measures and performance in cognitive and linguistic tasks, as well as psychopathology, were run. Results showed significant correlations between 1) MMN and both cognition (especially verbal memory and attention) and pragmatics, in particular the comprehension of figurative expressions; 2) alpha activity and the severity of psychopathology (especially negative symptoms); 3) aperiodic activity and both cognition especially working memory, attention, and psychomotor speed) and pragmatics, in particular figurative language interpretation.

**Conclusions:** Our results show the relationship between different electrophysiological indexes and both pragmatics and cognition, thus paving the way for increasing the knowledge on the neurocognitive architecture of the mind, as well as for the identification of possible treatment targets and markers for more refined prediction of diagnosis and treatment outcome. The identification of electrophysiological correlates of pragmatic and cognitive impairments may provide novel targets for treatment, including the use of combined rehabilitative interventions with neuromodulation techniques, such as transcranial magnetic stimulation and neurofeedback, which currently represent a promising therapeutic avenue for cognitive deficits, but still hampered by the lack of reliable markers.

**Monika Zdravkovic: LINKING ADVERSE CHILDHOOD EXPERIENCES TO BORDERLINE PERSONALITY DISORDER FEATURES. THE ROLE OF ATTACHMENT ANXIETY AND PERCEIVED SOCIAL SUPPORT**

Leiden University, Institute of Psychology, Department of Clinical Psychology, Leiden, Netherlands

**Introduction/Objectives:** Adverse childhood experiences (ACE) have been consistently mentioned as risk factor for the development of borderline personality disorder (BPD). However, the exact developmental pathways, as well as the question how the severity and type of abuse and neglect are related to different features of BPD, are still not well understood. An important underlying mechanism might be an insecure attachment, while perceived social support is believed to function as protective factor. Thus, the present study examined the predictive effects of distinct ACE on individual BPD features, and the role of attachment anxiety and perceived social support in linking ACE to BPD.

**Participants, Materials/Methods:** Questions were investigated using multivariate, mediation, and moderated mediation analyses in a large, diverse sample of international participants (N = 1966).

**Results:** Differential effects of distinct ACE were found with emotional abuse demonstrating the strongest effects on all four BPD features. Sexual abuse was positively related to some BPD features, while physical abuse showed a negative relationship to all four BPD features. No effect of emotional nor physical neglect was apparent. Attachment anxiety mediated the relationship, whereas no moderated mediation effect in combination with perceived social support was observed.

**Conclusions:** Given these findings, the prevention of ACE seems critical and should be regarded as first-line intervention in stopping the vicious cycle of BPD symptom manifestation. Still, adequate treatment with a focus on developing secure attachment could be beneficial to counterbalance the effects of ACE.

**SPORTS PSYCHIATRY SYMPOSIUM****Darko Marčinko: HEALTHY AND PATHOLOGICAL NARCISSISM IN FOOTBALL PLAYERS**

University Hospital Centre Zagreb, Department of Psychiatry and Psychological Medicine, Zagreb, Croatia

**Introduction/Objectives:** The prevalence of personality problems in the general population seems to be substantial such as in the population of football players. Investigations suggest that underlying personality pathology is associated with greater dropout from sport activities and poorer outcomes for results.

**Participants, Materials/Methods:** One of the most influential approaches to personality within the framework of psychopathology is Kernberg's psychodynamic model of personality dysfunction largely based on object relations theory, describing personality pathology as being influenced by an interrelated constellation of neurobiological and environmental factors. To elaborate on the development of personality impairment, Kernberg introduced the concept of personality organization (PO). An individual's levels of PO can be described by its position along three dimensions: identity diffusion, primitive defense, and reality testing. The levels of PO with accompanying three dimensions span across a continuum according to severity, ranging from neurotic PO to higher and lower level of borderline PO and psychotic PO. Pathological narcissism is dominantly situated at the higher and lower level of borderline PO. Although some pathological narcissism traits can also be found at the level of neurotic PO. Detailed investigation of the underlying psychological mechanisms by which PO contributes to more acute psychological reactions, particularly anxiety, impulsive behavior and mood disturbances are important for distinction between healthy and pathological narcissism in football players. One of the more prominent negative emotions arising in football players with personality pathology seems to be shame, a painful emotion, often associated with narcissistic defences. Shame can

range from mild to intense and can facilitate other difficult emotions such as feelings of helplessness and inferiority, with a strong need to hide these inadequacies.

**Conclusions:** During the presentation I will present some of our investigations regarding personality organization and parameters of pathological narcissism and shame.

### **Stipe Drmić: MENTAL BENEFITS OF SPORTS-SPORTS THERAPY IN MENTAL ILLNESS**

University Hospital Dubrava, Department for psychiatry, Zagreb, Croatia

**Introduction/Objectives:** Mental illness is a global issue that affects millions of people worldwide. While there are various treatments available, sports therapy has emerged as a powerful tool in combating the debilitating effects of mental illness.

**Participants, Materials/Methods:** Sports and physical activity have been shown to have a positive impact on mental health by reducing stress, anxiety, and depression. When you exercise, your brain releases chemicals called endorphins, which are natural painkillers that promote feelings of happiness and wellbeing. Regular exercise also helps to improve sleep quality, reduce stress levels, and boost self-esteem. Sports therapy is a form of therapy that uses physical activity and exercise as a way of promoting mental and emotional wellbeing. It can be used in conjunction with traditional forms of therapy or as a standalone treatment. Studies have shown that sports therapy can be effective in treating a variety of mental health conditions, including depression, anxiety, and post-traumatic stress disorder (PTSD). Sports therapy can also be particularly beneficial for individuals with substance use disorders. It provides a healthy and productive outlet for energy that might otherwise be channeled into negative behaviors. Additionally, exercise has been shown to reduce cravings and promote recovery in individuals with addiction issues.

**Conclusions:** In conclusion, sports therapy is an exciting and effective tool in the treatment of mental illness. It provides numerous mental health benefits, including reducing stress, anxiety, and depression. Moreover, it can be tailored to meet the unique needs and preferences of each individual. By incorporating sports therapy into traditional treatment plans, we can help individuals lead healthier, happier lives.

### **Katarina Šore, Frane Franić, Stipe Drmić, Darko Marčinko, Valentin Z. Markser, Tomislav Franić: HOW TO ACCESS MENTAL HEALTH IN ATHLETES - THE ROLE AND PROBLEMS OF ASSESSMENT AND SCREENING TOOLS**

Split University Hospital, Split, University of Split School of Medicine Croatia,  
School of Medicine, Psychiatry department, Split, Croatia

**Introduction/Objectives:** Mental health problems in athletes recently became a field of interest and the number of research in this field is increasing rapidly. Studies performed concluded that there are mental health problems among athletes. Influential international organizations such as World Health Organization (WHO) and International Olympic Committee (IOC) got involved in this raising issue. WHO issued several documents in which it is promoting physical activity as a way to support health in general as well as mental health. IOC developed the SMAHT-1 questionnaire that should help identify athletes who may develop mental health problems. Since we are not aware of the survey conducted among Croatian athletes that aims to explore their mental health we decided to do it by using the SMAHT-1 questionnaire.

**Participants, Materials/Methods:** We decided to conduct a study on competing athletes in Croatia by using the SMAHT-1 questionnaire. The questionnaire is in English, so we will first translate it (forward, backward), then pilot it, develop it, and validate it. Our hypothesis is that SMAHT-1 will have a structural model comparable to the English

model with high sensitivity and specificity. We expect to observe an association between the athletes and their mental health that will be presented in scores.

**Results:** We expect the SMAHT-1 questionnaire to prove comparable to the English model and reveal mental health symptoms among competing athletes in Croatia. We also expect it to find correlations between gender, age, sport type, and specific mental health symptom.

**Conclusions:** We expect to prove that the use of the SMHAT-1 questionnaire among competing athletes in Croatia will help in the early detection and consequentially in the early treatment of mental health symptoms among competing athletes in Croatia.

## NEUROPSYCHIATRY SYMPOSIUM (ORAL PRESENTATIONS)

### **Valentino Rački, Gloria Rožmarić, Eliša Papić, Mario Hero, Bojana Petek, Borut Peterlin, Vladimira Vuletić: OBTAINING A GENETIC DIAGNOSIS OF DYSTONIA: A SINGLE TERTIARY CENTRE EXPERIENCE**

Clinical Hospital Center Rijeka / Faculty of Medicine, University of Rijeka, Department of Neurology, Rijeka, Croatia

**Introduction/Objectives:** Advent of next-generation sequencing has greatly impacted gene discovery and enabled more genetic diagnoses of dystonia than ever before. Our aim was to assess the clinical impact of whole-exome sequencing in our tertiary centre.

**Participants, Materials/Methods:** Our study cohort includes patients from the Clinic of Neurology at the Clinical Hospital Centre Rijeka, referred to genetic testing from 2020 to 2022. Exome sequencing was performed at the Clinical Institute of Genomic Medicine, UKC Ljubljana using standardized protocols and using a determined hereditary dystonia gene panel. Identified variants were classified according to the ACMG and AMP 2015 joint consensus recommendation, along with ACGS recommendations where applicable.

**Results:** We have performed exome sequencing in 20 patients. Causative pathogenic and likely pathogenic mutations have been confirmed in 7 patients (35%, GNAO1, CHD8, GNAL, YY1, KMT2B and GNB1), while variants of uncertain significance (VUS) were found in 2 patients (10%, ADCY5 and SPG7). Regarding dystonia type, the diagnostic yield for generalized dystonia was 77.7%, with one additional VUS finding (11.1%). In segmental dystonia there was one VUS and one carriership, while in focal dystonia there was no findings. Retrospectively, using the proposed dystonia clinical score (Zech et al., 2020) would have been highly predictive in our patients.

**Conclusions:** Genetic testing using whole-exome sequencing is recommended for dystonia patients, especially in generalized and segmental dystonia, which is in line with previous findings in the literature. This enables a complete and accurate genetic diagnosis in patients, which has real-life implications given the younger patient population.

### **Kenan Galijašević, Emira Švraka, Belma Šljivo: THE INFLUENCE OF DAILY LIFE ACTIVITIES ON THE MENTAL HEALTH OF STUDENTS**

Faculty of Medicine, University of Zenica, Department of Health care, Zenica, Bosnia and Herzegovina, Zenica, Bosnia i Hercegovina

**Introduction/Objectives:** The general factors that lead to the appearance of depression and anxiety in the student population are related to academic stress arising from pre-exam and exam activities of students. Also, the excessive use of electronic devices in the process of learning and reading can lead to the appearance of depressive symptoms among students. The aim of the study: To determine the differences in the length of students' daily activities, to assess



the degree of depression of students, to correlate the length of students' daily activities with the degree of depression of students.

**Participants, Materials/Methods:** Cross-sectional study, conducted in the period May - June 2021 at the University of Zenica, at four faculties (Medicine, Economics, Mechanical Engineering and Law). The total number of students voluntarily included in the research was 147. Research instruments: General questionnaire for assessing the length and duration of students' daily activities (length of sitting, studying, working on the computer and mobile phone), and the Patient Health Questionnaire (PHQ-9).

**Results:** The amount of student stress increases with the prolonged duration of daily activities related to studies. The daily length of activity over four hours was found in 12.2% of students in sitting, in 38.1% in studying, in 36.1% in using a computer and in 60.5% of students in using a mobile phone. According to the results of the Patient Health Questionnaire, 27.2% of students do not have depression. Mild depression was found in 45.6%, moderate in 18.4%, moderately severe in 5.4%, and severe in 2.7% of students, with a statistically significant difference in the relationship between the degree of depression and the years of study ( $p < 0.05$ ).

**Conclusions:** A low positive correlation was found in the relationship between the daily length of sitting, studying and working on the computer with the degree of depression, and a moderately strong positive correlation between the use of mobile phones and the degree of depression of students.

#### **Jure Koprivšek, Andreja Čelofiga: DO CHANGES IN LEARNING AND TRAINING OF STAFF COMMUNICATION SKILLS AFFECT THE INCIDENCE OF AGGRESSIVE BEHAVIOR ASSOCIATED WITH CERTAIN MENTAL DISORDERS IN HOSPITAL INTENSIVE PSYCHIATRIC SETTINGS**

University Medical Centre Maribor, Department of Psychiatry, Maribor, Slovenia

**Introduction/Objectives:** As most guidelines for the management of aggressive behaviour in acute psychiatric patients describe the use of de-escalation as the first-choice method, with inconsistent evidence for its effectiveness, we assessed the effect of verbal and non-verbal de-escalation on the incidence and severity of aggression and the use of physical restraints in acute psychiatric wards in all psychiatric hospitals in Slovenia, after performing comprehensive education and training of verbal and non-verbal communication and de-escalation (manual, workshops, video materials, role-playing, etc.), without changes in the structure of staff or units.

**Participants, Materials/Methods:** Patients on intensive wards in all Slovenian psychiatric hospitals observed by number of aggressive incidents and coercive measures in the baseline and intervention periods of the study, and the severity of aggressive incidents (SOAS-R) and the duration of coercion in the baseline and intervention periods of the study in a multicenter, randomized controlled trial with cluster randomization. Statistics: regression analysis - negative binomial regression model.

**Results:** The use of de-escalation techniques stops the progression of already perceived aggression into more serious forms. The impact of de-escalation on the reduction of repeated incidents is significant - increased staff attention, the success of de-escalation is greater in these patients when using techniques that were already effective in previous incidents. In the most serious forms of aggression, the use of de-escalation is less effective, similar to other non-pharmacological measures.

**Conclusions:** The research results so far show that de-escalation is effective in reducing the incidence and severity of aggression and the use of physical restraints. When planning changes in the teaching, training, and implementation of these methods, available institutional and staff resources must be considered. It is also necessary to monitor how efficiency of taught methods performed by staff changes over time, so future continual education can be planned based on the gathered data. This evaluation should be the subject of future research.

**Igor Mošič: “Thukdam” - introduction to the post-mortem altered state of the mind**

N2SED, NAM Emotional Hygiene, Rijeka, Croatia

**Introduction/Objectives:** The main intention of this presentation is to introduce the participants to an extraordinary state of human mind named “thukdam”. “Thukdam” is an altered state of human mind, mostly experienced by advanced Tibetan meditators, during which a person is declared clinically dead, but the body remains fresh for days or weeks without any signs of decomposition or discolouration. While deceased person is in “thukdam” post-mortem body changes, “rigor mortis” does not set in.

**Participants, Materials/Methods:** Scientific inquiry into “thukdam” phenomenon has begun a few years ago under the initiative of His Holiness the Dalai Lama and leading American and Russian neuroscientists. “Thukdam” is a Tibetan word where “thuk” is a honorific word for mind, and “dam” literally means promise, but in this context it means calm abiding (samadhi) meditative state. “Thukdam” is an observable reality and efforts are made by scientific community to understand the phenomenon and its implications. Most rigorous, long-term ongoing research project on “thukdam” is called “The Thukdam Project” and is created at the “University of Wisconsin-Madison’s Center for Healthy Minds“ in Madison, WI, USA. The Thukdam Project” combines the knowledge and skills of neuroscientists, forensic anthropologists, doctors, psychologists, philosophers with the teams of Tibetan monk-researchers in India. At the same time, the Russian scientists, particularly leading experts from the Institute of the Human Brain, St Petersburg established research laboratories in the Tibetan settlements in Bylakuppe and Mundgod in India. Investigating “thukdam” opened many important and profound questions about the process of dying, such as: When should we harvest organs?, Could there be a meditation practice that makes the body go into a state of metabolic suspension?, Where exactly to measure the activity of the mind which stays in “thukdam”? And another very important question: Is the phenomenon of “thukdam” a counterexample to the belief that the human mind is an epiphenomenon of the brain?

**Results:** During the presentation many documented examples of people abiding in “thukdam” will be presented, followed by the scientific findings, and first-ever scientific study into thukdam. While it is explored by scientists, many experienced practitioners and meditators are continually dying with “thukdam”.

**Conclusions:** From the side of the practitioner, “thukdam” is a post-mortem altered state of subtle mind which is calmly abiding in relaxed, stable, single-pointed concentration during such a stressful situation like physical death. Single-pointed concentration is also known as calm abiding meditation. Since it is the potential of the mind on a subtle levels, we can infer that developing calm abiding is also potential of the mind on a coarser levels of everyday waking activity. Calm abiding of the mind is completely opposite to scattered and distressed state of the mind. It is well known that stress activates a complex network of hormones known as the hypothalamic–pituitary–adrenal (HPA) axis. Prolonged activation of the HPA axis leads to dysregulation and has many clinical consequences. Therefore, exploring “thukdam” can be very useful to better understand the process of dying, but it can also give us many insights into ways to lead a happier and more fulfilling life.

**Lea Murn, Roberto Mužić: Will Artificial Intelligence Treat Mental Disorders efficiently as Professionals?**

Clinical Hospital Dubrava, Department of Psychiatry, Zagreb, Croatia

**Introduction/Objectives:** We are living in a technological age where artificial intelligence is getting more noticed by different services providing health care. One such field of possibility is the treatment of mental illnesses. Although the way for clinicians to fully understand the potentials of AI in their everyday practice is still wide open, computer scientists and mental health experts are collaborating to use machine learning for the diagnosis, treatment, and prediction of psychiatric disorders. The aim of this study was to explore the challenges and limitations associated with the usage of AI in treating mental illnesses.

**Participants, Materials/Methods:** A literature review was conducted to gain insight into the current state of knowledge regarding the use of AI in mental health care. PubMed and Google Scholar were used to locate studies that conducted original clinical research in an area relevant to AI and mental health.

**Results:** Research has shown that machine learning algorithms can facilitate early disease detection, better understand disease progression, optimize medication and treatment dosages, and uncover novel treatments. AI-based techniques have been effectively used in the prediction of psychiatric symptoms including psychosis. Another possible application of machine learning algorithms is the prediction of suicide. Language models can identify „the language of suicide” with great success of accuracy. On one hand, innovations such as computer-assisted therapy and moderated online social therapy have proven successful in ameliorating symptoms of depression, anxiety, and psychosis through online peer support. This could present an opportunity to facilitate the delivery of tailored therapy content while facilitating privacy and autonomy. On the other hand, some of the applications that were designed created a therapeutic alliance with clients despite lacking memory and processing power. However, the impact of these chatbots on a large number of people using them is yet to be fully assessed.

**Conclusions:** We are facing a future where AI will be an inevitable partner to clinicians in diagnosing, preventing and treating mental health disorders. AI has the potential to help redefine mental illnesses more objectively, identify them at an earlier stage, and personalize treatments based on individual characteristics. Despite its possibilities, artificial intelligence technology holds potential pitfalls and ethical implications to consider. Further assessment is necessary to fully understand how AI can supplement clinical practice and where additional research is needed.

#### **Eliša Papić, Valentino Rački, Vladimira Vuletić: FUNCTIONAL DISORDERS IN PARKINSON'S DISEASE PATIENTS WITH DEEP BRAIN STIMULATION – A CASE SERIES**

KBC Rijeka, Department of Neurology, Rijeka, Croatia

**Introduction/Objectives:** Functional neurologic disorders (FND) are disorders with a neurologic presentation but without a clear organic cause. They mostly present as symptoms mimicking actual disorders and can have an organic background, making their proper diagnosis especially challenging. A specifically interesting phenomenon is the emergence of FNDs in patients with Parkinson's disease (PD) with deep brain stimulation (DBS). We report 3 such cases.

**Participants, Materials/Methods:** We present three patients that were treated at the Clinic for Neurology in Rijeka and presented with FND-s after DBS. First is a 62-year old female patient with bilateral STN-DBS that presented with severe right-sided tremor, the second is a 54-year old male with STN-DBS that presented with extreme „stiffness“, hypophonia and a history of dopamine abuse and the third is a 50-year old bilateral STN-DBS patient that presented with bilateral leg weakness which would emerge only in walking, but not in other activities.

**Results:** After using broad diagnostic methods and excluding other potential causes for the symptoms, we utilized a multidisciplinary approach including physical therapy and work therapy, psychological support as well as methods such as „sham“ stimulation, distraction and suggestion, achieving a beneficial therapeutic effect in the end and the improvement of the symptoms over time.

**Conclusions:** FND-s pose a challenging diagnostic and therapeutic problem in modern neurology and even more so in patients with underlying conditions such as PD, especially in those with DBS. A multidisciplinary approach should be utilized when treating these complex patients and for the best therapeutic effect.

## SYMPOSIUM - PROFESSIONAL MEDICAL ETHICS: CURRENT VIEWS, APPROACHES, AND CHALLENGES

### Lectures:

- A. (Bio)ethics and professional medical ethics - a very short introduction (Marko Ćurković<sup>1,2</sup>)
- B. Duties of physicians towards oneself (Ana Borovečki<sup>2</sup>, Ivan Pavao Gradiški<sup>1</sup>)
- C. Ethics at the end-of-life - general and specific views (Marko Ćurković<sup>1,2</sup>, Diana Špoljar<sup>3</sup>)
- D. Medical professionalism – legal framework (Sunčana Roksandić Vidlička<sup>4</sup>, Aleksandar Maršavelski<sup>4</sup>)
- E. E-professionalism - professional medical ethics in emerging digital landscapes (Kristijan Sedak<sup>5</sup>, Marko Marelić<sup>2</sup>, Tea Vukušić Rukavina<sup>2</sup>)

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<sup>2</sup>School of Medicine, University of Zagreb, Zagreb, Croatia

<sup>3</sup>Faculty of Law, University of Zagreb, Zagreb, Croatia

<sup>4</sup>Croatian Catholic University, Zagreb, Croatia

Professional medical ethics (or as commonly referred to – medical professionalism) is critically relevant and essential for contemporary healthcare. As such, professionalism has many different faces and many interrelated roles and is inevitably and often inextricably related to a broader societal context.

Within this symposium, a diverse group of authors from various backgrounds and perspectives aims to present some of the current views and approaches to professional medical ethics while discussing some of its most pressing challenges.

In that sense, within the lecture under the title: "(Bio)ethics and professional medical ethics - a very short introduction" the author explores possible philosophical and ethical foundations of professional medical ethics. Presumably, there is an important distinction between ethics in medicine and ethics of and for medicine. Ethics in medicine is ethics applied to and used in the field of medicine (or ethical issues occurring within it). Today, ethics in medicine yielded many different approaches underpinned by many different moral theories and practices. However, ethics for and of medicine, that is, professional medical ethics is ethics that underpins, emerges from, and guides everyday medicine. It construes medicine as a fundamentally moral endeavor, and can be conceived either as an internal (meta) organizing principle or a shared justificatory structure of medicine.

Lecture: "Duties of physicians towards oneself" deals with the pressing topic of physicians' wellbeing and related duties. Increasing evidence indicates that many physicians are unwell, with high reported rates of physicians' stress, fatigue, burnout, substance abuse, and depression. Despite being internally worrying, all of those also significantly negatively affect healthcare systems and patient care (its very purpose). There are many possible reasons beneath such occurrences. However, the more fundamental question is what physicians do for themselves, their close, near and dear ones, their colleagues, and their patients ought to do about them. Answers to those questions are further sought through discussion of recent empirical findings of the survey conducted on medical students from the School of Medicine of the University of Zagreb.

Within the lecture titled: "Ethics at the end-of-life - general and specific views", the authors present various general theoretical and practical views on prototypical ethical issues in contemporary medicine – that of decisions of and at end-of-life. Concepts of medically assisted dying (physician-assisted suicide and euthanasia) are laid out as well as their ethical (counter)arguments. More specific views are presented from the perspectives of recent comprehensive empirical findings, namely, those of healthcare professionals and the general public in Croatia.

The lecture titled: "Medical professionalism – legal framework" presents the evolution of medicine from mostly an unregulated profession, in which responsibility was based on the ethics of its agents (physicians), that is, on specific

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prevailing social rules at a given time towards the introduction and implementation of legal frameworks designed to foster and ensure medical professionalism. Thus, the rise of medical professionalism witnessed in the last century cannot be attributed only to the development of medicine but also to the development of the legal framework. Today, several legal regulations, on regional and international levels, help ensure the professional provision of health care and the right to health care for all. However, for medical professionals to be willing and able to apply necessary standards in their medical practice, in nearly all contexts, medical profession is strictly regulated through the prescription of special (two-track) conditions based predominantly on a human rights perspective.

Lastly, the lecture "E-professionalism - professional medical ethics in emerging digital landscapes" present the challenges healthcare professionals face within new and emerging, technologically mediated contexts. More specifically, the benefits, as well as dangers of social media, on medical professionalism are further explored and summarized. All of these urge for new and novel conceptualizations of medical professionalism, those built around and within digital landscapes, such as those currently commonly encompassed within the notion of e-professionalism.

## POSTERS PSYCHIATRY

**1. THE ROLE OF INTERPERSONAL ANS CO-REGULATION IN THE ETIOLOGY AND TREATMENT OF FIBROMYALGIA - A CASE REPORT.****Špela Brecelj**

Mokša, Institute for integrative medicine, psychotherapy and education, Ljubljana, Slovenia

**Introduction/Objectives:** After decades of looking into the mystery of the pathological processes that bring about the tormenting, yet invisible and hard-to-objectify symptoms of fibromyalgia (FM), the theory of central sensitization syndrome has been proposed as the main underlying pathophysiological process. It has also been observed that psychological trauma and adverse childhood experiences might be linked to chronic low-grade inflammatory processes in the brain, resulting in chronic central pain, fatigue, fibro-fog and depression later on in life. With relational psychotherapy being the therapeutic modality of choice in etiological treatment of psychological trauma, what is its role in the treatment of fibromyalgia?

**Case report:** This case study presents a 57-year-old married, well-educated woman with FM and no significant psychopathology, but with marked alexithymia and denial of unpleasant emotions. She was prescribed duloxetine 120 mg, NSAIDs, an occasional tramadol/paracetamol and pantoprazole. She started her weekly psychotherapeutic process with the author, an MD, then resident in psychiatry, certified integrative psychotherapist 3 years ago. Emotional education for alexithymia was key, as well as creative exploration of the yet unconscious affective wealth of information about the patient's own needs, wants and boundaries. A therapist with a well-regulated autonomic neural state, being open for contact, is a valuable source of co-regulation for the client through processes of interpersonal physiological attunement made possible by mirror neurons. Continuous contact with a mindful, regulated, affectively, developmentally and rhythmically attuned therapist provides the patient with a reliable source of relational harmonizing the ANS and stress-response axis. It also provides a model for future self-regulation.

**Results:** New ways of emotional processing and deeper, more secure connections to significant others allow her to access the regulated autonomic states inside the window of tolerance daily. This results in significantly higher quality of life, less pain, less stiffness and more self-attuned, self-protecting behavior going forward. Her integration process also promises an option of potentially, eventually reducing the need for less-than-optimally effective pharmaceuticals

and thus ameliorating their unwanted side effects. **Conclusions:** Psychotherapy is already recognized as one of the essential elements of an interdisciplinary treatment of FM and similar syndromes. Could relational integrative methods offer not only symptomatic relief, but etiological treatment of such syndromes? Humans being relational creatures, the case for relational therapy of essentially relational diseases seems strong and we are excited to put it to test with further research.

**2. DEPRESSIVE SYMPTOMS IN GLIOBLASTOMA MULTIFORME - A CASE REPORT.****Nikola Sikirica, Tonči Mastelić**

University Hospital of Split, Psychiatry Department, Split, Croatia

**Introduction/Objectives:** Although data are scarce, some studies indicate that in 60% to 85% of cases, psychiatric symptoms precede brain tumors. However, such symptoms rarely cause suspicion of a tumor process. Our goal is to raise awareness of this problem and present the case of a patient in whom glioblastoma multiforme (GBM) manifested itself in depressive symptoms.

**Case report:** An elderly female patient comes to the emergency psychiatric admission accompanied by her son. 8 days before, she was discharged from the Day Hospital of the Psychiatry Department. She was treated for alcoholism. A few days before admission, she hardly communicates, has difficulty forming sentences, withdraws into herself. She has a reduced affect, listlessness, weaker appetite. The patient was also examined by a neurologist. Speech was described as scarce but properly articulated. MSCT and MR revealed a high-grade primary glial process (glioblastoma multiforme) left frontally, with edema and compression of the frontal horn of the left lateral cerebral ventricle and consequent subfalcine herniation to the right side.

**Results:** In our patient, GBM was manifested by depressive symptoms. There are very rare cases, such as this one, in which there is no clear neurological outcome. Data so far suggest that localization of the tumor process frontally, as in the case of our patient, leads to a depressed clinical picture and personality changes. Symptoms such as loss of energy and appetite, which is also present in our patient, make the depressive clinical picture more often than cognitive or affective symptoms. Although it is not an official diagnosis, the literature refers to Disorders of diminished motivation (DDM). It is a spectrum consisting of apathy, abulia and akinetic mutism. Glioblastomas usually present with these symptoms, which share anhedonia and psychomotor retardation with depression. However, it is specific for DDM that patients, even in the case of akinetic mutism,

follow commands, i.e. react to auditory stimuli. The Neuropsychiatric Inventory has been mentioned as a possible useful tool for differentiating between DDM and depression.

**Conclusions:** GBM is an aggressive tumor that is often diagnosed late. Given the frequency of psychiatric symptoms, it is necessary to be aware of the possibility of tumor development. We should be especially careful when symptoms from the DDM spectrum are present, if they appear suddenly and at an unexpected age, if they are therapeutically resistant and if the person has already been treated psychiatrically.

### 3. WHAT IS THE MIND ? A SYNTHESIS OF COGNITIVE AND AFFECTIVE SCIENCE AND NEUROBIOLOGY.

**Mirko Čorlukić, Danko Nikolić, Mara Tripković, Marta Stojanović, Jelena Krpan**

Special hospital for children with neurodevelopmental and motor disorders, Department: Social-psychological, Zagreb, Croatia

**Introduction/Objectives:** There is no single theory of what the mind is, just as there is no single theory of (different aspects of) cognition, emotion, self, consciousness or human behavior. This poster will outline the answer to the question of what drives human behavior and how the mental world of the mind is generated. We can say that both the mind and behavior are biological, just as they are mental. A series of biological systems and processes creates the neurobiological machinery that is the basis of behavior and mental phenomena. We can imagine the mind as a spatio-temporal platform of various mental phenomena and processes - perception, cognition and affects - played out in the field of consciousness. Throughout the poster, the neurobiological machinery - the system of unconscious cognition - is highlighted as a key element in the equation of behavior and the mental. The brain produces the mind in a very specific way, where neurobiological processes generate intelligent behavior and mental phenomena of the mind.

**Participants, Materials/Methods:** We used the works of many researchers and theoreticians of neuro, cognitive and affective science. We strive to connect these works and present a schematic theory of the mind through understanding, conceptualizing, connecting, differentiating, and categorizing different neurobiological and mental systems in the generation of behavioral patterns and the mind. In the textual part of the poster, we highlighted three authors, N.Chater, G.Buszakia and a new theory by D.Nikolić. on the generation of intelligent behavior by

activating subnetworks through metabotropic receptors and G protein gated ion channels.

**Results:** The works of N.Chater talk about how cycles of thought and other mental contents of the mind are often very fluid and unstable, without knowing about it. The inner world of the mind is actually a collection of mental fragments, which the brain instantly repackages into a narrative, a story, which relies on reality with the help of imagination. G. Buzaki points out that the brain creates behavior and mind not dominantly through inputs from the outside, but through intrinsic activity inside-out. Humans do not have a direct, exact and completely accurate approach to neither their own nor other people's minds. We try to understand our behavior through introspection and reflection of our behavior, and other people with theory of mind and compassion.

**Conclusions:** Here we show how behavior and the mind are created from molecular systems, neural networks of the brain, drive-motivation systems, survival circuits, conglomerates of different cognitive subsystems, the self and the affective system. Although it is not known how mental phenomena and intelligent behavior are selected, we believe that it is necessary to better conceptualize the understanding of neurobiological and mental systems in human behavior and mind maintenance. The mind is the result of the interaction between the intrinsic brain, the body, behavior, and the environment.

### 4. SEVERE GBL (GAMMA-BUTYROLACTONE) WITHDRAWAL DELIRIUM - A CASE REPORT.

**Ilonka Vučko Miklavčič, Matija Smrečnik**

University Psychiatric Clinic Ljubljana, Intensive care unit, Ljubljana, Slovenia

**Introduction/Objectives:** The following case report focuses on the association between GBL (gamma-butyrolactone) withdrawal and the subsequent development of delirium and its management in the closed ward of the University Psychiatric Clinic. It presents and takes into account the restrictions according to the Slovenian Mental Health Act. According to data of National Institute of Public Health in Slovenia the intoxication with GHB in years 2013 and 2014 was the most common cause of intoxication among drug users, consequently we record an increase in GHB (gamma-hydroxybutyric acid)/GBL dependence among young adults, without prior experience with other psychoactive substances. Severity of withdrawal symptoms, which we face with, can be considered as a medical emergency and usually treated in our inpatient closed ward of University Psychiatric Clinic.

**Participants, Materials/Methods:** The paper presents a case of young male with a known substance abuse disorders who developed severe withdrawal symptoms after abruptly stopping GBL use. The patient had regularly used GBL for a year before admission, with heavily increased doses and dosing frequency in the final three months. Before seeking help, he tried home GBL reduction titration with little success. He was admitted to our inpatient closed ward for easier detoxication. Soon after the admission he became agitated, disoriented, disorganized, psychotic and delirious and had to be physically restrained. The patient was administered high doses of diazepam, clonazepam and risperidone, without any benefit. He also received intravenous baclofen twice, after which the symptoms seemed to subside, however, he later developed an acute swelling of the tongue, which lead us to stop baclofen. On the fourth day he was transferred to intensive care unit due to suspected respiratory infection and possible malignant neuroleptic syndrome. There, he was sedated and mechanically ventilated for 24 hours, using propofol and dexmedetomidine. He received antibiotic treatment for the respiratory infection. On the second day he seemed to recover completely, reporting no withdrawal symptoms, and presenting with a perfectly lucid consciousness, and no signs or laboratory findings suspect of malignant neuroleptic syndrome. He was later transferred back to the psychiatric closed ward at our clinic where he continued treatment and was discharged on the 6th day.

**Results:** Recent studies suggest that high doses of benzodiazepines (100-300 mg of diazepam daily) are effective in treating GBL and GHB withdrawal. However, in Slovenia we are limited by the Mental Health Act which doesn't allow exceeding maximum daily doses of psychopharmaceuticals in closed wards. When needed to exceed the maximum daily doses the medical consultations is established, but in everyday clinical practice is time-consuming and useless.

**Conclusions:** We treated the patient using maximum allowed doses of different benzodiazepines which resulted in a less than optimal outcome. The treatment was further complicated by the aforementioned respiratory infection and possible malignant neuroleptic syndrome.

**5. POST RESUSCITATION MANIFESTING DELIRIUM CONCERNING SURVIVED PATIENT WITH CARDIOGENIC SHOCK AFTER MYOCARDIAL INFARCTION - A CASE REPORT.**  
**Marija Kostadinovska, Tanja Angjuseva, Tanja Gramosli**

Zan Mitrev Clinic, Department of Psychiatry, Intensive Care Unit, Skopje, N. Macedonia

**Introduction/Objectives:** Patients surviving resuscitation after cardiac arrest (acute heart failure) are at risk of delirium. Delirium is a clinical syndrome caused by a disturbance in the normal functioning of the brain, represented by reduced awareness and reaction to the environment, which can manifest as disorientation, delusions, incoherence and memory impairment.

**Participants, Materials/Methods:** A 65-year-old man admitted to a cardiac surgery hospital after myocardial infarction. On admission to the hospital, there was cardiogenic shock, resuscitation was performed, and the patient was placed on mechanical ventilation. No significant association was found between delirium and the primary cardiac condition; the occurrence of delirium was more related to the presence of hemodynamic or electrical instability, resuscitation, and mechanical ventilation. There were some pre-existing conditions that may predispose to delirium (mild cognitive impairment, depression - due to the loss of his son) untreated medically.

**Results:** He was in cardiogenic shock on hospital admission, resuscitation was given, and the patient was placed on mechanical ventilation. Delirium is common in these patients: the more complex and debilitated the patient, the higher the rate of delirium. Consequently, the occurrence of this syndrome is strongly associated with a worse outcome—mortality or an increased risk of worsening cognitive impairment.

**Conclusions:** Monitoring of risk factors, early recognition and treatment of delirium, as well as regular medical examinations after discharge from the hospital are recommended.

**6. DYNAMIC ROLES OF COGNITIVE ELEMENTS AS ADAPTIVE MODES OF INFLUENCE IN PSYCHOSIS PROGNOSIS.**

**Sriram Balasubramanian**

Chennai, Tamil Nadu, India

**Introduction/Objectives:** The adaptive nature of psychosis development via cognitive and environmental factors and its influence on evolution of the psychotic illness is indicated as a basis of diagnostic importance. There is a conditional dependence of the psyche on its manner of interaction with the environment that can influence the morbidity of neurochemical psychosis onset.

**Participants, Materials/Methods:** The period immediately adjunct to nascent psychosis onset is crucial in determining



the prognosis and evolution of neurological configurations that influence psychiatric morbidity outcomes.

**Results:** The nature of the interaction is complicated via issues of propensity of psyche and biasing towards environmental and cultural variables via surge type relation that influence the manner of the outcome in the diagnostic schemes of morbidity. The integrative cerebral influence on the cognitively adaptive, psychosis influenced, and pathologically progressing mind manifests sensorially in visual, auditory, olfactory and cognitive regimes. Changes such as difference in visual acuity, photisms in the occipital manner of dependence and auric phenomenon in auditory dependence are complexly linked in the schema of adaptive cognitive modes of morbidity progress. These are neurochemical variables that induce novelty and complications in the manner of psychosis evolution that complicate morbidity and diagnosis of the psyche-based experiential being, the patient.

**Conclusions:** These account for unique neurological configurations in the brain as an outcome of psychosis and complications thereof due to the manifestation of cognitive input based adaptive elements.

#### 7. „CHEMOBRAIN“ ASSESSMENT USING NOVEL TOOL – COMPLEX REACTIOMETER DRENOVAC. Maja Ploh, Ana Petranović, Duška Petranović

Faculty of Medicine, University of Rijeka, Rijeka, Croatia

**Introduction/Objectives:** Cognitive impairment extended than expected cognitive decline of normal aging can be noticeable in 25% of patients during cancer-related therapy, which progresses during treatment. Most common problems are related to memory, language, thinking, and judgment, associated with the impaired overall quality of life. The aim of this study was to assess and compare cognitive function in cancer patients initially and during the treatment.

**Participants, Materials/Methods:** The study engaged 100 oncologic patients one month after starting active treatment and 100 healthy participants. Cognitive function was assessed in these patients was assessed Mini-Mental State Examination (MMSE) test and using Complex Reactiometer Drenovac (CRD) – Croatian computational product designed for chronometric testing of participant's performance in convergent thinking, spatial visualization, visual orientation, learning and memory, operative thinking, reaction on the sound, reaction on light, by measuring time to complete the test. Data were analyzed using Microsoft Excel (Microsoft Office) and Statistica v10.0 (StatSoft Inc., Tulsa, Oklahoma, United States).

**Results:** Cancer patients engaged in this study show 58% of impairment in convergent inductive thinking tests, 50% of

impairment in spacial visualization, 55% decline of visual orientation, 32% of regression in learning and memory abilities, 49% come-down in operative thinking test, no impairment in sound reaction, and 36% of debilitation in light reaction test, compared to healthy participants, measured with chronometric instrument. Paper-and-pencil test (MMSE) results reveal that patients combatting cancer, in difference from healthy participants, have a 20% of decline in calculation abilities, 33% impairment in visual recognition, 25% lower results in learning and memory tests, and 33% lower result in verbal instruction test, but without a noticeable difference in spatial visualization and visual recognition, as well as in following visual (written) instructions.

**Conclusions:** This study reveals measurable cognitive impairment in cancer patients, most pronounced in convergent inductive thinking, learning and memory abilities, and operative thinking in both conducted tests. CRD testing appears more sensitive in all testing categories but does not include language, verbal and speaking tests. Therefore, this chronometric instrument can be helpful and complementary to other cognitive assessment instruments in daily clinical practice.

#### 8. MDMA & DEPRESSION – FROM A PARTY-DRUG TO A POSSIBLE TREATMENT.

Emio Halilović, Dino Žujić, Marina Šagud

School of Medicine, University of Zagreb, Zagreb, Croatia

**Introduction/Objectives:** Nowadays there are at least 14 groups of antidepressants according to their mechanism of action, but still, 10-30% of the patients don't have an adequate response to them. This leads to the development of new drugs or the reusing of existing ones. One of the potential new antidepressants is the psychedelic drug 3,4-methylenedioxymethamphetamine (MDMA). The Food and Drug Administration granted breakthrough therapy status to MDMA in 2017 in treating post-traumatic stress disorder (PTSD). This narrative review aims to analyze the potential of MDMA in the treatment of treatment-resistant depression.

**Participants, Materials/Methods:** A search of the available literature was performed using the PubMed database from January 2018 to December 2022 for the terms “Depression”, “Therapy”, and “MDMA” and there were 61 results.

**Results:** All clinical trials for MDMA were investigating the treatment of traumatic disorders, primarily PTSD. The primary focus of MDMA-assisted therapy (MDMA-AT) is to diminish symptoms related to unresolved trauma and improve the overall well-being and quality of life of the patients. It is due to the action of MDMA to increase the

endogenous release of serotonin, norepinephrine, dopamine, and oxytocin. Because of this, it has been proven that patients had insight and self-awareness improvements, and it allowed them to revisit past distressful memories. Also, it showed an immediate and significant antidepressant effect of MDMA-AT measured by the Beck Depression Inventory-II (BDI-II), suggesting the potential role of MDMA in the treatment of depression. In most cases, the score measured by BDI-II decreased by half with a clinical improvement remaining stable after one year, which was the duration of the follow-up of the research participants. Furthermore, between 5 and 15 percent of the patients have shown complete remission of depressive symptoms. In clinical trials, MDMA has not been associated with severe toxicity, nor have participants displayed drug abuse. Side effects were dehydration, nausea, headaches, vomiting, and an increase in blood pressure, which can persist for a few days after a dosing session.

**Conclusions:** Given the well-established role of past trauma in the development of depression, and that MDMA helped patients to express their emotions and facilitated the reexperiencing of trauma, MDMA-AT is a good candidate for future studies in the treatment of depression, particularly comorbid with stress-related disorders.

## 9. PINEAL GLAND CYST AND MEMORY LOSS – A CASE REPORT.

**Marija Kostadinovska**

Zan Mitrev Clinic, Department: Psychiatry, Skopje, N. Macedonia

**Introduction/Objectives:** A pineal gland cyst is a usually benign (non-malignant) cyst in the pineal gland, a small endocrine gland in the brain. These fluid-filled bodies appeared on 1-4% of magnetic resonance imaging (MRI) brain scans. Pineal cysts are rarely symptomatic; however, the larger pineal cyst is more likely to produce symptoms. Larger cysts can cause symptoms that affect activities of daily life for some people. Symptoms of pineal cysts are nausea; fatigue and drowsiness, seizures, headaches, mood or personality changes, vision impairment, and memory loss.

**Participants, Materials/Methods:** A female at 21 years of age, on first psychiatric examination, complains of severe anxiety, a feeling of separation of the body from the mind, and alcohol abuse. During the examination, forgetfulness is dominant in addition to anxiety. Can not recall the date of her birthday, is time disoriented, with difficulties in understanding tasks and performing them, unable to do mathematical operations. The first changes in her mental state appeared 8 months before the first psychiatric check-

up, in a way that was not able to understand the offered answer to a question, nor to perform some everyday operations.

**Results:** Mini-mental Test Examination 20/30. MRI findings showed a pineal cyst filled with a slightly thicker (oily) liquid. Cystic lesion dimensions were 12mm (LL) x 9mm (CC) x 8mm (AP), without diffusion restriction and post-contrast signal enhancement.

**Conclusions:** Symptoms of memory problems in a young person should not always be attributed to confusion, lack of resourcefulness, or abuse of alcohol or psychoactive substances, nor should they be considered part of severe anxiety. Forgetfulness and memory problems must be approached seriously in the interest of the patient's health.

## 10. THE POSITIVE EFFECT OF SPERMIDINE IN OLDER ADULTS SUFFERING FROM DEMENTIA.

**Thomas Pekar, Aribert Wendzel, Reinhart Jarisch**

University of Applied Sciences Wiener Neustadt, Department: Biomedical Sciences, Wiener Neustadt, Austria

**Introduction/Objectives:** The worldwide prevalence of dementia is estimated at 35.6 million and will rise to 115 million by 2050. There is therefore an urgent need for well-founded dementia diagnostics and wellresearched therapeutic options. Previous studies have highlighted that spermidine has the ability to trigger the important process of dissolving amyloid- $\beta$  plaques by autophagy. They also confirmed that nutritional intervention with the natural polyamine spermidine can prevent memory loss in aging model organisms.

**Participants, Materials/Methods:** The following multicentric, double-blind preliminary study focuses on the effect of oral spermidine supplementation on older adults' cognitive performance. Memory tests were carried out on 85 subjects aged between 60 and 96 years in six nursing homes in Styria. Blood samples were taken for the determination of spermidine concentration and measurement of metabolic parameters.

**Results:** The results demonstrate a clear correlation between the intake of spermidine and the improvement in cognitive performance in subjects with mild and moderate dementia in the group treated with the higher spermidine dosage. The most substantial improvement in test performance was found in the group of subjects with mild dementia with an increase of 2.23 ( $p = 0.026$ ) in Mini Mental test and 1.99 ( $p = 0.47$ ) in Phonematic Fluidity. By comparison, the group which had a lower spermidine intake showed consistent or declining cognitive performance. The results after one year show a continuation of the positive effect of oral spermidine intake for patients with neurocognitive impairment.

**Conclusions:** Based on our results, we see great therapeutic potential in spermidine supplementation in older adults at risk of dementia. However, further studies are needed – also to check whether the shown positive effect of spermidine on the cognitive function is specific or non-specific.

## 11. NEUROSCIENCE AND ALZHEIMER'S DISEASE.

**Ruth Švarc, Ljubomir Radovančević, Vesna Lecher-Švarc**

School of Medicine, Zagreb, Croatia; DZ Zaprešić, Croatian Association for the Promotion of Patient Rights, Zaprešić, Croatia

**Introduction/Objectives:** In this paper the authors answer the question when and how neuroscience meets Alzheimer dementia. The authors describe, analyze, discuss, interpret, comment and operationalize the touching points of the link between the two subjects; modern neuroscientific approach and symptoms of Alzheimer disease.

**Conclusions:** All nosological signs – mental and physical have their basis in the body. Pathomorphological substrates revealed on autopsy results and in fluids of organism, are mostly detectable in laboratory and neuropsychological testings. Organic changes are necessarily reflected in nosological manifestations, In Alzheimer's disease postmortal neurological brain changes are manifested in bodily and mental spheres in the form of dementia senilis. Neuroscience in its instrumentarium and armementariums can succeed detectable possibilities through (neuroimaging, PET CT, doppler, etc). Signs of Alzheimer dementia are seen through their pathoanatomophysiological basis on structures of the brain. In our paper the following is mentioned: 1) organic changes seen after pathoanatomic or microscopic techniques in postautopsy proceedings; 2) psychologic/mental changes discovered through clinical and psychological testing. As all nosological entities, so Mb.Alzheimer has great benefits from neuroscientific methods. The contribution of contemporary neuroscience is not measurable with classical investigations in diagnostical and therapeutical techniques and approaches.

## 12. THE USE OF TRANSCRANIAL MAGNETIC STIMULATION IN THE COMPLEX TREATMENT OF PATIENTS WITH DEPRESSIVE DISORDER IN PARKINSON'S DISEASE.

**B.D. Tsygankov, A.O. Prosvetov**

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Psychotherapy of the Faculty of Additional Professional Education. Moscow, Russian Federation

**Introduction/Objectives:** In 2019, the number of people diagnosed with Parkinson's disease was estimated at over 8.5 million, according to WHO. The prevalence of depression in PD ranges from 10 to 90% of cases (Reijnders, Jennifer SAM, et al., 2008). The development of depression in patients with Parkinson's disease is a serious problem, and the treatment of depressive conditions in such patients is an integral part of the treatment of Parkinson's disease. Antidepressants of the class of selective serotonin reuptake inhibitors are the first-line treatment for depression in such patients, but antidepressant therapy is ineffective in about half of patients. (Barone R., Antonini A., Colosimo C., et al., 2009.). The use of transcranial magnetic stimulation for the treatment of depressive disorder has shown its effectiveness and safety and has been used in many countries, including Russia, since 2012. (Order of the Ministry of Health of the Russian Federation N 1705n 2012.). However, transcranial magnetic stimulation as a treatment for depression in Parkinson's disease is little covered in modern clinical studies. The use of transcranial magnetic stimulation as a treatment for depression in Parkinson's disease is being actively studied in many countries (Brys M, Fox MD, Agarwal S, et al., 2016) and others.

**Participants, Materials/Methods:** The treatment program included patients with previously registered primary Parkinson's disease, manifesting at the age of 45 years and older, having complaints of low mood, anxiety and not receiving psycho- and/or pharmacotherapy for this reason. In the main group, patients receive complex therapy with TMS according to the iTBS protocol for 10 sessions, and standard treatment with antidepressants from the SSRI group. In the control group, patients receive medical treatment with antidepressants from the SSRI group without TMS. In the course of the study, clinical-psychopathological, clinical-dynamic methods using psychometric scales are used to identify the clinical variant of a depressive disorder, to determine the socio-demographic and clinical factors that affect the effectiveness of therapy, and to assess the dynamics of clinical manifestations. Statistical data processing was carried out using the SPSS software. When analyzing statistically significant differences in the groups, the T-test for related samples was used - the Wilcoxon test. When analyzing statistically significant differences between groups, a nonparametric test for unrelated samples, the Mann-Whitney test, was used. The relationship was considered significant for  $p < 0.05$ . The formation of a multifactorial model was carried out by constructing a multiple linear regression equation for a quantitative trait.

**Results:** The sample consisted of 88 people, 44 patients in the main and in the control group. Assessment of the patients' condition, as well as psychometry according to the CGI, BDI and BAI scales, was carried out on day 1, 5 days, 10 days, 1 month from the start of therapy. After 10 days, the indicators of the main group moderately improved on the BDI scale compared to the initial state, the control group had minimal improvements on both scales. After 1 month, the indicators of the main group improved significantly compared to the initial state on the BDI scale. 47.73% of patients after 1 month on the BDI scale scored less than 9 points, which corresponds to the absence of depressive symptoms. In the control group during the same period, 29.55% of patients scored less than 9 points on the BDI scale. A statistically significant difference between the main group and the control group on the BDI scale was recorded on the 10th day of therapy and 1 month after the start of therapy ( $p < 0.05$ ). The findings indicate that treatment with iTBS and SSRIs is significantly more effective and rapidly at reducing depressive symptoms than SSRIs alone within 10 days of starting therapy. The main and control groups did not differ in the profile of side effects, which indicates the safety of using iTBS for this sample of patients. It was shown for the first time that the right laterization of PD symptoms at the onset of the disease and the apathetic clinical variant of a depressive disorder are factors affecting the effectiveness of complex therapy. Patients with these factors demonstrate a faster and deeper degree of symptom reduction in the main group. Further research is required to improve knowledge in the field of therapy of affective disorders in patients with Parkinson's disease using TMS.

### 13. DIFFERENTIAL EFFECT OF CHILDHOOD TRAUMA ON BRAIN FUNCTION IN MAJOR DEPRESSIVE DISORDER AND BIPOLAR DISORDER.

**Laura Raffaelli, Marco Paolini, Valentina Bettonagli, Irene Bollettini, Elisa Melloni, Sara Poletti, Francesco Benedetti.**

Vita-Salute San Raffaele University Milan, Italy; IRCCS San Raffaele Scientific Institute, Department of Psychiatry and Clinical Psychobiology, Milan, Italy

**Introduction/Objectives:** Adverse childhood experiences (ACE) are a transdiagnostic environmental risk factor for major depressive disorder (MDD) and bipolar disorder (BD); furthermore, they have been associated with long-term changes in brain structure and brain function (Teicher et al., 2016). In a previous study by our group (Poletti et al., 2022), ACEs differently affect white matter (WM)

microstructure in MDD and BD patients, with a negative association between childhood trauma and Fractional anisotropy (FA) found only in BD. However, it is still unclear if this different effect also translates to brain function. FA, widely regarded as a measure of white matter integrity, has also been linked to changes functional connectivity, suggesting an association between structural and functional abnormalities (Porcu et al., 2021). Therefore, the aim of the present study was to investigate the effect of ACE on BF in MDD and BD, testing a possible differential effect.

**Participants, Materials/Methods:** A sample of 127 patients (52 BD, 75 MDD) underwent 3T MRI scan and ACE assessment through Childhood Trauma Questionnaire. Fractional amplitude of low-frequency fluctuation (fALFF) maps were extracted using the SPM CONN toolbox. To investigate the possible differential effect of ACEs on brain function in BD and MDD, second-level analyses were performed in a general linear model with a continuous covariate interaction design, entering CTQ total and subscales scores as predictors and fALFF maps as dependent variables. The effect of CTQ scores was then tested separately in the two groups. FA values were extracted from the WM tracts mostly affected by childhood trauma in BD, and a possible mediating effect of FA between CTQ scores and brain function was tested.

**Results:** was found in 4 clusters (supramarginal gyrus,  $p=0.039$ ; middle temporal gyrus,  $p=0.039$ ; superior frontal gyrus,  $p=0.038$ ; cerebellum,  $p=0.0389$ ), with a positive association in BD and a negative one in MDD. Furthermore, single-group analyses showed that CTQ and physical neglect were positively associated with fALFF in BD, while emotional neglect and sexual abuse resulted negatively linked to fALFF in MDD. Finally, we found a significant mediating effect of FA on the relation between CTQ and fALFF in BD ( $b=0.0008$ , BCa CI [0.0002, 0.0018]).

**Conclusions:** Our findings suggest that the detrimental effect of ACE on FC differs between mood disorders, and it may be mediated by a reduction of WM integrity.

### 14. CHILDHOOD TRAUMA AND SUICIDAL IDEATION IN BIPOLAR DISORDER - THE ROLE OF GENETIC AND COGNITIVE FACTORS.

**Laura Raffaelli, Alice Pelucchi, Cristina Lorenzi, Sara Poletti, Francesco Benedetti**

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**Introduction/Objectives:** In recent years, growing evidence has highlighted the key role played by genes, early stress, and their interaction in the onset and development of bipolar disorder (BD) (McClung, 2007). Adverse Childhood Experiences (ACE) have long been recognized as an important risk factor for the outcome of mood disorders (Garno et al., 2005); indeed, BD patients with a history of ACE significantly exhibit suicidal ideation and widespread negative cognitive bias, mostly during depressive episodes. Genetic polymorphisms affecting CLOCK gene expression have also been associated with greater cognitive distortion and a severely compromised clinical profile in BD (Suzuki et al., 2017). In the present study we aimed at testing the effect of ACE on suicidal risk, considering the mediating effect of a negative cognitive bias during a depressive state and the moderating role of the rs1801260 polymorphism of the CLOCK gene.

**Participants, Materials/Methods:** We studied 85 inpatients who were consecutively admitted to the mood disorder unit of San Raffaele Hospital in Milan and who met the criteria for a major depressive episode without psychotic features. Patients were assessed for suicidal ideation, patients' hopelessness across situations, and ACE through Beck Depression Inventory (BDI), Cognitions Questionnaire (CQ), and Risk Family Questionnaire (RFQ), respectively. The analysis of moderated mediation was performed with the PROCESS macro for SPSS adding age, onset, and frequency of episodes as nuisance covariates.

**Results:** The relationship between ACE and suicidal ideation was found to be completely mediated by a negative cognitive bias related to the subjective perception of reality. Furthermore, the CLOCK gene polymorphism was found to moderate the relationship between childhood adverse events and cognitive bias, with a significant positive association only in homozygous CC subjects ( $b = 0.006$ ;  $SE = 0.003$ ;  $CI\ 95\% 0.003-0.013$ ). Moreover, CLOCK gene rs1801260 \*C carriers showed a worse cognitive distortion for the perception of reality as compared to \*TT carriers when exposed to the same amount of ACE. Finally, the moderate mediation index of the model was found to be significant ( $b = 0.0034$ ;  $SE = 0.003$ ;  $CI\ 95\% 0.002-0.01$ ).

**Conclusions:** These findings underline the relevance of the interaction between environmental risk factors and genetic components for understanding the symptomatology of BD. From a clinical perspective, they might help to identify a subset of patients who are more likely to experience cognitive distortion and might benefit from a targeted therapeutic intervention.

## 15. LOCAL FUNCTIONAL CONNECTIVITY AT REST OVERLAPS ACROSS UNIPOLAR AND BIPOLAR DEPRESSION.

**Giulia Gulino, Andrea Scalabrini, Marco Paolini, Mariagrazia Palladini, Francesco Benedetti**

Ospedale San Raffaele, Department of Psychiatry and Clinical Psychobiology, Milan, Italy

**Introduction/Objectives:** Resting state functional connectivity (rsFC) perturbations at the local level have been already reported in association with depressive symptomatology in major depressive disorder (MDD) as well as bipolar disorder (BD). However, it is still unclear whether rsFC alterations may vary according to diagnosis or constitute an endophenotype of the depressive state. By evaluating the level of intra-regional neuronal synchronization, regional homogeneity (ReHo) is a high test-retest reliable local measure of the cortical neural coherence, thus potentially providing insight into spontaneous-spatial processing at the local level. We thus aimed to evaluate ReHo functional variations as a potential transnosographic endophenotype of the depressive state across unipolar and bipolar disorders.

**Participants, Materials/Methods:** We evaluate whole-brain regional rsFC connectivity patterns in a group of 70 patients with a clinical diagnosis of MDD, a group of 70 patients with a clinical diagnosis of BD in depressive phase and a group of 70 healthy controls (HC). All participants completed the resting-state 3T-fMRI acquisition. We implemented all pre-processing procedures of fMRI data in Analysis of Functional Neuroimaging software (AFNI), controlling for impact of motion, global signal regression and medication load. To properly compare ReHo between groups, we operate a two-sample t-test for all the possible combinations of groups, resulting in a total of three comparisons (i) MDD vs HC, (ii) BD vs HC (iii) MDD vs BD. Results were thresholded at a voxel-wise  $p < 0.001$  uncorrected and a cluster-level FDR corrected (min. cluster size of 40 voxels).

**Results:** as compared to HC, MDD exhibited significant decreases in ReHo values located in posterior frontal (i.e., precentral gyrus) and middle frontal clusters both bilaterally represented, and left-located peaks in middle occipital gyrus, inferior parietal lobule, middle temporal gyrus, posterior cingulate, caudate, cerebellum. Largely overlapping results were found in the comparison between BD and HC with widespread ReHo decreases in the former. No statistically significant differences were found in the comparison between MDD and BD patients.

**Conclusions:** Overall, as compared to healthy controls and independently from diagnosis (i.e., MDD or BD), all patients with an ongoing major depressive episode,

exhibited decreased levels of ReHo at rest. These findings suggest that local rsFC changes may be considered a common denominator of the depressive syndrome occurring independently from diagnosis (i.e., MDD or BD), thus constituting a transdiagnostic and transnosographic characteristic. Future evidence might be helpful to corroborate such a hypothesis and further elucidate links with global measures of connectivity and the expected association with depressive symptomatology.

**16. FROM ACTING OUT IN AN ONLINE GROUP SETTING TO SUBLIMATION - CASE REPORT MODIFICATION OF GROUP PSYCHOTHERAPY IN THE DAY HOSPITAL FOR PSYCHOTRAUMA DUE TO THE COVID 19 PANDEMIC. Anamarija Milun, Nikolina Menegoni, Goran Tošić**

Neuropsychiatric Hospital Dr. Ivan Barbot, Department of Psychotherapy, Popovača, Croatia

**Introduction/Objectives:** Posttraumatic stress disorder (PTSD) is a disturbing disorder with a delayed response triggered with stressful life-threatening events. Main symptoms of PTSD are categorized into three groups: re-experience (intrusive trauma memories and dreams, flashbacks) avoidance and hyperarousal (arousal alteration). Traumatic experience is so painful that those people cannot integrate it, nor they can move on. Group psychotherapy of patients with PTSD in the setting of the Day Hospital for Psychotrauma requires numerous modifications and frequent supportive interventions.

**Participants, Materials/Methods:** Case report: Group psychotherapy in the Day Hospital for Psychotrauma includes 10 patients, (7 male and 3 female patients) therapists and co-therapists. Due to the appearance of positive COVID-19 patients in February 2022 at the Department of Psychotherapy, according to anti-epidemic measures, the treatment is being moved from the real to the online setting, which despite its benefits in terms of continuity of therapy, maintaining the object's constancy, however, it makes adaptation difficult with the appearance of numerous resistances related to real technical limitations, possibilities and skills of members, but also the change from concrete to virtual /non-concrete, frustrations with the emerging COVID situation, separation fears related to members and therapists. After three weeks of work in an online format (virtual, fantasy), the idea arises among the members of the group that the whole group and all members can see each other again in real time and space (concrete), but at the exhibition of a famous Croatian painter in Zagreb, which all members individually very quickly accepted. The

resulting acting out of the entire group and the abandonment of the online setting is, however, understood as an inevitable part of their basic psychopathology, but also a way of sublimating the resulting separation and existential fears, and the need to transfer aggressive urges from fantasy to the concrete, but through the process of sublimation and creative progress.

**Conclusions:** Group psychotherapy of patients with PTSD in the setting of the Day Hospital for Psychotrauma requires occasional modification in terms of frequent supportive interventions, but also understanding and containing the group's aggressive and destructive impulses that correspond to the unconscious pre-oedipal phantasms of these patients, which are re-actualized due to war traumas and recent threatening situations. The damaged ego and superego of traumatized patients who do not have the possibility of reparation and integration of the trauma, can no longer effectively suppress and control such aggressive and destructive contents, and they quickly come from the fantasy to the concrete level, which in this case is manifested as group acting out. However, due to group and therapeutic support, aggressive impulses are not realized through the destruction of the object, but through a concrete but also more mature and adequate mechanism of sublimation in socially acceptable behavior.

## POSTERS NEUROLOGY

**17. CLOSTRIDIUM DIFFICILE INFECTION AND NEUROLOGICAL DISORDERS - A CASE REPORT.****Dobrinka Petković, Borislav Vuković, Ivana Vuković**

General County Hospital Požega, Department of Infectology, Department of Neurology, Požega, Croatia

**Introduction/Objectives:** Clostridium difficile is a spore-forming, toxin-producing, gram-positive anaerobic bacterium that causes antibiotic-associated colitis. Up to 25 percent of patients experience recurrent C. difficile infection (CDI) within 30 days of completing treatment. Extracolonic manifestation of CDI are rare, but recent studies suggest toxin-mediated pathogenic process involving cardiac, renal and neurologic impairment. Objectives: Review of clinical manifestations and treatment of patient with dyskinesia as a neurological complication of recurrent CDI.

**Case report:** A 63-year-old female with previous history of arterial hypertension and a condition after a transient ischemic attack, presenting with a moderately severe enterocolitis, dehydration, general weakness and temporary involuntary movements of the left foot, left hand and oral dyskinesias. A clinical examination revealed a left-side hemichorea/athetosis. Three weeks earlier oral vancomycin therapy was administered for the first episode of CDI. Diagnosis was based on laboratory, physical and neurological examinations. The laboratory diagnosis of CDI was confirmed by a positive stool test-enzyme immunoassay for C. difficile toxins A i B (reference interval: negative 0,37).

**Results:** Hematological-biochemical tests registered a mild increase inflammatory markers and neutrophilia. Thyroid function tests, oncomarkers, electrophoresis of serum proteins and vitamin D3 test were normal. Covid 19 was excluded. A positive stool test-enzyme immunoassay for C. difficile toxin A i B (8,38) was confirmed a second episode of CDI. Ophthalmological examination, ultrasound of the heart, MSCT and MRI of the brain, electromyography, MR angiography of the brain were normal. Cerebrospinal fluid analysis excluded infection with neurotropic microorganisms and the antibody panel for autoimmune encephalitis was negative (anti-NMDAR, anti-AMPA-R1, anti-AMPA-R2, anti-GABABR, anti-LGI1, anti-CASPR2 antibodies). CDFI of the carotid arteries verified stenosis of the ACI on the right 40%. Electroencephalogram was diffuse irregular. Molecular genetic analysis for Huntington disease was negative (triplet CAG repeat numbers :17/23 in HTT gene). The patient was treated with vancomycin in tapering and pulse doses, and haloperidol 2 mg orally 2 times a day and chlonazepam 0,5 mg orally 2 times a day for

three months. Eradication of CDI and complete recovery of neurological deficit was achieved within four months.

**Conclusions:** We presented a patient with recurrent CDI and dyskinesia as a rare neurological complication most likely induced by C. difficile toxin. Other neurological diseases were excluded by extensive diagnostic work-up. Rational use of antimicrobial therapy and adherence to infection control measures are important in reducing the spread of C.difficile.

**18. DUAL ANTIPLATELET THERAPY AND THROMBOLYSIS - A CASE REPORT.****Andrija Meštrović, Ana Sruck, Gordana Sičaja, Zurap Raifi, Fabijan Đumbir, Hrvoje Budinčević**

Sveti Duh University Hospital, Department of neurology, Zagreb, Croatia

**Introduction/Objectives:** As per the latest guidelines by the AHA/ASA (American Heart Association/American Stroke Association) for high-risk TIA (transient ischemic attack), published in 2021, it is recommended to start dual antiplatelet therapy (DAPT) within 24 hours after a TIA in patients who have an ABCD2 score of 4 or higher. The same is recommended for patients with a minor stroke, defined by an NIHSS (National Institutes of Health Stroke Scale) of 3 or less. Similar recommendations have been published by the ESO (European Stroke Organization), with the main difference being in the doses of medications. According to a meta-analysis by Bhatia et al., DAPT decreases the risk of stroke in TIA patients without increasing the risk of an intracranial hemorrhage.

**Case report:** In this case report, we present the case of a 60-year-old male who presented to our emergency department with a history of several episodes of right-sided hemihypesthesia within the last 12 hours. A brain CT was done, showing no abnormalities; the ABCD2 score was 4. The patient was admitted, and DAPT with acetylsalicylic acid and clopidogrel was started. However, the patient started to have stroke symptoms: right-sided hemiparesis and hemihypesthesia, with an NIHSS of 6. The patient had undergone systemic thrombolysis, resulting in an NIHSS of 0 after 24 hours. A wide battery of tests was performed during the hospitalization, resulting in the findings of hypertension, hyperlipidaemia, and a positive „Bubble test". The patient was discharged with DAPT up to 21 days after the stroke, along with rosuvastatin, bisoprolol, and perindopril. A check-up after two months revealed he had had a transesophageal ultrasound, which revealed an opened foramen ovale, and had no new episodes of neurological symptoms.

**Conclusions:** Dual antiplatelet therapy is an important tool

in secondary stroke prevention, and its broader use has yet to reveal its full potential. One of the advantages of DAPT is that it does not prevent the application of alteplase, which has been shown to be beneficial in this case.

### 19. THE IMPACT OF THE COVID-19 PANDEMIC ON NEUROLOGICAL HOSPITAL ADMISSIONS AND MEDICAL CONSULTING AT SVETI DUH UNIVERSITY HOSPITAL.

Tea Plišić, Fran Naletilić, Sanja Tomasović, Hrvoje Budinčević

University of Zagreb, School of Medicine, Zagreb, Croatia  
Sveti Duh University Hospital, Department of Neurology, Zagreb, Croatia

**Introduction/Objectives:** Due to restrictions related to the coronavirus pandemic beginning in March of 2020, most Croatian hospitals deliberately curtailed noncritical medical services to prevent the breakthrough of the virus among hospitalized patients and staff. The aim of this study was to analyse the number of neurological ward admissions and medical consultations during the COVID-19 restrictions period and compare them to the pre-pandemic years of 2018-2019 at Sveti Duh University Hospital.

**Participants, Materials/Methods:** We present a study of the number of neurological ward admissions and consultations provided by the Department of Neurology at Sveti Duh University Hospital from 2018-2022 divided as follows: ward admissions in general, major diagnosis among admissions, medical consultations at various infirmaries with total admissions.

**Results:** Total admissions increased in 2019 compared to 2018 by 4,19%. A significant decrease in admissions took place during the year 2020, with a total decrease of 11.9% in comparison to 2019. Admissions steadily decreased throughout the years of 2021 and 2022, with a total decrease of 28,9% and 33,6%. When analyzing specific outpatient clinic work in a mentioned period of five years, only day hospital showed an increase in number of examinations during the pandemic years in comparison to the pre-pandemic years. All other outpatient facilities (ER/EEG/Ultrasound/EMNG) and in-hospital neurological consultancy presented with a decrease in numbers of examined patients in 2020. Due to COVID-19 restrictions being loosened, an increase in outpatient clinic admissions occurred, the highest being in the Ultrasound laboratory (+44,2%) in 2022 compared to 2019. Throughout the years analyzed, ischemic stroke continues to be the most common neurological diagnosis. In the pandemic years of 2020-2022, multiple sclerosis was presented as the third most common

diagnosis, its incidence increasing from fifth place during 2018 and 2019.

**Conclusions:** COVID-19 restrictions affected the total number of admissions and medical examinations from 2020 to 2022 in comparison with pre-pandemic years of 2018 and 2019. As COVID-19 related restrictions enveloped hospitals in Croatia in March 2020, a significant decrease in admissions presented in 2020, with a total of 11.9% in comparison to 2019. The number of admissions continued to decline throughout the years of 2021-2022, with a total of 28,9% and 33,6%, which leads to the conclusion that COVID-19 restrictions affected the number of admissions. Day hospital showed an increase in admissions during the pandemic years compared to pre-pandemic. The most common diagnoses remain the same throughout the examined five-year period with slight changes in order of occurrence.

### 20. TWO CASES OF NEW ONSET PSYCHOGENIC NON-EPILEPTIC SEIZURES IN PREGNANCY.

Thomas Ryle, Deirdre Muller Neff

Cork University Maternity Hospital, Department of Perinatal Mental Health, Cork, Ireland

**Introduction/Objectives:** Psychogenic Non-Epileptic Seizures (PNES) are movements or behaviours that resemble seizures but do not have epilepsy or associated abnormal electroencephalography (EEG) changes. They are triggered by emotional and psychological events over which the patient does not have conscious control. The literature data shows a high prevalence of associated psychiatric comorbidity. Objectives We will present two cases of psychogenic non-epileptic seizures (PNES) in women during pregnancy, discuss the clinical features, management, and outcomes with reference to relevant clinical studies and literature.

**Participants, Materials/Methods:** The first case was a 26-year-old multiparous woman at 20 weeks gestation who presented with a history of new onset PNES. The second case was a 22-year-old primiparous woman at 6 weeks gestation who presented with an 8-week history of new onset PNES and multiple medical admissions

**Results:** The PNES were precipitated or increased in context of unexpected pregnancies. Neither case had a past medical or family history of epilepsy Both had predisposing factors including past history of anxiety depression, borderline personality traits, significant childhood adversity, past suicidal behaviour, and deliberate self-harm. Studies to guide treatment are limited but an individualised biopsychosocial approach to address concurrent stressors, risk factors and comorbidities aided acceptance of diagnosis and symptomatic improvement. Psychoeducation around



condition and early communication of the diagnosis with non-stigmatising language was reported as helpful by patients in both cases. One case engaged with individualised Cognitive Behavioural Therapy (CBT) with therapeutic benefit. At 4 week follow up neither case had represented to an emergency department which reduced the risk of iatrogenic harm from others unaware of PNES.

**Conclusions:** Conclusions New onset PNES in pregnancy can herald an opportunity to identify and offer therapeutic interventions to vulnerable women with a high prevalence of psychological difficulties and psychiatric comorbidities. Pregnant women with PNES are also at risk of adverse consequences to mother and foetus with unnecessary medical interventions, premature delivery or treatment with potentially teratogenic antiepileptic medications. Reaching an early and definitive diagnosis is therefore of heightened importance for women with documented PNES during pregnancy. There is potential for enhanced cross speciality education and communication between neurologists and psychiatrists to inform and optimise collaborative therapeutic approaches and outcomes in individual patients.

## 21. MEMORY CLINIC EXPERIENCE DURING THE COVID-19 PANDEMIC- DATA FROM A CROATIAN REGIONAL CENTER.

**Mario Hero, Eliša Papić, Valentino Rački, Klara Radović, Zoran Tomić, Vladimira Vuletić**

Clinic of Neurology, Clinical Hospital Centre Rijeka, Department of Neurology, Faculty of Medicine, University of Rijeka, Rijeka, Croatia

**Introduction/Objectives:** The COVID-19 pandemic has greatly changed people's daily lives and made it difficult to carry out examinations in hospitals. In this observational study, we presented patients who underwent a complete diagnostic process for dementia through our memory clinic over the last 2 years.

**Participants, Materials/Methods:** We collected patient data from the hospital electronic records system in the period from 1.1.2020. until 31.12.2022. Patients included in this study had to undergo a complete diagnostic workup, which included: extended laboratory tests, lumbar puncture, MoCA test, MRI and FDG PET scan of the brain, psychological examination and cognitive evoked potentials.

**Results:** In the period of two years, 107 patients underwent complete diagnostic workups. Of these patients, 49 (45,79%) were diagnosed with Alzheimer's disease, 33 (30,84%) with mild cognitive impairment, 12 (8,42%) with unspecified dementia and needed further monitoring and evaluation, 2 (1,87%) with extrapyramidal disease and 2

(1,84%) with normal findings of diagnostic tests. The average MoCA score at the first examination was 18,37.

**Conclusions:** The COVID-19 pandemic has made the work of the memory clinic more challenging. Low MoCA scores indicate that patients showed up relatively late for their first examinations, which can be partly attributed to the fear of the coronavirus and pandemic lockdowns. Furthermore, the pandemic has shown that telemedicine and technical devices would be helpful in monitoring these patients if epidemiological factors prevent examination. Finally, more importance should be given to public health promotions in order to raise awareness among people.

## 22. A POSSIBLE CASE OF MULTIPLE SCLEROSIS WITH INITIAL STROKE-LIKE CLINICAL AND RADIOLOGICAL FEATURES - A CASE REPORT.

**Valbona Govori, Kastriot Rexhepi, Esra Zhubi**

University Clinical Centre of Kosova, Faculty of Medicine, University of Prishtina, Neurology Clinic, Prishtina, Kosovo

**Introduction/Objectives:** Multiple sclerosis (MS) and stroke represent two common causes of death and disability worldwide. Multiple sclerosis (MS) is an inflammatory demyelinating disease of the central nervous system (CNS) that is characterized by inflammation, demyelination, and degenerative changes. MS usually begins between the ages of 20 and 40, whereas stroke typically occurs after the age of 55 years. MS affects two to three times as many women as men, and its diagnosis is based on the 2017 McDonald's Criteria. Distinguishing multiple sclerosis from alternative diagnoses can sometimes be challenging.

**Participants, Materials/Methods:** This is a case report from a patient admitted to the Neurology Clinic at the University Clinical Center of Kosovo after presenting with sudden onset of persistent focal neurological symptoms. The initial clinical presentation and imaging findings resulted in a diagnostic dilemma between multiple sclerosis and acute infarction.

**Results:** We presented a case of a 24-year-old female patient, with an onset of symptoms two weeks before their admission to our clinic. She presented with a motor weakness of the left side of the face and body, blurred vision, gait disturbances, headache, and dizziness. Her family history was negative for any hereditary disease. The patient denied recent illnesses, travel, or vaccinations. She has previously visited other clinics but the attempts to diagnose the patient were unsuccessful. Slightly decreased muscle strength and decreased sensation to light touch and pinprick throughout the left side of the body were evident in the neurological examination. Coordination testing demonstrated decreased fine-finger movements, finger-to-nose, rapid alternating movements, and heel-knee-shin all in

proportion to weakness on the left side. Since the patient appeared in the clinic outside of the time window of 4.5 hours, she was not considered for intravenous thrombolysis. An MRI was performed and it showed a hyperintense lesion on the right hemisphere in the FLAIR, T2 and DWI sequences. The lesion demonstrated restricted diffusion, appearing hyperintense on diffusion-weighted imaging and hypointense on apparent diffusion coefficient mapping, suggestive of an acute ischemic stroke and therefore stroke diagnostic workup was done. A transthoracic and transesophageal echocardiography was performed, and they showed normal echocardiographic findings, with an ejection fraction of 56%. The autoimmunity evaluation, tests of hemostasis and thrombosis, and peripheral blood smear showed normal results. During the hospitalization, the patient experienced worsening symptoms, with left hemiplegia. An additional MRI was performed, which showed no sign of a recurrent ischemic stroke. A lumbar puncture was performed for further etiologic differentiation and the tests of cerebrospinal fluid did show the presence of oligoclonal bands. Treatment with high-dose intravenous corticosteroids (pulse therapy) was initiated and an improvement in the clinical outcome was evident.

**Conclusions:** This case illustrates a potential example of multiple sclerosis with radiological and clinical signs of a stroke. The distinction is important because a false diagnosis could result in ineffective or even harmful treatment. For example, the tissue plasminogen activator, which is used to treat acute ischemic strokes, may have a negative effect on the patient with a demyelinating condition. Similarly, intravenous steroids, which are typically given during multiple sclerosis episodes, would worsen the outcome of a patient experiencing an ischemic stroke. Prompt and adequate patient management can be made easier with a better understanding of multiple sclerosis's unusual clinical and radiographic presentations. Further study is required to more precisely establish the standards for multiple sclerosis diagnosis in atypical cases.

### 23. A CASE REPORT ON THE ETIOLOGICAL ASSESSMENT OF NONCONVULSIVE STATUS EPILEPTICUS.

**Fabijan Đumbir, Ana Sruk, Zurap Raifi, Meštrović Andrija, Gordana Sičaja, Hrvoje Budinčević**

Sveti Duh University Hospital, Department of Neurology, Zagreb, Croatia

**Introduction/Objectives:** Nonconvulsive status epilepticus (NCSE) is defined as a persistent change in the level of consciousness or mental status with subtle or no motor

symptoms associated with continuous epileptiform discharges on electroencephalogram (EEG) monitoring. The threshold for NCSE is 10 minutes. It can be divided into NCSE with coma and NCSE without coma, further divided into generalized (absence status) and focal status. The causes of NCSE can be classified as cryptogenic and symptomatic, including structural, metabolic, malignant, inflammatory, infectious, toxic, or traumatic abnormalities. **Results:** A 64-year-old female patient with hypertension, hyperlipidemia, atrial fibrillation, and previous alcoholism, without a prior seizure history, presented in the emergency department with sudden consciousness disorder (Glasgow Coma Score 3) and respiratory failure (pH 7.129, pCO<sub>2</sub> 12.5 kPa, pO<sub>2</sub> 6.21 kPa, SaO<sub>2</sub> 0.589). MSCT pulmonary angiography revealed a nonocclusive subsegmental pulmonary embolism. She was intubated and ventilated and transferred to the cardiology department. Concurrently, she was observed by a neurologist; an MSCT of the brain showed an irrelevant chronic ischemic lesion at the right basal ganglia, while the neurologic examination did not show any lateralization. Two days after admission, she was presented with periodic ocular deviation and myoclonic jerks of the left hemiabdomen. EEG showed generalized spike-wave discharges, and she was diagnosed with NCSE. She was transferred to the neurology department and treated with levetiracetam, clonazepam, and continuous midazolam sedation. We spent an extensive workup to diagnose potential causes of NCSE. Laboratory tests showed hyponatremia, hypokalemia, and hypomagnesemia. Cerebrospinal fluid analysis showed proteinorachia (1,66 g/L) and pleocytosis (mononuclear leukocytes: 99x10<sup>6</sup>/L). A panel on autoimmune encephalitis arrived negative, but serology of neurotropic pathogens showed positive PCR and IgM antibodies to West Nile virus. MSCT of the thorax revealed suspicious primary pulmonary malignancy. MRI revealed multiple pathological changes: acute pontine infarction, brain metastases in the left occipital lobe and right basal ganglia, hemorrhage in the supramarginal gyrus, and gyral enhancement of the right cerebral hemisphere (most likely encephalitis). Although repetitive EEGs confirmed a resolution of the status epilepticus, multifactorial and incurable pathology caused a lethal outcome.

**Conclusions:** NCSE is relatively common, especially in elderly and critically ill patients, with a prevalence of approximately one-third of all cases of status epilepticus. However, NCSE is still challenging to recognize and diagnose, with a mortality rate of approximately 25%.

**24. INTERACTIVE MATHEMATICAL SOFTWARE FOR THE PREDICTION OF THE RISK OF EARLY IN-HOSPITAL MORTALITY IN PATIENTS WITH INTRACEREBRAL HEMORRHAGE BASED ON PRO-INFLAMMATORY AND OXIDATIVE STRESS MARKERS: A CHALLENGE IN MODERN CLINICAL THERAPEUTIC STRATEGIES.**

**Vladimir Rendeovski, Boris Aleksovski, Ana Mihajlovska Rendevska, Nikola Hadzi-Petrushev, Icko Gjorgoski**

University Clinic for Neurosurgery, Medical Faculty, Ss. Cyril and Methodius University in Skopje, Skopje, North Macedonia; Faculty of Natural Sciences and Mathematics-Skopje, Institute of Biology, Ss. Cyril and Methodius University in Skopje, Skopje, North Macedonia; University Institute of Radiology, Medical Faculty, Ss. Cyril and Methodius University in Skopje, Skopje, North Macedonia

**Introduction/Objectives:** Prognostic models for in-hospital mortality after intracerebral hemorrhage (ICH), mainly based on clinical evaluation, still remain essentially confounded by subjective scoring assessments and limited accuracy. This study aimed to develop a prognostic model for estimating the risk for in-hospital mortality after ICH based on biochemical markers, i.e., peripheral blood inflammatory and oxidative stress markers three days after the hemorrhage.

**Participants, Materials/Methods:** Prospective, longitudinal study included a cohort group of seventy-three conservatively-treated patients with ICH (2019-2021), without hematoma expansion or intraventricular bleeding. Study procedures included multilevel comprehensive analyses of clinical and neuroimaging data, aligned with the exploration of 19 inflammatory and five oxidative stress (OS) markers. The levels of IL-6 (interleukin 6) and IL-10 (interleukin 10) were determined by the enzyme-linked immunosorbent assay (ELISA) method. The levels and activity of OS markers: catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GPx), malondialdehyde (MDA) and advanced oxidation protein products (AOPP) were measured by enzyme kinetic spectrophotometric methods.

**Results:** Based on the multivariate nominal logistic regression model, we generated quantification and prediction formula for quantification of the probability and odds ratio of early in-hospital mortality with overall prediction accuracy rate is 93.75%. The variables: edema volume (V edema, 5 th day), absolute plasma neutrophil count (ANC, 3 rd day), the interaction  $ANC \times AOPP$  (3 rd day) and  $ANC \times IL-10$  (3rd day) were assessed as significant predictors in the model. Using receiver operating

characteristic (ROC) analysis, we calculated optimal values of edema volume (V edema 5 th day) and absolute plasma neutrophil count (ANC 3 rd day) as cut-off points for discrimination between surviving patients and those with in-hospital mortality, with a satisfactory rate of discrimination between the two groups of patients (ROC AUC = 0.9778). The confirmatory canonical discriminant analysis (CDA) model also confirmed that the two outcomes (surviving patients and patients with in-hospital mortality) can be discriminated and determined based on the proposed 4 markers.

**Conclusions:** Interactive software application, based on mathematical predicting formula and 3D graphics plots is able to make decisions and distinguish two different subgroups: surviving patients and patients with early in-hospital mortality. The clinical application of these models will help in the future, in the clinical strategy in the treatment of patients with hemorrhagic stroke in terms of conservative or early operative treatment.

**25. RESISTANT HYPERTENSION AND SMALL CEREBRAL VESSEL DISEASE OF THE BRAIN IN OLDER CARDIOVASCULAR PATIENTS.**

**Vesna Đermanović Dobrota, Ingrid Prkačin, Iva Mucalo, Vesna Lukinović - Škudar, Juraj Jug, Ivana Jurca, Kristijan Peroš, Dario Rahelić**

Clinical Hospital Merkur - University Clinic Vuk Vrhovac, Department of Diabetic Complication, Zagreb, Croatia

**Introduction/Objectives:** Resistant hypertension is one of the most important modifiable risk factors for cerebral small vessel disease (CSVD), which is the most common chronic and progressive vascular disease, causing silent strokes, gait disturbances, cognitive impairment, and dementia in the older cardiovascular patients. All patients with CSVD have similar vascular risk factors such as hypertension, diabetes mellitus, hyperlipidaemia, and smoking. Non-pharmacological treatment in the form of Mediterranean diet, sodium restriction, increased physical activity, and smoking cessation is also important.

**Participants, Materials/Methods:** The study was conducted at a Croatian primary care ambulatory clinic, Healthcare Centre Zagreb – Centre. Patients aged 65 to 80 years were divided into an intervention and control group and followed-up for one year. In addition to standard care, patients in the intervention group received medication management services (MMS) provided by a pharmacist, while the control group, assigned in a non-randomised fashion, received the usual care. Pharmacists provided face-to-face consultations and a minimum of 3 consultations were held for each patient following the pharmaceutical care

framework. Groups were compared with regards to the clinical parameters (blood pressure, HbA1c, LDL, TC), ambulatory blood pressure monitoring (ABPM), and cerebral microbleeds (CMBs), using the paired t-test, two-way ANOVA, and Fisher's LSD test at a 5% statistical significance level.

**Results:** A total of 60 patients in the intervention group and 60 patients in the control group completed the study. Baseline demographic and clinical parameters were similar between the two groups ( $p > 0.05$ ). The MMS intervention significantly improved systolic and diastolic blood pressure ( $p = 0.039$ ,  $p = 0.002$ ), cholesterol ( $p = 0.015$ ), low-density lipoprotein cholesterol ( $p = 0.006$ ) and glycosylated hemoglobin ( $p = 0.047$ ), compared to the control group. Patients included in MMS had statistically and clinically significant lower systolic ( $-9.22$  mmHg,  $p < 0.001$ ) and diastolic blood pressure ( $-4.98$  mmHg,  $p < 0.001$ ) at the end of the study. The MMS intervention group showed less "non-dipping" pattern of hypertension on ABPM ( $p < 0.001$ ). Between groups there were no statistical difference in cerebral microbleeds on brain MRA.

**Conclusions:** Resistant hypertension and cerebral small vessel disease (CSVD) is a very common problem in older patients. Better control of hypertension certainly improves the quality of life in the older cardiovascular patients and their families, thus potentially contributing to health care savings.

## 26. SUBGROUP ANALYSES OF PARKINSON'S DISEASE PATIENTS AMONG THYROID DISEASES GROUP AND CONTROLS WITH CEREBRAL INFARCTION ACCORDING TO COMORBIDITIES.

Iva Šarac, Ida Ivek, Helena Šarac, Fran Borovečki.

Lucija Bagaric-Krakan, Zdravko Krešić, Mateja Iveta, Tea Sukobljević

School of Medicine, University of Zagreb, Zagreb, Croatia

**Introduction/Objectives:** We have found, in our prior study, significantly increased prevalence of thyroid diseases in patients with Parkinson's disease (PD) in comparisons to controls with acute acute cerebral infarction (33.33% vs. 17.14%). The main goal of this study was to perform subgroup analyses of associations between PD and thyroid diseases amongst PD patients and controls according to age, sex, Charlson Comorbidity Index (CCI) score and comorbidities.

**Participants, Materials/Methods:** A total of 222 PD patients at first presentation and 175 age- and sex-matched patients with cerebral infarction (CVI) as controls were studied. They were analysed according to sex, age, CCI score and comorbidities including hypertension, diabetes,

dyslipidemia.

**Results:** The rates of Hashimoto thyroiditis (HS), hypothyroidism and hyperthyroidism were significantly higher in the PD patients than in the CVI group (24.32, 24.32 and 3.60% vs. 4.0%, 4.57% and 1.17%, respectively,  $p < 0.05$ ). Significant differences in the prevalence of subclinical hypothyroidism and subclinical hyperthyroidism were found between PD patients and CVI group (0.9% and 0.05% vs. 4.57% and 3.43%,  $p < 0.05$ ). The adjusted odds ratios (ORs) for Hashimoto thyroiditis, hypothyroidism and hypothyreosis in the PD group were 7.71 (95% confidence interval (CI) 3.41-17.44,  $p = 0.00$ ), 6.67 (95% CI 3.08-14.5,  $p = 0.00$ ) and 15.04 (95% CI 2.09-73.27,  $p = 0.001$ ), respectively. In subgroup analyses, the association between Hashimoto thyroiditis and PD was maintained in patients with diabetes. Also, the association for subclinical hypothyroidism and PD was found for patients with CCI score  $\geq 3$ .

**Conclusions:** Hashimoto thyroiditis, hypothyroidism and hyperthyroidism were more common in PD patients than in controls with acute stroke, particularly Hashimoto thyroiditis for PD patients with diabetes. Also, hypothyroidism and hyperthyroidism were associated with hypertension, diabetes and dyslipidemia in stroke subgroups.

## 27. OLIVO-PONTOCEREBELLAR ATROPHY IN A PATIENT WITH X-LINKED AGAMMAGLOBULINEMIA.

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**Introduction/Objectives:** Progressive neurodegenerative disease (PND) may develop in patients with X-linked agammaglobulinemia (XLA) during treatment with intravenous immunoglobulin (IVIG). Here, we report a case of olivo-ponto-cerebellar atrophy on 27-year-old male with Bruton agammaglobulinemia. We aimed to demonstrate the clinical course of neurological complications and neuroradiological findings associated with Bruton agammaglobulinemia.

**Participants, Materials/Methods:** Diagnostic tests of blood and cerebrospinal fluid included chemistry, cytology and cultures and PCR for viral genomes. Neuroimaging studies through magnetic resonance imaging (MRI), diffusion tensor imaging (DTI), tractographic reconstruction of neural connections by diffusion tensor imaging (DTI) were performed. In addition, neuropsychological tests were

performed.

**Results:** No evidence of any infectious disease was found in CSF and serum. MRI showed advanced atrophy of the cerebellum, especially of the cerebellar peduncles and brainstem. For age, advanced brain atrophy with enlarged cerebrospinal fluid spaces and a wider ventricular system. There is no crossed T2 hyperintensity of the pons. Increased T2 hypointensity in terms of metal deposition in the globus pallidum and substantia nigra bilaterally. Diffusion tensor and tractography show thinned but maintained transversal fibers of the pons and atrophy of the corticospinal tract and middle cerebellar peduncles. There were no significant progression of findings through 3 years of follow-up. Neuropsychological testing revealed clinically significantly impaired non-verbal functions, visual memory deficit, visuospatial disturbances and sensorimotor dysphasia.

**Conclusions:** Olivo-pontocerebellar atrophy may develop in patients with XLA during IVIG treatment. Diffusion tensor imaging (DTI) and tractography reconstruction is recommended to further improve diagnostic accuracy and monitoring of neurodegeneration.

## 28. POST-COVID-19 SYNDROME IN NEUROLOGY PATIENTS - A SINGLE CENTER EXPERIENCE.

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**Introduction/Objectives:** COVID-19 pandemic greatly influenced the whole society and neurology due to common and sometimes debilitating post-COVID-19 syndromes. Our aim was to determine the frequency and characteristics of neurological post COVID-19 syndrome and which diagnostic and therapeutic measures were used in the treatment of these patients.

**Participants, Materials/Methods:** Data was collected for 243 patients examined in the in the period from 11 May 2021 to 22 June 2022. Inclusion criteria were COVID-19 illness, neurological symptoms lasting after the recovery of COVID-19 or symptoms that occur after acute infection. Exclusive criteria were symptoms that were not neurological, patients who did not suffer from COVID-19, and symptoms that occurred after vaccination against the SARS-CoV-2 virus.

**Results:** Data for 227 subjects (158 women and 69 men) with neurological post COVID-19 symptoms were analyzed, with a mean age of  $51.89 \pm 15.67$  years. The majority of subjects presented with multiple symptoms, most often

headache (30%), cognitive impairment (29%), loss of smell (17%), paraesthesia (16%), fatigue (15%), dizziness (15%) and insomnia (11%). Patients were most often referred for consultative examinations (41%), neuroradiological methods (37%) and EEG (31%). The therapy was mostly symptomatic, with vitamin supplements most often prescribed. Most patients had no change in symptoms on follow-up visits (53.21%), while positive outcome was found in 44.95% of patients. Worsening was only seen in 1.83% of patients.

**Conclusions:** This study found that neurological post-COVID-19 syndrome is more common in women and that generally the most common symptoms are headache and cognitive impairment. Most common diagnostic procedures are consistent with these findings. Also, the gender distribution of symptoms is clearly visible and should be further investigated. Most patients had persistence of symptoms on follow-up visits. There is a need for longitudinal follow-up studies to better understand the disease dynamic.

## 29. EFFICACY OF FIBRINOLYTIC NONIMMUNOGENIC STAPHYLOKINASE IN THE TREATMENT OF ISCHEMIC STROKE: FIRST RESULTS OF APPLICATION IN REAL CLINICAL PRACTICE.

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**Introduction/Objectives:** Intravenous thrombolytic therapy (ITT) for acute ischemic stroke (AIS) continues to evolve. New fibrinolytic agents for AIS treatment appeared: tenecteplase, nonimmunogenic staphylokinase. Nonimmunogenic staphylokinase (STA) has been used in stroke unit of the Republic of Tatarstan since 2022. According to randomized clinical trials, STA has a good level of safety and efficacy in the treatment of AIS. There is no analysis of the results of STA use in the treatment of AIS in real clinical practice.

**Participants, Materials/Methods:** From August 2022 to March 2023, 460 patients with AIS were treated at the Interregional Clinical Diagnostic Center of Kazan. ITT was performed in 57 patients. 29 patients received thrombolysis with tissue plasminogen activator (TAP-group). 28 patients underwent thrombolysis with STA (STAP group). The overall rate of thrombolysis was 12.4%. One patient died after ITT. Mortality after thrombolysis was 1.8%.

**Results:** In TAP-group (n=29), the mean NIHSS on admission was 10.0±4.7 (NIHSS from 2 to 25). In TAP-group, 13 patients had a modified Rankin Scale (mRS) of 0-2 on discharge (rate of good outcome in TAP-group was 44.8%). One patient died, mortality in TAP-group was 3.4%. In TAP-group, 1 patient had 5-6 mRS on discharge (rate of miserable outcome in TAP-group was 3.4%). In STA-group (n=28), the mean NIHSS on admission was 8.0±4.6 (NIHSS from 2 to 22). In STA-group, 13 patients had a mRS of 0-2 on discharge (rate of good outcome in STA-group was 60.7%). In STA-group, 0 patient had 5-6 mRS on discharge. The rate of symptomatic hemorrhagic transformations in the TAP-group was 3.4%. There were no symptomatic hemorrhagic transformations in the STA-group.

**Conclusions:** The analysis was performed on a small sample (n=57), so the data obtained are preliminary. But the first analysis of the results of STA application in real clinical practice confirms high safety and high efficiency of the new fibrinolytic agent nonimmunogenic staphylokinase in the treatment of AIS.

### 30. PARADOXICAL CEREBRAL EMBOLIZATION AS A RISK FACTOR FOR THE DEVELOPMENT OF VASCULAR DEMENTIA - A CASE REPORT.

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**Introduction/Objectives:** Paradoxical brain embolization usually occurs due to a positive right-left shunt through the patent foramen ovale (PFO) and can be the cause of subclinical, cumulative damage to the white brain mass, as well as the occurrence of a stroke. Damages localized periventricularly and in subcortical regions increase the risk of impaired cognitive functions. There are studies that point to the paradoxical, brain embolization as a preventable cause above all of vascular dementia.

**Case Report:** We present a case of a 73-year-old with: impaired memory, psychiatric symptoms and residual hemihypesthesia on the right.

**Results:** MR of the brain with advanced lacunar status, cumulative damage to the periventricular and subcortical white matter of the brain as well as advanced cortical atrophy with secondary hydrocephalus. Neuropsychological testing indicates an initial global impairment of cognitive functions. TCCD Bubble test confirms significant right-left shunt, third degree, confirmed with TEE. Shunt

uncorrectable with cardiosurgical intervention due to age. Also confirmed thrombophilic condition. Holter ECG 24-hour monitoring negative for atrial fibrillation. Psychiatric and vitamin therapy, with secondary NOAC prophylaxis were initiated.

**Conclusions:** Conclusion: timely diagnosis of paradoxical brain embolization and other vascular risk factor is a good strategy for the prevention of vascular dementia.

### 31. COVID-19 RELATED PERIPHERAL FACIAL PARALYSIS AND UNILATERAL ANTERIOR UVEITIS - A FOLLOW-UP: A CASE REPORT.

**Dino Papišta, Marijan Borić, Martina Britvar, Josipa Dujmić, Katarina Opačak, Vlatka Brzović Šarić, Hrvoje Budinčević**

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**Introduction/Objectives:** Peripheral facial paralysis is a neurological disorder that causes paralysis or weakness on one side of the face. Anterior uveitis is an eye inflammatory process that can lead to glaucoma, cataract, or retinal edema, and may cause permanent visual loss. The aim of this case report is to highlight potential post-COVID-19 complications.

**Case report:** We present the case of a 44-year-old male who was admitted to the Neurological Emergency Department with symptoms of right-sided facial paralysis, headache, and lagophthalmos in November 2020. He had tested positive for COVID-19 three weeks prior to his admission. Electromyography and blink reflex tests revealed a lesion of the right facial nerve. A biomicroscopic examination of the right eye showed mild conjunctival redness, an unstable tear film, and punctiform defects in the lower third of the corneal epithelium. Multiple keratic and pigmented precipitates were distributed over the central part of the cornea as well. Based on these clinical findings, a diagnosis of anterior uveitis in the right eye was made. The patient was treated with topical dexamethasone 0.1% and tropicamide, as well as intravenous methylprednisolone. A follow-up examination two weeks and a year later showed that corneal epithelium had been repaired, and there were no signs of inflammation in the right eye.

**Conclusions:** Early recognition and treatment of post-COVID-19 complications such as uveitis can result in complete recovery.

### 32. HEMORRHAGIC STROKE CAUSED BY BACTERIAL ENDOCARDITIS-A FOLLOW UP - A CASE REPORT.

**Marijan Borić, Dino Papišta, Martina Britvar, Josipa Dujmić, Andrija Meštrović, Gordana Sičaja, Hrvoje Budinčević**

Faculty of Medicine Osijek, Josip Juraj Strossmayer University of Osijek, Osijek, Croatia; Sveti Duh University Hospital, Department of Neurology, Zagreb, Croatia

**Introduction/Objectives:** Endocarditis can be a cause of cardioembolic stroke, usually ischemic stroke. Septic emboli might cause hemorrhagic infarction too. The aim of this case report is to present a patient with septic embolism which was initially presented as hemorrhagic stroke.

**Case report:** We present a case of a 41-year-old male patient who presented to Emergency Department with fever and confusion. Blood tests revealed elevated C-reactive protein (186) and liver enzymes (AST 67, LDH 302, GGT 81, ALP 156, bilirubin 78). Neurological examination was unremarkable. Initial computed tomography of the brain showed left occipital intracerebral hematoma with frontotemporal subarachnoid hemorrhage. During hospitalization he became septic with tachycardia and developed icterus. Echocardiography showed a floating formation in the area of the posterior cuspis of the mitral valve with consequent significant mitral regurgitation. *Staphylococcus aureus* was isolated in blood culture. An infectious disease specialist was consulted and targeted antibiotic therapy with ceftriaxone and fluoxacilline was started. A follow-up magnetic resonance imaging of the brain revealed brain abscesses localized left occipital in the area of previous intracerebral hemorrhage and right frontal. Cardiac surgeon was consulted, and a transfer was planned for operative treatment of mitral valve vegetations. Further regression of the described lesions was monitored with brain magnetic resonance. The follow up exam showed normal neurological status.

**Conclusions:** Septic emboli can lead to the formation of brain abscesses. In our case, infective endocarditis was initially manifested by an intracerebral hematoma underlying a septic embolism, which should be considered in febrile patients.

### 33. HIRAYAMA DISEASE - A CASE REPORT.

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**Introduction/Objectives:** Hirayama disease, also recognized as monomelic amyotrophy is a rare disease which is identified by slowly progressive muscle weakness and atrophy in one upper limb, usually in the muscle groups of the forearm and wrist. Cold skin and excessive sweating are also observed as a result of the presence of objective autonomic dysfunction.

**Participants, Materials/Methods:** Description of the Hirayama Disease case report in North Macedonia.

**Case report:** We report a Hirayama Disease in 57-year-old-male who presented with moderate right upper limb weakness and wasting in the distal muscles, that was established by radiological and electrophysiological examinations too. The first symptoms of the disease appeared 7 years ago with a progressive development. Electromyography (EMG) and magnetic resonance imaging (MRI) of the cervical area, native and after contrast enhancement of the image, in a flexion and neutral position, have a crucial place in the process of diagnosis. As far as differential diagnostic view, advanced carpal tunnel syndrome, spinal muscular atrophy (SMA) and amyotrophic lateral sclerosis (ALS) should be appraised. Although considered to be with a self-limited background, the long-term effects warrant treatment.

**Conclusions:** Generally, this diseases is diagnosed as a motor neuron disease, which can increase the psychological stress for the affected patients. Early diagnosis and intervention has been shown to regulate the progression and reduce the degree of disability.

### 34. PATHOPHYSIOLOGICAL CHANGES OF THE MICE SPINAL CORD AFTER SINGLE AND REPETITIVE BRAIN TRAUMA.

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**Introduction/Objectives:** Traumatic brain injury (TBI) occurs as a consequence of a mechanical force to the skull and causes life-long changes in the central nervous system (CNS). Neurodegenerative sequelae of TBI commonly include proteinopathies, such as the one involving the TAR DNA binding protein 43 (TDP-43). TDP-43 proteinopathy results in both gain of function, because of the formation of cytosolic aggregates that inhibit normal cellular mechanisms, and loss of function, with the lack of TDP-43 physiological properties. Repetitive brain traumas, which are common after sport and violent injuries, have been

recognized as a risk factor for amyotrophic lateral sclerosis (ALS). There is less evidence of the association of a single brain trauma with TDP-43 proteinopathy. Studies have shown that brain injury can induce changes in the parts of the CNS that are distant from the initial trauma site, e.g., the hippocampus and cerebellum. The aim of this study was to investigate pathophysiological changes, including the ones related to the TDP-43 proteinopathy, of the mice spinal cord after single moderate and repetitive mild TBI.

**Participants, Materials/Methods:** Single moderate brain trauma was induced over the left parietal cortex by the lateral fluid injury (LFPI) apparatus. A separate cohort of mice received repetitive mild TBI (RT) using the weight drop method, twice a day for five days in a row. Animals were sacrificed 14 days after LFPI or the last mild brain trauma and their spinal cords were prepared for immunohistological analyses. For both trauma models, sham-injured mice were used as the control group.

**Results:** Cresyl violet staining did not reveal any significant morphological changes in the spinal cords of both trauma groups compared to their matching controls. Also, differences in the spinal cord white matter were not detected for RT and LFPI trauma groups of mice at this time point. The significant mislocalization of spinal cord TDP-43 was observed after both single moderate and repetitive mild brain injury. Cytoplasmic TDP-43 staining was evident in neurons but not in astrocytes of tested trauma groups.

**Conclusions:** Our preliminary results suggest that both single and repetitive brain trauma can induce subtle pathophysiological changes, such as TDP-43 mislocalization, in CNS regions distant from the initial site of trauma.

This work was supported by the University of Rijeka, Croatia, project uniri-biomed-18-199 to K.P. and uniri-biomed-18-204 to P.D.

### 35. FREQUENCY OF THE D313Y MUTATION IN THE GLA GENE IN NEUROLOGICAL PATIENTS FROM EASTERN CROATIA.

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**Introduction/Objectives:** Anderson-Fabry disease is a rare X-linked recessive progressive multisystem lysosomal

storage disorder caused by enzyme  $\alpha$ -galactosidase A ( $\alpha$ -Gal A) deficiency, due mutations in  $\alpha$ -galactosidase A (GLA) gene. Progressive accumulation of globotriaosylceramide and related glycosphingolipids leads to damage in brain, heart, kidney and other organs. The aim of this study was to estimate the frequency of hemizygous variant c.937G>T (D313Y) mutation in the GLA gene in neurological patients from Eastern Croatia.

**Participants, Materials/Methods:** A prospective screening study was carried out measuring the  $\alpha$ -Gal A activity in dried blood spot (DBS) samples of 665 patients (mean age 45±16 years, 61.2% females) undergoing neurological care in Clinical Hospital Centre Osijek. Those patients in which DBS  $\alpha$ -Gal A level was low, underwent GLA genetic testing.

**Results:** Genetic testing showed a D313Y mutation in the GLA gene in 23 patients (15 women and 8 men). In some patients in whom the D313Y mutation was observed, the following were registered: ischemic attacks - consequent zones of demyelination, areas of acute ischemia, diffuse atrophy of the brain parenchyma, chronic gliotic lesions of vascular etiology, acroparesthesia, kidney symptoms and corneal opacity.

**Conclusions:** In this study, we report for the first time the frequency of the D313Y mutation in the Croatian population of patients who underwent neurological care. The frequency of the D313Y mutation in neurological patients from Eastern Croatia is 3.45%.

### 36. CHEYNE STOKES BREATHING IN STROKE - A CASE REPORT.

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**Introduction/Objectives:** Cheyne-Stokes breathing is a breathing pattern characterized by a gradual increase and decrease in the depth and rate of breathing, followed by a period of apnea. This type of breathing is often associated with certain neurological conditions, including stroke. The aim of this report is to point out the possibility of polygraphy test use instead of sleep apnea screening.

**Case report:** We report a case of a 78-year-old female who was presented to the Neurological Emergency Department with aphasia and right-sided hemiplegia. Neurological examination revealed that she was soporose, with right-sided supranuclear facio paresis and severe ipsilateral hemiplegia. Her NIHSS was 20 at time of admission. Her



brain CT showed infarction in the irrigation of left middle cerebral artery with hemorrhagization. She was treated with acetylsalicylic acid; low-molecular weight heparin was used for prevention of deep venous thrombosis and pulmonary embolism. During hospitalization rivaroxaban was introduced for secondary stroke prevention due to atrial fibrillation. At discharge patient's NIHSS was 16. The patient was returned from Rehabilitation center due to suspicion of Cheyne-Stokes breathing which was confirmed with polygraphy test. Serial arterial acid-base status was satisfactory. She was returned to rehabilitation center.

**Conclusions:** Cheyne-Stokes breathing can be a significant concern for patients who have experienced a stroke because it can be related to poor prognosis. Polygraphy test might be useful tool for detecting breathing patterns in patients with stroke, and it shouldn't be reserved for sleep apnea screening only.

### 37. SCREENING TOOLS FOR SARCOPENIA IN NEUROLOGIC PATIENTS – A CLINICAL CHALLENGE.

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**Introduction/Objectives:** Sarcopenia is the gradual loss of muscle mass, muscle strength and function and can greatly affect the quality of life in patients, regardless of age. Recognizing and treating sarcopenia in neurologic patients is an often overlooked and a challenging issue, due to a varied presentation of symptoms leading to disability and feeding problems. So far, there has been a number of diagnostic and clinical tools that can help in the recognition of sarcopenia. We conducted a screening for sarcopenia to evaluate their applicability and veracity in neurologic patients.

**Participants, Materials/Methods:** For our screening, we randomly selected 50 patients (male n=30, female n=20) with varied neurologic disorders. The dominant disorders represented in our screening were Parkinson's disease, dementia and stroke. To screen for sarcopenia and the risk for sarcopenia we used BMI, SARC-F, NRS-2002, grip strength and lower leg circumference.

**Results:** In more than a half of the patients (n=28), SARC-F was equal or higher than 4, however, in a lot of the cases it was due to acute onset neurologic deficits and could be interpreted falsely. Lower leg circumference has been shown as a better predictor for sarcopenia, with 18 patients having a score lower than 31 cm.

**Conclusions:** We posit that besides SARC-F and NRS-2002, lower leg circumference could be a good prediction tool in neurologic patients since it can be measured in immobile patients. Using these tools, caloric support can be prescribed to these patients, helping increase the overall functional status and quality of life.

### 38. STRESS IN PARKINSON'S DISEASE – A PROSPECTIVE COHORT STUDY.

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**Introduction/Objectives:** Parkinson's disease has been shown to be greatly linked to stress, be it as a risk factor for the initial development of the disease, or as a factor exacerbating earlier symptoms. We tested for its potential effects on patients in a cohort study of drug-naive Parkinson's disease (PD) patients over a period of one year.

**Participants, Materials/Methods:** We enrolled 20 drug-naive PD patients and tested for stress levels at the time of the initial diagnosis of PD and after one year. We used the National Stress Assessment Day (NSAD) questionnaire and the Holmes-Rahe Life Stress Inventory (HRLSI). We evaluated symptoms of Parkinson's disease using the Unified Parkinson's Disease Rating Scale (UPDRS III) and the Non-Motor Symptoms Questionnaire (NMSQ).

**Results:** Looking at the NSAD results, 45 % of the patients showed no change in the score, while 30% showed a reduction. We found that UPDRS III and NMSQ scores decreased in patients that had no changes or lower scores in NSAD. On the other hand, the HRLSI scores increased in 50% of the patients and decreased in 30% of the patients. HRLSI results showed a less reliable link to UPDRS III and NMSQ after one year.

**Conclusions:** Fewer patients have shown an increase in stress when using the NSAD questionnaire than in HRLSI. This can be due to more confounding outer factors present in HRLSI, something less pronounced in NSAD. Additionally, a stronger correlation between stress and PD symptoms was shown using the NSAD stress questionnaire. Further study is required to elucidate this connection.

### 39. DEMENTIA OR PSEUDODEMENTIA.

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**Introduction/Objectives:** Alzheimer's disease (AD) is a progressive, irreversible neurodegenerative disease characterized by disturbances in memory, learning, thinking

and daily functioning. About 70% of dementia sufferers aged 70 and over have AB or AB combined with cerebrovascular disease or another form of dementia. About 30% of patients have other dementias, of which about 5-6% are of metabolic, infectious or traumatic etiology. According to the data of the Reference Center of the Ministry of Health for AB from 2021., there are over 100,000 dementia patients in Croatia, so it can be estimated that around 6,000 patients have dementia that is potentially reversible. Primary hyperparathyroidism (pHPT) is characterized by elevated levels of parathyroid hormone (PTH) and hypercalcemia. It is clinically presented by the appearance of kidney stones or osteoporosis. It is rarely initially presented with dementia. In elderly patients, cognitive deficits, various psychiatric symptoms, muscle weakness and pain may be the only symptoms of the disease, which can easily be overlooked and attributed to "age". PHPT can also be asymptomatic. The aim of this work is to draw attention to the importance of early detection of this disorder, because the cognitive deficit caused by it is curable if detected in time.

**Participants, Materials/Methods:** The patients presented in this work are 3 women and 1 man, they are older than 80 years, they have had cognitive difficulties for at least a year (1-7). One patient has been treated for the last 6 years under the diagnosis of AB. A year ago, she needed the help of another person to perform daily activities, while the others were mostly independent. It is characteristic that the cognitive difficulties in all 4 patients are of an oscillating nature, they all have psychiatric symptoms, depression, anxiety, mood changes, and hypertension. MMSE and CDT were used to assess cognitive status. Standard laboratory processing and MSCT of the brain were performed.

**Results:** MMSE was from 18-29. Brain MSCT in all patients indicates chronic microangiopathic changes. All 4 patients were found to have elevated levels of serum calcium (2.55-3.40 mmol/L) and elevated PTH (12.1-47.1 pmol/L). Endocrine examination (UZV, SPECT) showed pHPT in 3 patients. One patient underwent surgery (extirpation of the lower right parathyroid gland), one is being prepared for surgery, the third is on zoledronate therapy, and the male patient is still being treated by an endocrinologist. After the correction of serum calcium in all patients, there was a significant improvement in cognitive and psychological status.

**Conclusions:** The connection between hypercalcemia, pHPT and dementia is known and proven in several studies, which is also evident in this small sample. People over the age of 70 should undergo a short cognitive test and laboratory workup with calcium analysis at least once a year by a competent physician. In this way, potentially reversible cognitive disorders would be detected in time and their treatment started.

#### **40. THE CAROTID INTIMA-MEDIA THICKNESS AS A PREDICTOR OF CEREBROVASCULAR AND CARDIOVASCULAR EVENTS: STATE OF THE ART.**

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The intima-media thickness (IMT) of the carotid arteries as measured by non-invasive B-mode ultrasound is an established marker of carotid and coronary atherosclerosis. Carotid IMT has been found strongly associated with the risk of myocardial infarction and stroke both in asymptomatic and symptomatic adults. In addition, it is an established measure for assessing the extension of atherosclerosis and, importantly, it retains predictive power of coronary, cerebrovascular, and peripheral arterial occlusive disease, and their complications. Despite this, the utility of this marker in defining cardiovascular risk is still debated. IMT is measured in several ways that differ in the involvement of the number of segments of carotid arteries (common carotid artery, bifurcation), types of measurement (manual or automatic IMT detection), and types of summary measure (average IMT, maximal IMT). In this regard, it has been demonstrated that a composite IMT measurement obtained by assessing IMT in different segments of carotid arteries, predicts future cardiovascular events with more accuracy than simple measurement in the common carotid artery. Interestingly, carotid IMT appeared to be a more accurate predictor of cerebrovascular events than of coronary events.

#### **41. SECONDARY CENTRAL NERVOUS SYSTEM INVOLVEMENT IN SYSTEMIC ALK-POSITIVE ANAPLASTIC LARGE CELL LYMPHOMA: A CASE REPORT.**

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**Introduction/Objectives:** There are very sporadic reports of central nervous system (CNS) involvement in systemic

anaplastic large cell lymphoma (ALCL). ALCL is a rare T-cell non-Hodgkin lymphoma who commonly spreads to bone marrow, skin, lung, liver, and rarely other sites. CNS involvement of systemic lymphoma most often occurs in advanced disease. According to the last World Health Organization Classification, there are four types of ALCLs; systemic ALK-positive ALCL, systemic ALK-negative ALCL, primary cutaneous ALCL, and the provisional entity breast implant-associated ALCL. Epidemiology of ALK-positive ALCL accounts for approximately 3% of adult non-Hodgkin lymphomas and 10-20% of childhood lymphomas with a male-to-female ratio of 1.5:1.

**Participants, Materials/Methods:** A 39-year-old woman presented with pain and lump in right inguinal region with on and off fever for one month. Contrast-enhanced Computed Tomography of the thorax and abdomen revealed bilateral cervical, axillary, mediastinal, retroperitoneal and inguinal nodes along with mild hepatomegaly and bilateral pleural effusions. The cervical node biopsy showed total replacement of architecture by a population of large polymorph atypical lymphoid cells, immunohistochemically stained positive with CD30, CD4, CD7 and ALK, so a diagnosis of ALK+ anaplastic large cell lymphoma (common type) was confirmed. Peripheral blood and bone marrow examination showed no evidence of tumour infiltration. The patient received induction chemotherapy CHOEPx1 and BV-CHEPx1. After one cycle of chemotherapy, the patient had complained of severe headache and vomiting. Contrast-enhanced Computed Tomography of the brain did not reveal any significant findings, however Magnetic Resonance Imaging of the brain delineated intracerebral lesions and focal leptomeningeal enhancement, so secondary CNS lymphoma is considered and cerebrospinal fluid (CSF) examination was advised. The cytocentrifuge preparation of the CSF showed large atypical lymphoid cells with marked pleomorphism and nuclear irregularity, immunocytochemically stained positive with CD30, CD7 and ALK partially as a prove of infiltration by ALCL cells.

**Conclusions:** Establishing a diagnosis of CNS infiltration by ALCL has a substantial prognostic and therapeutic significance, therefore in a case of clinical symptoms detailed neurological assessment, neuroimaging, and cerebrospinal fluid cytology are essential.

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**OFFICIAL LANGUAGE**

The official language is English.

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**REGISTRATION FEES**

Registration Fees	Until May 1st, 2023	After May 1st, 2023
Delegates (specialists) - specijalisti	€ 350,00	€ 450,00
Members of: Croatian Stroke Society/Central and Eastern European Stroke Society	€ 250,00	€ 450,00
Residents (trainees)/Young Researchers (<35y) - specijalizanti	€ 100,00	€ 150,00
Undergraduated Students	€ 30,00	€ 50,00
Nurses/Physioterapists/ Allied Health Professionals/Accompanied Persons	€ 100,00	€ 150,00

\* Payments of Registration fees can be made only in Cash in Euro.

**REGISTRATION FEE INCLUDES**

Admission to the Congress Sessions, Schools, Workshops and Courses and the Exhibition Area

Refreshments as indicated in the program.

Welcome Reception and other social events.

Conference bag, Final program, and Book of Abstracts (online)

Certificate of Attendance (online form)

**REGISTRATION DESK - WORKING HOURS:**

Thursday 17:00-19:00 / Friday 08:00-18:00 / Saturday 08:00-18:00 / Sunday 08:00-10:00

**POSTER PRESENTATIONS:**

Neurology and Psychiatry: Friday, May 19th, 2023, 17:30-19:00

During the indicated time of poster session there will be a poster guided tour selecting best posters that will receive the Best Poster Prizes! The poster guided tour requires a presence of one of the poster authors or will not be considered as a prize nominee.

Maximal poster dimensions are 90 (width) and 120 (height) cm.

The posters can be mounted from 9:00, Friday, May 19th, and can stay exhibited until the Closing ceremony, Sunday, May 21st, 2023.

**CERTIFICATE OF ATTENDANCE**

Before obtaining the Certificate of Attendance and CME Credits, you will be requested to complete the online evaluation questionnaire. Link will be available on our web site after the Congress (until May 28th, 2023):

<https://www.pula-cong.com/program/certificate-2023> or on <https://forms.gle/jPrb67YoMeFmddM28>



**CROATIAN MEDICAL CHAMBER CREDITS:** 20 points for active participants / 12 points for passive participants

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**ACCOMODATION:**

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**TECHNICAL ORGANIZER:**

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Reference: 1. Sažetak opisa svojstava lijeka za AJOVY<sup>®</sup> odobren 7.6.2022. 2. Ferrari MD et al. Lancet 2019; 394(10203): 1030-1040.

\*Bolesnici čiju je migrenu teško liječiti bili su oni s epizodnom i kroničnom migrenom kod kojih je dokumentiran neuspjeh 2 do 4 skupine lijekova za prevenciju migrene<sup>2</sup>

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**Datum sastavljanja:** ožujak 2023, AJO-HR-00102

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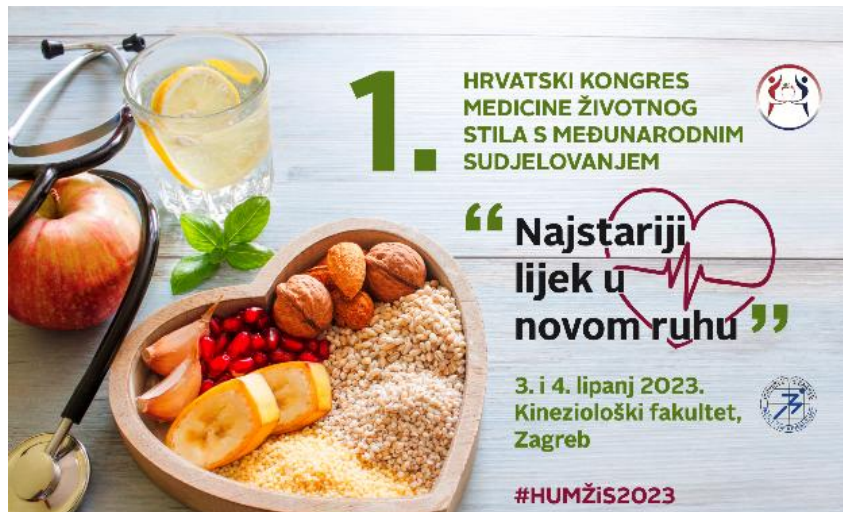
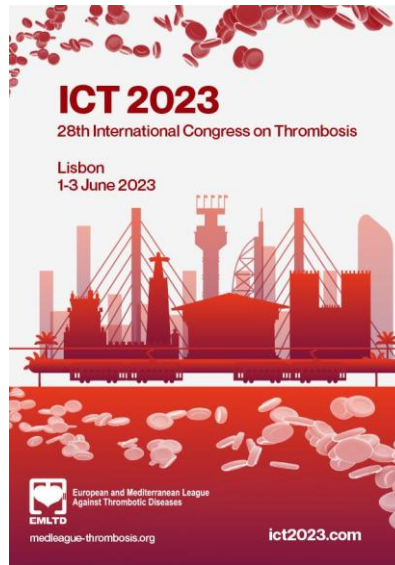
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